Assessment of the relationship between aortic pulse wave velocity and aortic arch calcification

Aort nabız dalgası hızı ile aort yayı kalsifikasyonu arasındaki ilişkinin değerlendirilmesi

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ABSTRACT

Objectives: We aimed to assess arterial stiffness parameters and to investigate the relationship between these parameters and aortic calcification in patients with aortic arch calcification and without symptomatic atherosclerotic disease.

Study design: The population of this study consisted of 41 patients with aortic arch calcification verified by chest X-ray (group I, 17 males, mean age 70±5 years) and individuals without aortic arch calcification (group II, 17 males, mean age 68±6 years). Subjects with symptomatic or known vascular disease were excluded from the study. The arterial stiffness parameters of all subjects were measured non-invasively with a SphygmoCor device. Aortic pulse wave velocity (PWV), augmentation pressure (AP), augmentation index (AIx) and heart rate normalized augmentation index (AIx@75) were used as parameters of arterial stiffness.

Results: The two groups were compared according to demographic characteristics, medications currently being taken, and levels of serum lipids. There was no significant difference between the groups. AP in group I was significantly higher than that of group II (p=0.002). AIx and AIx@75 were similar in both groups. Aortic PWV of group I was significantly higher than that of group II (p<0.0001).

Conclusion: According to the results of this study, the presence of aortic calcification, verified by chest radiography, was associated with increased aortic PWV.

ÖZET

Amaç: Semptomlu aterosklerotik hastalığı olmayan hastalarda arteryel sertlik parametreleri ile aort kalsifikasyonu arasındaki ilişkiyi incelemeyi amaçladık.

Çalışma planı: Çalışma popülasyonu göğüs grafisinde aort yayı kalsifikasyonu olan 41 hasta (grup I, 17 erkek, ortalama yaş 70±5 yıl) ve kalsifikasyonu olmayan yaş ve cinsiyet eşleştirilmiş 41 kişiden (grup II, 17 erkek, ortalama yaş 68±6 yıl) oluşturuldu. Semptomlu veya bilinen vasküler hastalığı olanlar çalışmadan dışlandı. Tüm bireylerin arteryel sertlik parametreleri SphygmoCor cihazı ile ölçüldü. Aort nabzı dalga hızı (PWV), augmentasyon basıncı (AP), augmentasyon indeksi (AIx) ve kalp hızına göre düzeltilmiş augmentasyon indeksi (AIx@75) arteryel sertlik parametreleri olarak değerlendirildi.

Bulgular: İki grup demografik özellikler, ilaç kullanımı ve serum lipit düzeyleri açısından karşılaştırıldı, gruplar arasında anlamlı fark yoktu. AP grup I'de grup II'ye göre anlamlı olarak yüksek bulundu (p=0.002). AIx ve AIx@75 gruplar arası benzerdi. Aort PWV'si grup I de grup II'ye göre anlamlı olarak yüksek bulundu (p<0.0001).

Sonuç: Bu çalışmanın bulgularına göre göğüs grafisinde tespit edilen aort yayı kalsifikasyonu artmış aort nabzı dalga hızı ile ilişkilidir.

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Arterial stiffness is a sign of aging that develops as a result of various diseases, including atherosclerosis, diabetes mellitus (DM), and chronic renal disease. In addition, it indicates an increased risk of cardiovascular disease.[1] Although cellular and structural features can predispose a patient to arterial stiffness and have been shown to accelerate atherosclerosis in arterial vessels, there are few studies examining the relationship between arterial stiffness and atherosclerosis.[2] Increased arterial stiffness and wave reflection values can result in increased central blood pressure, which is associated with cardiovascular events such as stroke and myocardial infarction. In previous epidemiological studies, pulse wave velocity (PWV) has been shown to be an independent predictor of cardiovascular events.[3] PWV is a simple, reliable, reproducible, and noninvasive method that is often used for evaluating arterial stiffness.

Calcium accumulation on the walls of large arteries has long been recognized as having a role in the development of adverse cardiovascular events. Calcification of the aortic arch via chest X-ray, valvular calcification via echocardiography, or calcification of the carotid artery and vertebral arteries via computed tomography (CT) are considered to be markers of vascular atherosclerosis. One large study reported that calcium deposition in both non-coronary and coronary arteries indicated the extent of atherosclerotic lesions and could be a subclinical marker of cardiovascular disease.[4]

The current study was designed to investigate the correlations between arterial stiffness and the presence of aortic arch calcification in patients with aortic calcification on posterior-anterior (PA) chest X-ray.

