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Aortic arch calcification is strongly associated with obstructive sleep apnea

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ABSTRACT

Aim: Obstructive sleep apnea (OSA) is a common clinical condition that causes an increase in cardiovascular morbidity and mortality. OSA is likely to show increased arterial stiffness and progressive systemic atherosclerosis. Chest radiography reveals atherosclerotic changes in the aorta.The aim of this study was to investigate the relationship between aortic arch calcification (AAC) on chest radiography and OSA.

Material and Method: 204 patients (age: 55±14 years; 78 men) who were diagnosed with OSA by performing night polysomnography were evaluated. On the other hand 200 (age: 48±15 years; 94 men) patients were selected to the group non OSA. AAC was evaluated with chest radiography and inter-observer agreement was analyzed by using kappa statistics. Univariate and multivariate logistic regression analysis was conducted to assess the association of AAC and OSA. P-value <0.05 was considered statistically significant.

Result: The prevalence of AAC was 207 (51,2%). OSA group had significantly higher prevalence of AAC (79% vs. 32.5%, p <0.0001) as compared to the normal group. Presence of AAC was a strong and independent predictor of OSA (OR 3.923, 95%CI 2.396 to 6.328) in multivariate analysis.

Conclusion: Presence of AAC on plain chest radiography is strongly and independently associated with the presence of OSA.

Keywords: Aorta, thoracic, calcinosis, sleep apnea, obstructive.

INTRODUCTION

Obstructive sleep apnea (OSA) is a disease that causes complete or partial airway collapse during sleep and thus repetitive ventilation interruptions (1). OSA has been demonstrated to be involved with increased prevalence of cardiovascular disease (CVD) due to intermittent sleep interruptions, intermittent chronic hypoxia, and changes in intra-chest pressure (2,3). Oxidative stress and sympathetic activation occur in OSA due to fast reoxygenation following periods of hypoxia. These also lead to inflammation resulting in endothelial dysfunction and thus subclinical and clinical atherosclerosis (4).

In some studies, the relationship between OSA and coronary artery calcium level has been revealed and, as it is known, coronary artery calcium level is one of the indicators of subclinical atherosclerosis (5). There are previous studies evaluating the relationship between aortic calcification, coronary artery calcium level, and CVD (6). Calcium accumulation in the aortic arch can be evaluated by chest radiography. Calcification of the aortic arch gives preliminary clues about atherosclerosis. Based on all these, further investigation of the relationship between OSA and subclinical atherosclerosis markers is valuable in that it leads to evaluations for reducing possible future adverse events related to CVD in patients with OSA.

In this study, it was aimed to research its relationship with OSA by evaluating aortic arch calcification (AAC) on chest radiography.

MATERIAL AND METHOD

The study was carried out with the permission of Tokat Gaziosmanpaşa University Faculty of Medicine Clinical Researchs Ethics Committee (Date: 19.08.2020, Decision No: 20-KAEK-122). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

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Study Populations

The aortic arch was evaluated with posterior-anterior (PA) chest radiography of all participants included in the study. Patients older than 18 years of age and had night polysomnography from July 2018 to May 2020 were included in the study. The conditions for not being included in the study were as follows: inadequate chest x-ray, known aortic, coronary artery, cerebrovascular and peripheral vascular disease, open chest surgery, heart failure, moderate to severe cardiac valve disease, pregnancy, malignancy, and receiving dialysis. All participants were evaluated by transthoracic echocardiography. Participants were evaluated with medical history, physical examination and laboratory data.

Demographic and Laboratory Data

Biochemical parameters were automatically evaluated with the aid of the Beckman Coulter LH-750 Hematology Analyzer (Beckman Coulter, Inc, Fullerton, California). Routine biochemical parameters were evaluated by standard methods. Hypercholesterolemia was described as an initial cholesterol level of> 200 mg/dL and/or a low-density lipoprotein cholesterol level of> 130 mg/dL or pre-diagnosed and treated hypercholesterolaemia. Diabetes mellitus and hypertension were defined as drug users for the treatment of these diseases. In addition to these, presence of diabetes mellitus was determined based on when glucose level was ≥126 mg/dL in several measurements for fasting or glucose level >200 mg/dL at any measurement and hypertension was diagnosed based on when repeated systolic/diastolic blood pressure measurements was ≥140/90 mmHg. Current smoking was defined as smoking in the previous 6 months. Body mass index was expressed as kg/m².

Evaluation of Obstructive Sleep Apnea

All subjects were evaluated using polysomnography overnight using an equipped digital polygraph (SomnoStar Alpha Sleep System, SensorMedics Corp., Yorba Linda, CA, USA). Patients who were diagnosed with OSA according to the accepted definition and scoring methods were included in the study (7). Hypopneas were defined as a 30-80% reduction in nasal pressure flow for at least 10 seconds with oxygen desaturation ≥4%. A flow reduction of 80% in the nasal pressure signal for at least 10 seconds was defined as apneas. Oxygen desaturation scored if there is a ≥4% decrease. The apnea-hypopnea index (AHI) was defined as the number of apnea and hypopneas per hour of the analyzed recording time and it was used to determine the risk of OSA.

