

Relationship between Aortic Knob Calcification and Coronary Artery Calcium Scores Among Patients with Stable Angina Pectoris

Ahmet Karaduman,¹ Cemalettin Yılmaz,² İsmail Balaban,¹
Mustafa Ferhat Keten,¹ Muzaffer Kahyaoğlu,¹ Elnur Alizade,¹ Çetin Geçmen¹

¹Department of Cardiology, Kartal High Specialization Training and Research Hospital, İstanbul, Türkiye

²Department of Cardiology, Muş State Hospital, Muş, Türkiye

Abstract

Objectives: The deposition of calcium in the vascular bed can reflect the presence of atherosclerotic lesions, and aortic knob calcification (AKC) has been shown to correlate with a heightened risk of cardiovascular disease (CVD) events. This retrospective research was undertaken with the aim of evaluating the relationship between AKC and the coronary artery calcium score (CACS) by chest X-ray and investigating the possibility of using AKC to predict the risk of CVD. We hypothesized that AKC would be detected more frequently on chest X-rays among patients with severe CACS values.

Methods: The study included 282 consecutive patients diagnosed with stable angina pectoris (SAP) who had presented to our cardiology outpatient clinic between 2018 and 2020 and underwent cardiac computed tomography and chest X-ray. Those whose chest X-rays revealed small spots or singular areas of fine calcification were considered to have AKC. CACS values were classified according to the Agatston score and CACS severity was defined as none-mild (<100) or moderate-severe (>100).

Results: The mean age of the 282 enrolled patients was 47.5±11.3 years and 169 (59.9%) of the patients were male. CACS values of >100 signifying moderate-severe risk were observed more commonly among patients with diabetes mellitus, hypertension (HT), older age, and smoking habits (p<0.001). Thirty-five patients (12.4%) had AKC on a chest X-ray. Patients with AKC were more likely to be categorized in the moderate-high CACS severity group than those without AKC (p<0.001). Logistic regression analysis demonstrated that HT (odds ratio [OR]: 4.413; 95% confidence interval [CI]: 1.733–11.240; p=0.002) and AKC (OR: 5.619; 95% CI: 2.280–13.848; p<0.001) were independent predictors of moderate-severe CACS values.

Conclusion: It is important to establish the risk of CVD in patients with SAP using simple and non-invasive methods. Our study showed that the presence of AKC on chest X-ray is associated with higher CACS values in patients presenting with SAP. Therefore, AKC may be used more frequently for the evaluation of the risk of CVD.

Keywords: Aortic knob calcification; cardiac computed tomography; chest X-ray; coronary artery calcium score.

Stabil Angina Pectorisli Hastalarda Aort Topuzu Kalsifikasyonu ile Koroner Arter Kalsiyum Skorları Arasındaki İlişki

Özet

Amaç: Vasküler yatakta kalsiyum birikimi, aterosklerotik lezyonların varlığını yansıtabilir. Aort topuz kalsifikasyonu (AKC) ile kardiyovasküler hastalık (KVH) o arasındaki yüksek korelasyon daha önceki çalışmalarda gösterilmiştir. Bu çalışmamızda, AKC ile koroner arter kalsiyum skoru (CACS) arasındaki ilişkiyi göğüs röntgeni ile değerlendirmek ve AKC'nin KVH riskini öngörme olasılığını araştırmayı amaçladık. AKC'nin, yüksek CACS değerlerine sahip hastalarda göğüs röntgeninde daha sık tespit edileceği hipotezini öne sürdük.

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Address for Correspondence:

Ahmet Karaduman

Department of Cardiology, Kartal High Specialization Training and Research Hospital, İstanbul, Türkiye

E-mail: ahmetkaradumanmd@gmail.com

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Gereç ve Yöntem: Çalışmaya, 2018 ile 2020 yılları arasında kardiyoloji polikliniğimize başvuran ve stabil angina pectoris (SAP) tanısı konulan, kardiyak bilgisayarlı tomografi ve göğüs röntgeni çekilen ardışık 282 hasta dahil edildi. Göğüs röntgenlerinde küçük noktalar veya tekil ince kalsifikasyon alanları görülenler AKC'ye sahip olarak kabul edildi. CACS değerleri Agatston skoruna göre sınıflandırıldı ve CACS şiddeti, yok-hafif (<100) veya orta-şiddetli (>100) olarak tanımlandı.

