Coronary Computed Tomography Angiography-Adapted Leaman Score can Predict New-Onset Atrial Fibrillation in Patient with Low-to-Moderate Risk for Coronary Artery Disease

Koroner Bilgisayarlı Tomografi Anjiyografiden Elde Edilen Leaman Skoru, Koroner Arter Hastalığı için Düşük-Orta Riskli Hastalarda Yeni Başlayan Atriyal Fibrilasyonu Öngördürebilir

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ABSTRACT

Objective: Atrial fibrillation (AF) and coronary artery disease (CAD) are interrelated clinical conditions which increase mortality and morbidity globally. Coronary computed tomography angiography adapted Leaman score (CT-LeSc) is an important tool for CAD detection. Herein we report clinical impact of CT-LeSc on prediction of new-onset AF (NOAF) occurence in patients with low-to-intermediate risk for CAD.
Methods: We retrospectively analysed 1394 patients who underwent coronary computed tomography angiography (CCTA) for the detection of CAD. CT-LeSc was calculated for each patient. NOAF occurence following CCTA was obtained from medical records. Univariate and multivariate Cox regression analysis was used to determine the role of CT-LeSc in NOAF prediction.
Results: The mean age of the patients was 52.7±11.8 and 676 patients (48.5%) were male. NOAF occured in 22 patients (1.57%) during a median follow up of 828 (525-1227) days. Multivariate Cox regression analysis revealed that CT-LeSc (OR = 1.131, 95% CI: 1.020–1.255; P = 0.002), was the strongest independent variable for the development of NOAF.
Conclusion: CT-LeSc independently predicts development of NOAF in low-to-intermediate risk patients undergoing CCTA for the assessment of stable CAD.

Keywords: Atrial fibrillation, coronary artery disease, coronary computed tomography angiography, Leaman score

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ÖZET

Amaç: Atriyal fibrilasyon (AF) ve koroner arter hastalığı (KAH), küresel olarak mortalite ve morbiditeyi artıran birbiriyle ilişkili klinik durumlardır. Koroner bilgisayarlı tomografi anjiyografiye uyarlanmış Leaman skoru (BT-LeSc), KAH tespiti için önemli bir araçtır. Bu çalışmada BT-LeSc'nin düşük-orta KAH riski olan hastalarda yeni başlangıçlı AF (YBAF) oluşumunun öngördürücülüğü üzerine etkisi bildirilmiştir.
Yöntem: KAH tespiti için koroner bilgisayarlı tomografi anjiyografisi (KBTA) yapılan 1394 hastayı geriye dönük olarak analiz ettik. Her hasta için BT-LeSc hesaplandı. KBTA sonrası YBAF gelişimi tıbbi kayıtlardan elde edilmiştir. YBAF gelişimi tahmininde BT-LeSc'nin rolünü belirlemek için tek değişkenli ve çok değişkenli Cox regresyon analizi kullanıldı.
Bulgular: Hastaların yaş ortalaması 52.7±11.8 olup 676 hasta (% 48.5) erkekti. Median 828 (525-1227) günlük takip sırasında 22 hastada (% 1.57) YBAF meydana geldi. Çok değişkenli Cox regresyon analizi, BT-LeSc'nin (OR = 1.131, %95 GA: 1.020–1.255; P = 0.002) YBAF gelişimi için en güçlü bağımsız değişken olduğunu ortaya koydu.
Sonuç: BT-LeSc, stabil KAH değerlendirmesi için KBTA uygulanan düşük-orta riskli hastalarda YBAF gelişimini bağımsız olarak öngörmektedir.

Anahtar Sözcükler: Atriyal fibrilasyon, koroner arter hastalığı, koroner bilgisayarlı tomografi anjiyografi, Leaman skoru

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INTRODUCTION

Atrial fibrillation (AF) is the most common persistent arrhythmia worldwide (1, 2). AF is associated with reduced quality of life, the increased risk of ischemic stroke, heart failure and increased cardiovascular mortality. The prevalence of AF is related to age, hypertension, left ventricular dysfunction, diabetes mellitus, and coronary artery disease (CAD). Moreover, AF is an independent predictor not only for ischemic complications but also for long-term survival (3- 6). Acute myocardial infarction is an important risk factor for NOAF,[5] but the effect of stable CAD on NOAF is yet to be determined.