PATIENTS AND METHODS

The study design

This cross-sectional, case-controlled study was conducted at Karadeniz Technical University Faculty of Medicine between March 2008 and March 2009. Patients with abnormal sinus rhythm, malignant hypertension (>180/110 mmHg), known connective tissue disease, valvular or congenital heart disease, peripheral arterial disease, coronary heart disease (e.g., myocardial infarction, angina, or previous coronary angioplasty or coronary artery bypass graft surgery with a history of nitrate use), cerebrovascular disease (e.g., stroke, transient ischemic attack, or a history of carotid endarterectomy), chronic obstructive pulmonary disease, aortic wall disease (e.g., Marfan syndrome or aneurysm), an active infectious or inflammatory disease, and malignancies were excluded since these conditions could affect the arterial stiffness parameters. Subjects were assigned to either the study group or to the control group. The study group included those patients with aortic calcification verified by chest X-ray, while the control group consisted of patients who had no aortic calcification.

Abbreviations:

AIx	*Augmentation index*
AP	*Augmentation pressure*
BMI	*Body mass index*
CT	*Computed tomography*
DBP	*Diastolic blood pressure*
DM	*Diabetes mellitus*
PA	*Posterior-anterior*
PWV	*Pulse wave velocity*
SBP	*Systolic blood pressure*

Study population

A total of 177 consecutive patients with aortic calcification verified by chest X-ray were included in the study. One hundred thirty six of these patients were excluded from the study. A total of 41 patients with aortic calcification were assigned to the study group (17 males; mean age, 70±5 years). The control group consisted of 41 subjects (17 males; mean age, 68±6 years) matched according to age, smoking status, and the presence of hypertension or DM.

Evaluation of cardiovascular risk factors

Information related to smoking status, age, the presence of ischemic heart disease, hypertension, DM, stroke, or peripheral vascular disease was obtained from hospital records and/or patient reports. Arterial blood pressure measurements were taken twice with 5 minute intervals from the right arm in the sitting position. According to the report of the 7th Joint National Committee (JNC), patients having either systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg were defined as having hypertension.[5] Patients were defined as having diabetes if they had a fasting glucose level of ≥126 mg/dl or were undergoing pharmacological treatment in the area of diabetes. Each subject was classified as either a current smoker or nonsmoker, and the body mass index (BMI) of each subject was calculated as weight (kg)/(height [m])^2. Obesity was defined as a BMI ≥30 kg/m^2. Dyslipidemia was defined as having a total cholesterol level >200 mg/dl, low-density lipoprotein (LDL) cholesterol >160 mg/dl, and high-density lipoprotein (HDL) cholesterol <40 mg/dl for men and <50 mg/dl for women.[6]

Chest-X ray and detection of aortic arch calcification

A posterior-anterior chest-X ray was taken with the patient holding his/her breath and standing 2 m away from the X-ray tube. All chest films were evaluated by two radiologists. Aortic arch calcification was defined as the presence of a curvilinear density along the arch.[7]

Measurement of arterial stiffness parameters

Arterial stiffness was measured using a SphygmoCor device (AtCor Medical, Sydney, Australia) according to the manufacturer's instructions.[8,9] Each patient's gender, age, height, weight, and arterial blood pressure were entered into the SphygmoCor software program. All measurements were taken by the same person with each patient in a supine position after a 5-min acclimation period in a room maintained at 23-24°C. Radial artery pressure waveforms were recorded at the wrist using applanation tonometry with a high-fidelity micro-manometer (Millar Instruments, Houston, TX).[8,9] After 20 sequential waveforms had been acquired and averaged, a validated, generalized mathematical transfer function was used to synthesize the corresponding central aortic pressure waveform.[8] The point where the incident and reflected waves merged (the inflection point) was identified on the generated aortic pressure waveform.

Augmentation pressure (AP) was defined as the maximum SBP subtracted by the pressure at the inflection point. The augmentation index (AIx) was defined as the AP divided by the pulse pressure and was expressed as a percentage. Larger AIx values indicate either an increased wave reflection from the periphery or an earlier return of the reflected wave as a result of an increased PWV (attributable to increased arterial stiffness). The AIx is dependent upon the elastic properties of the entire arterial tree (elastic and muscular arteries). Because the AIx is influenced by heart rate, a normalized index for a heart rate of 75 bpm (AIx@75) was used in accordance with the report of Wilkinson et al.[10] The accuracy of the values obtained by the SphygmoCor device is indicated by a percentage. Since >80% is generally accepted as a high-quality recording, we applied this criterion to our study.