Bulgular: Çalışmaya katılan 282 hastanın ortalama yaşı $47,5 \pm 11,3$ yıl olup, 169'u (%59,9) erkekti. Orta-şiddetli riski gösteren >100 CACS değerleri, diyabetes mellitus, hipertansiyon, ileri yaş ve sigara içme alışkanlığı olan hastalarda daha yaygın olarak gözlemlendi ($p < 0,001$). Otuz beş hastada (%12,4) göğüs röntgeninde AKC tespit edildi. AKC olan hastalar, AKC olmayanlara göre daha yüksek CACS şiddet grubunda sınıflandırılma olasılığı daha yüksekti ($p < 0,001$). Lojistik regresyon analizi, hipertansiyonun (olasılık oranı [OR]: 4,413; %95 güven aralığı [GA]: 1,733–11,240; $p = 0,002$) ve AKC'nin (OR: 5,619; %95 GA: 2,280–13,848; $p < 0,001$) orta-şiddetli CACS değerlerinin bağımsız belirleyicileri olduğunu gösterdi.

Sonuç: SAP'li hastalarda basit ve invaziv olmayan yöntemlerle KVH riskini belirlemek önemlidir. Çalışmamız, göğüs röntgeninde AKC varlığının, SAP ile başvuran hastalarda daha yüksek CACS değerleri ile ilişkili olduğunu gösterdi. Bu nedenle, AKC KVH riskinin değerlendirilmesi için daha sık kullanılabilir.

Anahtar sözcükler: Aortik topuzu kalsifikasyonu; kardiyak bilgisayarlı tomografi; göğüs röntgeni; koroner arter kalsiyum skoru.

Introduction

Atherosclerotic cardiovascular disease (CVD) begins to develop long before symptoms appear. Early detection of the disease in this period prevents undesirable outcomes. Calcium deposits in the vascular bed are known to indicate the presence of atherosclerotic lesions.^[1] In addition, patients found to have aortic knob calcification (AKC) are also found to be at increased risk of cardiovascular events.^[2]

Conventional chest X-rays have a sensitivity of 50%, specificity of 70–80%, positive predictive value of 80%, and negative predictive value of 30–45% for the diagnosis of mild-to-severe AKC in place of cardiac computed tomography (CT) or transthoracic echocardiography.^[3,4] In other words, it is difficult to predict the severity of AKC from chest X-rays alone. Although chest X-rays are performed with regularity in cardiology outpatient clinics, the actual severity and possible consequences of AKC are not easily understood with this imaging approach alone. We designed this retrospective study to evaluate the relationship between AKC as determined by chest X-ray and the coronary artery calcium score (CACS) as determined by cardiac CT and to assess its potential role in predicting CVD risk. We hypothesized that AKC would be detected more frequently on chest X-rays among patients with higher CACS values.

Materials and Methods

Study Population

We analyzed the data of 341 consecutive patients who presented to our cardiology outpatient clinic between the years of 2018 and 2020 and underwent both cardiac CT and chest X-ray. Only patients admitted to the clinic with a diagnosis of stable angina pectoris (SAP) were included. SAP was defined as exertional chest pain and/or positive stress test without change in the frequency, intensity, and duration of symptoms in the previous 4 weeks. We subsequently excluded all patients who had aortic valve disease, had severe concomitant kidney disease (glomerular filtration rate of <60 mL/min), or presented with acute coronary syndrome. In addition, we excluded patients whose chest X-rays were not properly centered and those who had known diseases such as vasculitis affecting the aorta. Accordingly, 59 patients of the original 341 patients were excluded from the study based on these criteria and 282 patients were

included. All of the included patients provided informed consent and the study was approved by the local ethics committee (date: November 19, 2024; no: 2024/20/966), in accordance with the Declaration of Helsinki guidelines.