Coronary computed tomography angiography (CCTA) is a safe, non-invasive test commonly used to diagnose CAD (7). Unlike other non-invasive diagnostic methods, CCTA both indicates the severity of stenosis and provides information regarding coronary anatomy and morphology of plaque(s). The CCTA-adapted Leaman score (CT-LeSc) is a parameter used in determining the severity of CAD and has been proven as an independent predictor for cardiovascular events (8). Based on mentioned advantages, CCTA is recommended by the up-to-date guidelines as a primary test for diagnosis of stable CAD in patients with low-to-moderate risk (9). Discovering new parameters that would predict development of the NOAF is important to identify high-risk patients and in terms of preventive treatment.

In this study, we aimed to investigate the possible role of CT-LeSc on NOAF prediction.

METHODS

Study population

In this retrospective, single tertiary center, observational study; medical records of 1394 patients (>18 years old) were examined who underwent CCTA from 2013 to 2020 because of suspected stable angina pectoris according to their clinical presentation. Exclusion criteria were history of documented AF, CAD, heart failure, chronic kidney and liver disease, moderate-to-severe valvular heart disease, hypo-hyperthyroidism, neoplastic and systemic inflammatory disease. All patients were screened regarding the clinical data that addressed personal and general information such as; age, gender, diabetes mellitus, hypertension, smoking status, hyperlipidemia and family history of CAD. NOAF was defined as development of AF in a patient with no prior history of AF according to the medical history and review of the medical records. This research was approved by by the local Ethics Committee Faculty of Medicine, Gazi University (Date: 22 03.2021; Protocol Number: 275).

Table 1: Baseline clinical and laboratory parameters.

	NOAF (n = 22)	Non-AF (n = 1372)
Age (years)	54.9 ± 15.2	52.6 ± 11.7
Gender male, n (%)	11 (50)	665 (48.5)
Hypertension, n (%)	15 (68.2)	681 (49.6)
Diabetes, n (%)	0 (0)	157 (11.4)
Hyperlipidemia, n (%)	4 (18.2)	231 (16.8)
Fasting blood glucose, mg/dl	120.8 ± 60.1	99.6 ± 32.1
Haemoglobin, g/dl	13.3 ± 1.9	14.3 ± 1.5
Platelet count, $x10^3/mm^3$	289.8 ± 52.6	265.6 ± 68
WBC count, $x10^3/mm^3$	8.1 ± 3.1	7.5 ± 2.2
Creatinine, mg/dl	0.7 ± 0.1	0.7 ± 0.1
Uric acid, mg/dl	5.3 ± 1.8	5.4 ± 1.3
Total Cholesterol, mg/dl	193.7 ± 39.5	219.4 ± 46.6
LDL Cholesterol, mg/dl	116.1 ± 33.5	138.1 ± 39.5
HDL Cholesterol, mg/dl	49.2 ± 18.4	51.1 ± 13.2
Triglycerides, mg/dl	131 (108.8 - 194.2)	136.80 (99 - 184.8)
Follow-up period, day	206 (29 - 865)	835 (530 - 1239)
CHA_2DS_2VASc score	1.8 ± 1.1	1.4 ± 1.0

Results are expressed as: mean ± SD or median (IQR) or frequency (%) Abbreviations: HDL: high-density lipoprotein, LDL: low-density lipoprotein, NOAF: new-onset atrial fibrillation, WBC: white blood cell.

Coronary computed tomography angiography

One of the two multidetector computed tomography (MDCT) scanners a 64 MDCT Scanner [Lightspeed vct, General Electric Medical Systems (Milwaukee WI USA)] or dual-source 192 slice MDCT scanner [Somatom Force, Siemens Healthineers Germany]) was used to perform the cardiac exams. The CT scan was preceded by oral administration of metoprolol (up to 100 mg) if it was required to achieve optimal heart rate (< 70 beats/minute).

An ECG-gated unenhanced scan was performed before contrast-enhanced CT angiography in all patients for coronary artery calcium score (CACS) analysis with a tube current of 80 mAs, tube voltage of 120 kV and scan thickness of 3 mm. CCTA was performed on full inspiration and breath-hold and the scan parameters were as follows: a tube current of 250-650 mAs, tube voltage of 120 Kv and scan thickness of 0.6 mm. Contrast agents were instilled with an automated dual-rail injector (Medrad Stellant CT injection system, Bayer). A nonionic iodinated contrast agent (60-80 ml; 350 mg I/mL ioversol, Optiray, Guerbet, France) was administrated intravenously at a flow rate of 5 ml/s via an antecubital vein and next, the venous lumen was flushed with saline. The scan was started with a real time bolus tracking method. After these examination steps were completed, images were processed with software and read and interpreted by two experienced radiologists according to the Society of Cardiovascular Computed Tomography guideline (10).