Following radial artery pulse wave analysis, an electrocardiographic (ECG) device was immediately connected for PWV measurement. The aortic PWV was determined by the foot-to-foot method using the SphygmoCor system (AtCor Medical).[8] Consecutive registrations of the carotid and femoral artery pulse waves are electrocardiogram-gated, which allows the time shift between the appearance of a wave at the first and second sites to be calculated. For the aortic PWV, the carotid artery pulse wave was recorded with the ECG followed by the recording of the femoral artery pulse wave. The distance between the two sites was measured to determine the aortic PWV in m/s. The average of measurements taken over a period of 8 s (9-10 cardiac cycles) was calculated after the exclusion of extreme values.[8,9]

Statistical analysis

Continuous variables were expressed as means ± standard deviations (SD) and categorical variables were expressed as percentages. Comparisons of the categorical and continuous variables between the groups were performed using chi-square tests and unpaired t-tests, respectively. Normality of the continuous variables was determined by the Kolmogorov-Smirnov test. Logistic regression analyses were used to assess the relationships between arterial stiffness parameters (PWV, AIx@75, AP, aortic mean pressure), age, systolic and diastolic blood pressure, and aortic arch calcification. P values less than 0.05 were considered to be statistically significant. An SPSS software program (14.0, Inc., Chicago, Illinois) was used for all statistical analyses.

RESULTS

Patient demographics, laboratory analyses, and medication history are presented in Table 1. There were no significant differences between the ages, SBP, and DBP of the groups (p=0.162, p=0.097 and p=0.075, respectively). BMI, heart rate, SBP, DBP, lipid parameters, frequency of DM, hypertension, and smoking were similar between the two groups. Although not significant, the SBP values of the group with aortic arch calcification tended to be higher.

Arterial stiffness parameters of both groups are shown in Table 2. Although systolic pressures obtained from the SphygmoCor were similar in both groups (p=0.062), DBP were significantly different (p=0.042). Heart rate augmentation-adjusted index

Table 1. Patient demographics, laboratory characteristics, and medications

	Aortic calcification (+) (n=41)			Aortic calcification (–) (n=41)			*p*
	n	%	Mean±SD	n	%	Mean±SD	
Age			70±6			68±6	NS
Gender (male)	17	41		17	41		NS
Hypertension	33	80		29	70		NS
Diabetes mellitus	5	12		4	10		NS
Obesity (BMI ≥30)	12	29		14	34		NS
Cigarettes	4	9		5	12		NS
BMI (kg/m^2)			28±4			30±5	NS
Heart rate			69±10			67±11	NS
SBP (mmHg)			134±13			129±13	NS
DBP (mmHg)			82±7			79±9	NS
LDL (mg/dl)			121±21			132±40	NS
HDL (mg/dl)			47±12			46±8	NS
Total cholesterol (mg/dl)			182±32			199±44	NS
Triglycerides (mg/dl)			136±58			151±74	NS
Aspirin	19			13			NS
Beta-blocker	6			3			NS
ACE inhibitor	12			9			NS
ARB	11			14			NS
Diuretic	7			6			NS
Calcium channel blocker	4			3			NS

NS: Non-significant; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; LDL: Low density lipoprotein; HDL: High density lipoprotein; ACE: Angiotensin converting enzyme; ARB: Angiotensin receptor blocker.

(Alx@75) was similar in both groups (p=0,755), but PWV was significantly (p=0.001) higher in the study group (Fig. 1). Logistic regression analyses were performed to investigate the independent markers of aortic arch calcification. Arterial stiffness parameters (PWV, AIx@75, aortic mean pressure) and clinical parameters (such as age, BMI, SBP and DBPs and aortic arch calcification) were included in the analysis. As a result, only aortic PWV was an independent predictor of the presence of aortic calcification (Table 3).

DISCUSSION

In the current study, we evaluated the relationship between aortic arch calcification and arterial stiffness

Table 2. The relationship between arterial stiffness parameters and aortic arch calcification

	Aortic calcification (+) (n=41)	Aortic calcification (–) (n=41)	*p*
Central aortic pressure			
Systolic (mmHg)	126±13	120±13	0.062
Diastolic (mmHg)	83±7	79±10	0.047
Pulse wave velocity (m/s)	13±2	10±1	**<0.001**
Augmentation index normalized to heart rate	29±10	28±9	0.755