The Aortic Arch Assessment

To all participants included in the study; standard PA chest radiography was taken while the participants were standing (AXIOM Aristos MX, SIEMENS, Germany). The AAC was evaluated in four categories: grade 0, no visible calcification; grade 1, the calcification appears as a small dot or thin line; grade 2, calcification at one or more points or in the form of a thick line; grade 3, circular prominent calcification of the aortic arch (8). AAC for each patient was assessed by two independent, experienced cardiologists in a blinded fashion.

Echocardiographic Examination

All echocardiographic evaluations (General Electric Vivid S5, Milwaukee, WI, USA) were performed on all participants in the left decubitus position using a 2.5-3.5 MHz transducer. The examination was performed using two-dimensional and pulsed Doppler measurements according to the American Echocardiography Association and the European Society of Cardiovascular Imaging criteria. Simpson's method was used to evaluate left ventricular ejection fraction (9).

Statistical Analysis

Statistical analyses were carried out using the SPSS 18.0 Statistical Package Program for Windows (SPSS Inc., Chicago Illinois, USA). Qulitative data are presented as medians with interquartile ranges. Quantitative variables were expressed as a mean value standard deviation and categorical variables as percentages. The distribution of continuous variables was determined with the Kolmogorov-Smirnov test. Student t-test was used to evaluate normally distributed data and Mann-Whitney U test was used to evaluate non-normally distributed data. Fisher's exact or chi-square tests were used to evaluate categorical variables . Multivariate logistic regression analyses were applied to determine independent factors. Data from univariate and multivariate logistic regression analyses were reported as odds ratios with 95% CI. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 404 participitians were included in this study. The mean patient age was 55±14 years, and 172 (42.5%) of the patients were men. Two hundred four patients (50.4%) with OSA were evaluated as an OSA (+) group. Those without OSA diagnosis, symptoms or signs were determined as the OSA (-) group. As compared to the OSA (+) group, the OSA (-) group was older (p<0.001). Basic characteristic features of the groups, demographic and laboratory data were similar except age. Patient characteristics are summarized in **Table 1**.

In the evaluations made on chest radiography, the frequency of AAC in the group with OSA (+) was statistically higher than the group with OSA (-) (p<0.001) (**Table 2**).

In univariate analyses (**Table 3**), AAC was positively and significantly correlated with age(r=0.172, p< 0.001, BMI (r=0.201, p<0.001), AHI (r=0.212, p<0.001), arousal index (r =0.282, p<0.01), and 3% ODI (r=0.224, p<0.01), as well as several clinical variables.

Table 1. Baseline characteristics of the study groups

	OSA (+) (n=204)	OSA (-) (n=200)	P value
Age (years)	55±14	48±15	<0.001
Male, n (%)	78 (38.2)	94 (47)	0.064
BMI, kg/m2	29±5	28±4	0.062
Smoker, n (%)	65 (31.8)	52 (26)	0.110
Hypertension, n (%)	104 (50.9)	83 (41.5)	0.051
Glucose (mg/dL)	106±30	102±29	0.086
Diabetes mellitus, n (%)	46 (22.5)	34 (17)	0.286
Total cholesterol (mg/dL)	189±40.6	194±40.4	0.198
Triglyceride (mg/dL)	191±39	174±81	0.019
Low-density lipoprotein (mg/dL)	116±38	118±37	0.902
High-density lipoprotein (mg/dL)	46±12	45±13	0.498
Creatinine (mg/dL)	0.82±0.18	0.82±0.27	0.880
Antihypertensive drug, n	47	35	0.049
Antidiabetic drug, n	2	1	0.988
AHI, /h	50.5±14.4	2.1±1.7	<0.001
Aurosal index, /h	48±17.2	19.8±9.6	<0.001
ODI (3%), /h	40.1±20.2	0.8±0.7	<0.001
Lowest SpO2, %	75±9.7	90.5±3.5	<0.001

AHI, apnea-hypopnea index; BMI, body mass index; ODI, oxygen desaturation index; SpO2, peripheral oxygen saturation

Table 2. Aortic arch calcification grades in the study groups

Aortic arch calcification (n, %)	OSA (+) (n=204)	OSA (-) (n=200)	P value
Grade 0	62 (30.3)	135 (67.5)	<0.0001
Grade 1	86 (42.1)	50 (25)	<0.001
Grade 2	45 (22)	14 (7)	<0.001
Grade 3	10 (4.9)	1 (0.5)	<0.001