Variables of Interest

From our institution's digital records, we collected clinical, epidemiological, laboratory, and procedural data for all included patients. Patients with systolic blood pressure above 140 mm/Hg or diastolic blood pressure above 90 mm/Hg were said to have hypertension (HT). Diabetes mellitus (DM) was recognized in the event of a fasting plasma glucose concentration above 126 mg/dL, random plasma glucose concentration above 200 mg/dL, HbA1c value above 6.5%, or the usage of antidiabetic medication. Smoking was defined as a present, ongoing habit of smoking at the time of presentation to the outpatient clinic.

Chest X-rays

All patients had chest X-rays recorded from a posteroanterior view. The resulting images were evaluated separately by two independent experienced cardiologists. The value of the

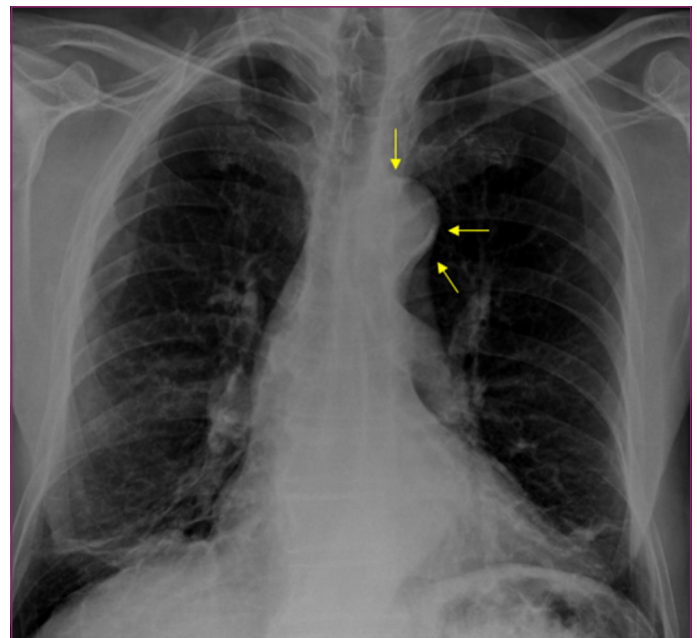


Figure 1. Chest radiographic view of aortic knob calcification (arrows).

widest point of the ascending aortic knob (AK) was obtained along the horizontal line from the lateral side of the trachea to the left border of the AK. When X-ray images revealed small spots or singular areas of fine calcification, the patients were considered to have AKC (Fig. 1).

CACS

All images were obtained using a 256-slice CT scanner. Cardiac CT images were interpreted by two experienced radiologists who were unaware of the patient characteristics and study design. The CACS is typically measured using the Agatston score based on the sum of attenuation in Hounsfield units and the area of all calcium lesions in the coronary arteries.^[5–7] The patients were categorized into one of two groups based on CACS values whereby the risk of coronary events was said to be none-mild for those with CACS values of <100 or moderate-severe for those with CACS values of >100.

Statistical Analysis

The IBM Statistical Package for the Social Sciences Statistics 19.0 for Windows (IBM Corp., Armonk, NY, USA) was utilized for the analyses of all study data. Descriptive statistics were presented as number and percentage values for categorical variables and as mean, standard deviation, minimum, maximum, and median values for numerical variables. To compare groups, chi-square tests were applied. The differences between the findings of two independent groups were evaluated with Student's t-test in the case of variables that conformed to normal distribution. For variables that did not conform to normal distribution, Mann–Whitney U tests were applied instead. Subsequently, univariate and multivariate logistic regression analyses were performed in an effort to identify variables that could independently predict the CACS. For multivariate logistic regression analysis, only variables previously shown in univariate analysis to have significance of $p < 0.05$ were included.