After the CT data were transferred to a workstation, the coronary plaques were analyzed with cardiac assessment software (syngo.via VB10, Siemens Healthineers Germany). Multiplanar reformatted, maximum intensity projection, 3-D volume-rendered and curved-multiplanar reformatted images were used for the evaluation. The recorded parameters were left or right dominancy or co-dominancy of coronary arteries and anatomic variations such as abnormal origin or course. Subsequently, the coronary arteries were examined regarding atherosclerotic plaque formation. The severity of stenosis and plaque morphology was recorded according to the Society of Cardiovascular Computed Tomography guideline (11). The evaluation included all segments of the coronary arteries > 2 mm in diameter. A plaque is defined as follows: a formation, measuring > 1 mm^2 in size, detected on the wall or in the lumen of the coronary artery and it can be distinguished from pericardial tissue or epicardial fat tissue. Plaques were classified according to the calcification; plaques with no calcification were called non-calcified plaque, while plaques with calcification below 50% were classified as non-calcified/mixed and plaques with calcification rate above 50% (density ≥ 130 Hounsfield unit in native scans) were deemed calcified plaque. The assessment criteria were the type of plaque (no plaque, non-calcified/mixed plaque and calcified plaque) and presence or severity of stenosis (no plaque, non-occlusive (luminal stenosis ≤ 50%), occlusive stenosis (luminal stenosis ≥ 50%)).

The extent of the CAD was determined with CT-LeSc (12). Estimation of CT-LeSc was followed by a calculation for each coronary segment. This score was calculated by multiplying A (localization of the lesion in the coronary artery) with B (the type of plaque) and C (severity of stenosis; >50%). Finally, scores of all segments were summed up to get patient-based CT-LeSC. CACS was estimated using the Agatston method with dedicated software (13).

Statistical analysis

The study data were analyzed by using the SPSS (SPSS Inc., Chicago, version 23.0) program. In order to test the normality of distribution Kolmogorov–Smirnov test was used. Values are presented as a mean and standard deviation for the variables normally distributed, and as median and interquartile range for variables that have not normal distrubition. categorical variables were shown as number and percentage values. Numerical variables between two groups were compared by using student t-test or Mann-Whitney U. Categorical variables were compared with Chi-square test. Independent factors were evaluated by univariate Cox regression analysis. Variables with P < 0.1 on univariate analysis were further included in the multivariate analysis. Tolerance and variance inflation factor were used to check the possible multi-collinearity. A tolerance <0.2 and a variance inflation factor ≥ 4 were selected to withdraw variables from the multivariate cox regression model (14). Two-sided P-value of < 0.05 was considered significant.

RESULTS

The study population consisted of 1394 patients who met the inclusion/exclusion criteria. The mean age of the patients was 52.7 ± 11.8 and 676 patients (48.5%) were male. Baseline demographics were depicted in Table 1. Median follow-up time for all patients was 828 (525 - 1227) days. NOAF occurred in 22 (1.57%) patients during the follow-up period. Median follow-up time in NOAF patients was 206 (29 - 865) days. While the CHA_2DS_2VASc score was 1.77 ± 1.06 in patients with NOAF, it was 1.36 ± 0.95 in patients without NOAF (Table 1).

NOAF was detected in 10 out of 815 patients with normal coronary artery while 5 out of 134 patients with severe stenosis determined in CCTA. The CCTA findings are summarized in Table 2.

Table 2: CT angiography findings of the study population

	NOAF (n = 22)	Non-AF (n = 1372)
Severe stenosis, any coronary artery	5 (22.7)	129 (9.4)
Coronary artery calcium score	0.5 (0 - 84.50)	0 (0 - 19.00)
CT-LeSc	1.9 (0 - 6.36)	0 (0 - 3.07)

Results are expressed as: mean ± SD or median (IQR) or frequency (%) Abbreviations: AF: atrial fibrillation, CT-LeSc: coronary computed tomography angiography-adapted Leaman score, NOAF: new-onset atrial fibrillation.

In a univariate Cox regression analyses, hypertension, haemoglobin, fasting blood glucose, total cholesterol, LDL cholesterol, CT-LeSc, CACS and severe coronary stenosis were found to be statistically significant for the development of NOAF. CACS and severe coronary stenosis were removed from multivariate analysis since high collinearity was found with CT-LeSc. Multivariate Cox regression analysis revealed that CT-LeSc (OR = 1.13, 95% CI: 1.02 - 1.25; P = 0.002), was the strongest independent variable for the development of NOAF (Table 3).