OSA, obstructive sleep apnea

Table 3. Univariate analysis for obstructive sleep apnea

Variables	β	P value
Age	0.172	<0.001
Male	0.006	0.056
BMI	0.201	<0.001
Smoker	-0.186	0.103
Hypertension (%)	0.526	0.048
Diabetes mellitus (%)	0.438	0.301
Total cholesterol (mg/dL)	-0.012	0.235
Triglyceride (mg/dL)	-0.002	0.089
Antihypertensive drug	0.490	0.044
Antidiabetic drug	0.042	0.382
AHI	0.212	<0.001
Aruosal index	0.282	<0.001
ODI (%3)	0.224	<0.001
Lowest SpO2	-0.134	0.001

AHI, apnea-hypopnea index; BMI, body mass index; ODI, oxygen desaturation index; SpO2, peripheral oxyen saturation

ACC was associated with OSA in univariate logistic regression analysis (**Table 4**). According to the results of multivariate regression analysis, AAC was also identified as an independent predictor for OSA (r =1.362, OR 3.923, 95%CI 2.396 to 6.328) (**Table 5**).

Table 4. Correlations between OSA and AAC

Aortic arch calcification (%)	β	P value
Grade 0	Reference category	
Grade 1	1.384	<0.0001
Grade 2	1.846	<0.0001
Grade 3	2.698	0.006

ACC, aortic arch calcification; OSA, obstructive sleep apnea

Table 5. Multivariate analysis for obstructive sleep apnea

Variables	β	OR	Lower	Upper
Age	0.014	1.014	0.978	1.034
Body mass index	0.035	1.036	0.987	1.089
Hypertension	0.060	1.062	0.658	1.690
Triglyceride	-0.002	0.985	0.989	0.996
Presence of aortic arch calcification	1.362	3.923	2.396	6.328
AHI	0.15	1.018	0.985	1.049
Male	0.15	1.008	0.964	1.027

AHI, apnea-hypopnea index

DISCUSSION

As far as we know, this study clearly reveals the relationship between AAC and OSA, which was detected for the first time via chest radiography. Therefore, the detection of ACC, which is one of the indicators of subclinical atherosclerosis, more frequently in OSA patients provides early treatment and approaches. Accordingly, this situation; it is important in terms of improving the morbidity and mortality of CVD.

The pathophysiology of OSA is not fully explained. Factors that reduce the width of the upper respiratory tract can cause OSA (10). The most important complications seen in patients with OSA are associated to the cardiovascular system (11). Cardiovascular diseases seen with OSA in order of frequency: hypertension (30-60%), CAD (20-30%), pulmonary hypertension (20-30%) (12,13).

Many risk factors for atherosclerosis are common with OSA; age, male gender, smoking, obesity, metabolic syndrome are parameters specific to both situations (14). Oxidative stress in OSA; there are data that it causes both endothelial dysfunction and LDL oxidation (15). CRP, fibrinogen, IL-6 are risk factors for atherosclerosis and these have also been shown to increase in OSA (16). In patients with CAD proven by coronary angiography, OSA has been found frequently (17).

Local endothelial damage, inflammation, oxidative stress, and vascular calcification are involved in the pathogenesis of atherosclerosis (18). Calcification of the

arterial wall is part of atherosclerosis and is not found in normal vessels (19).

Oxidative stress and inflammatory reaction in OSA lead to increased arterial stiffness , carotid intima-media thickness and CAD progression (20-22). OSA is frequently seen in patients with aortic aneurysms and dissection and it has been suggested that negative intrathoracic pressure may play a role in the development or worsening of these pathologies. Additionally, negative intrathoracic pressure is thought to cause basal atherosclerotic changes in the aorta (23,24).

AAC has been presented as a substitution marker for atherosclerosis to better reflect the total burden of atherosclerosis (25). Atherosclerosis may be suspected if ACC is present in the chest radiography evaluation in OSA patients, and so patients can be stratified by their risk of atherosclerosis (26). In addition, Patients with higher risk for atherosclerosis can be distinguished by investigating the presence of ACC in patients with OSA. Most of the parameters that are indicators of subclinical atherosclerosis do not provide additional information other than the prediction of subclinical atherosclerosis (27-29). On the other hand, chest radiography is generally used in OSA, health checks unrelated to OSA, and in various clinical settings.

In this study, we have demonstrated that the presence of AAC is strongly associated with OSA. New studies are also needed to confirm our findings and, in addition, to assess the possible relationship of AAC and OSA by classifying by severity.

Study Limitations

The main limitation of the study is the small number of participants included in the study. OSA is categorized as no/mild, moderate, and severe. However, we did not examine OSA by classifying it by severity.

CONCLUSION

OUA is strongly and independently associated with ACC presence on plain chest radiography. This simple assessment allows us to distinguish patients with OSA based on their risk of developing subclinical atherosclerosis.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Tokat Gaziosmanpaşa University Faculty of Medicine Clinical Research Ethics Committee (Date: 19.08.2020, Decision No: 20-KAEK-122).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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