Results

Table 1 presents data on the demographic characteristics of the patients and their risk factor profiles. The patients had a mean age of 47.5 ± 11.3 years and 169 (59.9%) of the patients were male. While 204 (72%) patients were concluded to be at very low risk (CACS: 0), minimal risk (CACS: 1–10) was determined for 16 (6%) patients, mild risk (CACS: 11–100) for 27 (10%) patients, moderate risk (CACS: 101–400) for 23 (8%) patients, and severe risk (CACS >400) for 12 (4%) patients according to their calculated CACS values (Fig. 2).

Moderate-severe risk was observed most commonly among patients with comorbid DM and HT, those of older ages, and those who smoked. No statistical differences were observed, however, between high and low CACS values in terms of renal function, triglycerides, total, high- and low-density lipoprotein cholesterol levels. Thirty-five patients (12.4%) were found to have AKC based on their chest X-rays. These patients with AKC had higher CACS values compared to those without such calcifications. In other words, patients with AKC were more

likely to be categorized within the moderate-severe risk group than those without calcifications ($p < 0.001$).

Logistic regression analysis showed that HT (odds ratio [OR]: 4.413; 95% confidence interval [CI]: 1.733–11.240; $p = 0.002$) and AKC (OR: 5.619; 95% CI: 2.280–13.848; $p < 0.001$) were independent predictors of moderate-severe CACS values (Table 2).

Discussion

This is the first clinical study to show that AKC as confirmed by routine chest X-ray is a useful predictor of high CACS based on cardiac CT among patients with SAP. We found the presence of AKC on chest X-ray to be more common among patients with SAP who had higher CACS values. In this study, we have demonstrated that AKC is capable of independently predicting a high CACS value.

CVD is not typically initiated with the first observed clinical event. It begins developing months or even years before such symptoms appear. Therefore, it is important to confirm the risk of CVD among patients with SAP and distinguish patients at high risk, especially without the need for invasive procedures.^[8,9] With that aim in mind, it is important to use simple diagnostic methods such as chest X-rays.

Arteries simultaneously exert effective conducting and efficient buffering actions.^[10] In younger individuals, the aorta and proximal elastic arteries expand by roughly 10% with every heartbeat.^[11] Muscle arteries, on the other hand, dilate by only 2–3%. Elastic lamellar fractures may occur in the aorta with aging and may be responsible for dilatation, stiffness, and calcification in the vessel.^[12,13] Arterial stiffness and calcification increase with age and these increases are exacerbated by the existence of cardiovascular risk factors.^[14]

The intima layer of an atherosclerotic plaque undergoes vascular calcification, a sophisticated and controlled biomineralization process. It is comparable to diffuse osteogenesis, with progressive characteristics.^[15,16] AKC is related to classical CVD risk factors such as smoking, advanced age, diabetes, high cholesterol, or high C-reactive protein.^[17] Individuals with atherosclerotic disease in one vascular bed are more likely to develop the same condition in another area of the body. Therefore, the development of calcification in the aorta is also associated with calcification in the coronary arteries. In our study, we have shown that AKC identified on chest X-ray is capable of independently predicting a higher CACS value.

Various studies in the literature were undertaken with the aim of examining the relationships between AKC as monitored by chest X-rays and many other conditions. For example, Kim et al.^[18] confirmed that AKC has the power to reliably predict the likelihood of intracranial stenosis following ischemic stroke. They suggested that chest radiography should be utilized more widely in this patient population for purposes of screening and risk factor assessments.