Table 3: Univariate and multivariate Cox regression analysis of independent factors for the development of new-onset atrial fibrillation

	Univariate				Multivariate			
		95% CI				95% CI		
	OR	Lower	Upper	P	OR	Lower	Upper	P
Age	1.02	0.98	1.05	0.302				
Gender	1.02	0.44	2.37	0.950				
Hypertension	2.41	0.98	5.92	0.055	1.90	0.67	5.37	0.222
Hyperlipidemia	1.18	0.40	3.50	0.759				
Diabetes	0.04	0.00	31.24	0.348				
Hemoglobin	0.69	0.54	0.88	0.001	0.80	0.61	1.03	0.890
Platelet count*10^3	1.00	0.99	1.01	0.900				
WBC count*10^3	1.06	0.94	1.20	0.329				
Fasting blood glucose, mg/dl	1.00	1.00	1.01	0.006	1.00	0.99	1.01	0.094
Creatinine	2.37	0.19	29.69	0.503				
Uric acid	0.96	0.68	1.34	0.815				
Total Cholesterol	0.98	0.97	0.99	0.024	0.99	0.96	1.01	0.536
LDL Cholesterol	0.98	0.97	0.99	0.022	0.99	0.96	1.02	0.702
HDL Cholesterol	0.99	0.95	1.02	0.679				
Triglycerides	1.00	0.99	1.00	0.880				
Leaman score	1.13	1.03	1.23	0.007	1.13	1.02	1.25	0.020

Abbreviations: HDL: high-density lipoprotein, LDL: low-density lipoprotein, WBC: white blood cell.

DISCUSSION

In the present study, we propose a novel non-invasive prediction tool for NOAF as we detected that CT-LeSc alone is an independent predictor for development of the NOAF.

The AF is increasingly getting more prevalent due to higher global life expectancy and overall advancing age. Many risk factors may play a potential role in the pathogenesis of AF. CAD is one of these risk factors. The relation between acute myocardial infarction and AF is well-known. Proximal lesions increase the risk of AF occurrence. An explanation of this condition involves improper generation and transfer of the stimuli secondary to ischemia of the sinus node (15). On the other hand, unlike acute myocardial infarction, the relation between stable CAD and AF has not been fully elucidated yet.

Many mechanisms have been suggested that explain the relationship between stable CAD and AF. The first one is heart failure due to CAD either by reduced or preserved ejection fraction. As the left ventricular filling pressure and left atrial pressure increase, it paves the way for the development of the AF (16,17).

On the other hand, atrial ischemia may play a role in the onset and maintenance of AF by supporting ectopic activity and causing structural changes in the atrial tissue (18). Aberg et al. reported that the most common conditions related to AF are previous myocardial infarction and the presence of CAD in their autopsy series (19).

Coronary angiography is the gold standard for diagnosis of CAD, but it has major complications due to its invasive nature. Recently, a non-invasive test, the CCTA, is effectively used to evaluate patients with low-to-moderate risk (20). CCTA both indicates the location and severity of stenosis also provides important information about the plaque morphology. CT-LeSc is a scoring system used to investigate the degree of CAD based on the severity and location of stenosis and plaque type (12). Mushtaq et al. found that the CT-LeSc is an independent predictor for the determination of long-term prognosis (21). To the best of our knowledge, the effects of the CT-LeSc on development of the NOAF have not been investigated.

In this study, many parameters that would be related to development of the AF were evaluated with univariate and multivariate analyses. Among those parameters, the CT-LeSc was proven to be the strongest independent parameter to predict the NOAF.

This may be due to CT-LeSc offers a more holistic approach, as it evaluates the localization and type of plaque along with the severity of the stenosis. It is known that non-calcified and mixed plaques are associated with low-grade vascular inflammation and more common in acute coronary syndrome (22). The ability of CT-LeSc to evaluate non-calcified and mixed plaques may offer superiority to other scoring systems. Besides low-grade chronic inflammation is held responsible for the pathogenesis of the AF (23). Indeed, inflammatory cell infiltration is demonstrated in the atrial myocardium of AF patients. The similar inflammatory process responsible for each condition can make stable CAD patients more prone to AF.

CONCLUSION

In this study, we found that the CT-LeSc can predict NOAF in low-to-intermediate risk population for stable CAD. High CT-LeSc can provide us additional information about the AF risk and lead us to effectively manage the underlying risk factors responsible for stable CAD.

Conflict of interest

No conflict of interest was declared by the authors.

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