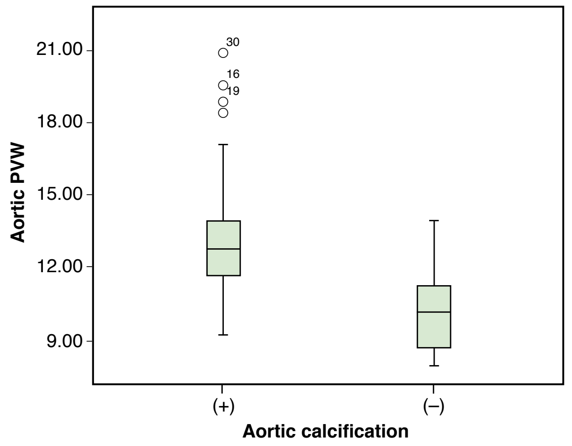

Figure 1. There is a significant relationship between aortic calcification and aortic PWV.

in patients with no clinical evidence of atherosclerotic disease. The AIx@75 was similar in both groups, but the PWV was significantly higher in the study group. Although the aortic PWV was independently correlated with the presence of aortic arch calcification, there was no significant correlation between the normalized heart rate (AIx@75) and aortic arch calcification.

In a recent study, McEniery et al.[11] reported that aortic calcification had a significant positive association with aortic PWV, but it was not related to the AIx. Similarly, we detected a significant relationship between aortic calcification and the aortic PWV, but not with the AIx@75. Interestingly, Raggi et al.[12] reported that the abdominal, but not the thoracic calcium score was independently related to aortic stiffness in hemodialysis patients. Here, abdominal calcification was assessed by standard radiography, while thoracic deposition was quantified by electron beam CT, which is an expensive and sophisticated method. In our study, aortic calcification was evaluated by chest X-ray, which is commonly used in clinics and is easily interpreted by most physicians. In another small study of healthy Japanese subjects, a relationship was reported between the brachial-ankle PWV and the length of the calcified abdominal aorta on standard radiographs.[13] However, that study was limited in that data on the aortic PWV, which is the gold standard for the measurement of arterial stiffness, were not available.

The Calcification Outcome in Renal Disease (CORD) study was the first large-scale clinical study to assess aortic calcification, PWV, and AIx of dialysis patients concurrently using widely available and relatively low-cost methods. CORD data was used to evaluate whether these surrogate measures for cardiovascular disease risk (aortic calcification, PWV, and AIx) provide complementary or overlapping information.[14] The differences in factors influencing PWV and AIx and their individual relationships with aortic calcification suggest that these three markers are complementary, rather than redundant to each other.[14] In our study, consistent with previous studies, patients with aortic calcification had higher aortic PWV than healthy individuals.[15-17] PWV does not always change in parallel with the AIx. Aortic PWV is affected by structural changes, while the AIx is mostly affected by endothelial function.[11-14] Also, as aortic calcification impairs the structural properties of the aorta, it is possible that PWV is initially affected by aortic calcification. However, increased cytokine and matrix metalloproteinase levels, the presence of in-

Table 3. The relationship between arterial stiffness parameters, age, BMI, SBP, DBP, and aortic arch calcification via multivariate linear regression analysis

	Odds ratio	95% CI	*p*
Age	1.028	0.879-1.201	0.732
Body mass index	0.874	0.736- 1.037	0.122
Systolic blood pressure	0.960	0.876-1.052	0.386
Diastolic blood pressure	0.967	0.846-1.107	0.628
Aortic mean pressure	1.093	0.952-1.254	0.206
AIx@75	0.913	0.827-1.009	0.075
PWV	2.137	1.390-3.285	**0.001**

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; CI: Confidence interval; AIx@75: Normalized for heart rate augmentation index; PWV: Pulse wave velocity.

flammation, and arterial stiffness also play important roles in the development of aortic calcification.[18,19] More comprehensive studies are needed to assess the relationship between the AIx and PWV. Both aortic calcification and the aortic PWV are associated with coronary artery disease and cardiovascular mortality.[4,16,17] Aortic PWV is an independent indicator of all-cause mortality and mortality due to cardiovascular causes.[15-20] Additionally, peripheral vascular disease and ischemic stroke have been found to be associated with aortic calcification.[21,22]

Limitations

The exclusive use of PA chest radiography was a limiting factor for the evaluation of aortic calcification, as it can also be detected via lateral chest radiography. An additional limitation of this study was the small number of subjects.

Conclusions

This study is the first to show a significant association between the presence of aortic arch calcification via chest X-ray and an increased aortic PWV. Also, carotid-femoral PWV measurements were performed using the SphygmoCor device for the first time. According to the results of the current study, aortic PWV is an early indicator of coronary artery disease and is associated with aortic arch calcification.

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Key words: Aorta/physiopathology; blood pressure; calcinosis/complications/physiopathology/radiography; elasticity; hypertension.

Anahtar sözcükler: Aort/fizyopatoloji; kan basıncı; kalsinoz/komplikasyonlar/fizyopatoloji/radyografi; elastisite; hipertansiyon.