Similarly, Higaki et al.^[10] reported that the existence of AKC significantly correlated with values of central systolic blood

Table I. Comparison of cardiovascular risk factors and laboratory findings according to the coronary calcium score

	CACS 0–100 (very low/mild risk) n=247		CACS >101 (moderate-severe risk) n=35		p
	n	%	n	%	
Baseline characteristic					
Age, (years)		46.5±11.8		54.8±7.6	<0.001*
Gender (male)	142	57	27	77	0.028*
Present smoker	67	27	21	60	<0.001*
Hypertension	53	21	26	74	<0.001*
Diabetes mellitus	31	13	17	49	<0.001*
Cerebrovascular disease	13	5	3	8	0.091
Laboratory findings					
Fasting blood glucose (mg/dL)		99 (91–109)		109 (93–132)	0.056
BUN (mg/dL)		18.4±7.17		16.7±6.94	0.115
Creatinine (mg/dL)		0.77 (0.64–0.89)		0.80 (0.63–0.88)	0.913
Hemoglobin (g/dL)		14.1±1.6		13.8±1.5	0.418
WBC (*10 ³ /μL)		8.53±3.22		8.57±6.18	0.732
Platelets (*10 ³ /μL)		257.88±71.24		271.8±88.08	0.390
Aspartate aminotransferase (U/L)		20 (15–24)		21 (17–25)	0.317
Alanine aminotransferase (U/L)		17 (11–24)		18 (15–23)	0.380
Sodium (mmol/dL)		137.9±2.7		137.1±8.7	0.589
Potassium (mmol/dL)		4.4±0.5		4.5±0.4	0.146
Calcium (mg/dL)		8.8±0.4		8.9±0.6	0.373
Magnesium (mg/dL)		1.9±0.4		2.1±0.5	0.78
Total cholesterol (mg/dL)		188.6±44.45		194.8±63.21	
Triglyceride (mg/dL)		154.2±103.46		174.1±142.77	0.291
HDL (mg/dL)		47.4±10.29		45.1±9.73	0.434
LDL (mg/dL)		132.9±41.10		129.1±40.93	0.776
Echocardiography					
Left ventricular ejection fraction (%)		64 (60–65)		63.5 (55–65)	0.098
Left atrial diameter (mm)		36.9±5.9		36.8±4.6	0.650
IVST (mm)		9.5 (9–10.5)		10 (9–12)	0.372
PWT (mm)		10.5 (9–12)		10.5 (8.5–12)	0.424
LVEDD (mm)		46 (38–52)		45 (44–55)	0.646
LVESD (mm)		29 (24–31)		32 (27–36)	0.461
E (m/s)		0.8 (0.7–0.9)		0.8 (0.8–0.9)	0.201
A (m/s)		0.7 (0.6–0.8)		0.6 (0.5–0.7)	0.363
E/A ratio		1.2 (0.8–1.4)		1.2 (1.1–1.5)	0.449
e' (cm/s)		12 (8–14)		13 (12–16)	0.715
a' (cm/s)		8 (6–12)		8 (6–10)	0.831
E/e' ratio		6.1 (4.9–7.5)		6.4 (6.1–7.5)	0.158
TAPSE (mm)		19.6±1.0		19.1±1.2	0.443
SPAP (mmHg)		26 (22–35)		29 (21–38)	0.345
Left ventricular hypertrophy	74	30.0	11	31.4	0.686
Heart valve disorder	15	6	3	8.5	0.344
Coronary artery calcium score		0 (0–0)		236 (148–655)	<0.001*
Risk-based on agatston score					
Very low-risk CACS:0	204	83	0	0	<0.001
Minimal risk CACS 1–10	16	6	0	0	
Mild risk CACS 11–100	27	11	0	0	
Moderate risk CACS 101–400	0	0	23	66	
Severe risk CACS >400	0	0	12	34	
Aortic knob calcification	22	9	19	54	

CACS: Coronary artery calcium score; BUN: Blood urea nitrogen; WBC: White blood cell; HDL: High-density lipoprotein; LDL: Low-density lipoprotein, IVST: Interventricular septal thickness; PWT: Posterior wall thickness; LVEDD: Left ventricular end-diastolic diameter; LVESD: Left ventricular end-systolic diameter; TAPSE: Tricuspid annular plane systolic excursion; SPAP: Systolic pulmonary artery pressure.

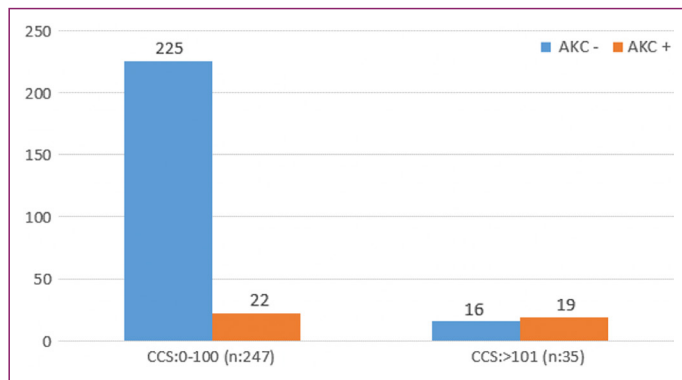


Figure 2. Number of patients with and without aortic knob calcification according to the coronary calcium score.

pressure. In that study, they used the aortic arch calcification score (AoACS) to define AKC. They found that as the AoACS increased, systolic blood pressure also increased. In another study, it was shown that the existence of AKC as revealed by chest X-ray yielded helpful predictions regarding the likelihood of arterial stiffness or subclinical atherosclerosis in hypertensive patients without symptoms.^[19] In the present study, we have shown that, in addition to AKC, HT is also associated with high CACS values. This may be due to the relationship between aortic calcification and blood pressure.

There is evidence of an independent association between metabolic and aortic calcification in terms of both the prevalence and severity of the latter.^[20] It is also known that dyslipidemia is among the major risk factors identified to date for CVD. In the present study; however, no relationship between lipid levels and CACS could be found. This may be due to the fact that some patients were receiving statin therapy when they presented to our clinic.

Smoking is one of the leading preventable causes of CVD. It contributes to approximately 30% of CVD-related deaths worldwide.^[21] Furthermore, smoking may also increase the risk of AKC.^[22] Tsai et al.^[23] demonstrated a dose-response relationship between active smoking and aortic calcification burden with partial protective effects for those who had never smoked or had quit smoking. However, smoking was not found to be an independent indicator of high CACS values in our study. This may be because we did not perform analysis for ex-smokers in this study and we did not know how many pack-years patients had smoked.

Limitations

Alongside that important finding, the present study has some limitations. First of all, it was designed as a retrospective study and retrospective studies carry the risk of information and selection bias. The patients included in this study do not represent the general population because they had presented to a cardiology outpatient clinic with chest pain and coronary CT was subsequently performed. Thus, AKC was more frequent among these patients than it would be in a more general population. Furthermore, we used chest X-rays to evaluate the presence

Table 2. Multivariate logistic regression analysis of the clinical factors for coronary artery calcium score

	OR	CI	p
Age	1.023	0.981–1.067	0.290
Male	1.405	0.533–3.703	0.492
Hypertension	4.413	1.733–11.240	0.002*
Smoker	1.987	0.803–4.918	0.138
Diabetes mellitus	1.783	0.659–4.826	0.255
Aortic knob calcification	5.619	2.280–13.848	<0.001*

OR: Odds ratio; CI: Confidence interval.

or absence of AKC. We were unable to confirm the existence of AKC with other approaches such as echocardiography or CT. Due to the small number of patients in this retrospective study, we did not attempt to evaluate the extent of aortic calcification. Finally, our study had a cross-sectional design. For that reason, causal relationships could not be established. A larger prospective study needs to be done to confirm our findings.

Conclusion

It is important to establish the risk of CVD in patients with SAP using simple and non-invasive methods. Our study showed that the presence of AKC as confirmed by chest X-ray is associated with high CACS values in patients presenting with SAP. Due to this correlation between AKC as seen by chest X-ray and high CACS values, AKC could be used more frequently for the evaluation of CVD risk.

Disclosures

Ethics Committee Approval: The study was approved by the Kartal High Specialization Training and Research Hospital Ethics Committee (no: 2024/20/966, date: 19/11/2024).

Informed Consent: Informed consent was obtained from all participants.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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