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Original Article

Aortic knob width and calcification is associated with the extensivity of lower extremity arterial disease

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Abstract

Aim: Aortic knob width (AKW) and calcification (AKC) were shown to be associated with atherosclerosis. We aimed to evaluate the relationship between AKW, AKC, and the extensivity of lower extremity arterial disease (LEAD).

Material and Methods: AKW and AKC were assessed in patients with LEAD who underwent conventional or CT angiography. Characteristics of patients were retrospectively reviewed.

Results: AKC was observed in 79 (42.2%) of 187 patients. Patients with AKC were older compared to those without (63.7±9.4 vs 60.2±8.9; p:0.009). Smoking was more frequent in patients with AKC whereas the frequency of coronary artery disease, hypertension (HT), dyslipidemia (DL), diabetes mellitus (DM) were similar. AKW was greater in patients with AKC (37.6±2.7 mm vs 36.7±2.4 mm; p: 0.013). Patients with AKC had higher TASC II class (2.8 ±0.9 vs 2.4±0.9; p:0.001). Patients were divided into low (A,B)(n:81) and high (C,D)(n:106) TASC II groups. Male patients were more common in both groups albeit statistical difference (%93.8 vs %82.1; p:0.017). DM, HT, and AKC were more common in high TASC II group. AKW was greater in high TASC II group (38.0±2.5 vs 35.8±1.9, p:0.001). HT [OR: 5,956 (2.800-12.671); p:0.001], AKW [OR: 1,583 (1.302-1.926); p:0.001] and AKC [OR: 2,540 (1.185-5.441); p: 0.017] were predictors for high TASC II class in multivariate logistic regression. In ROC analysis, AKW greater than 36.5 mm had 72.6% sensitivity and 69.1% specificity [AUC: 0.766, p:0.01, 95% CI (0.698–0.834)] to predict high TASC II class.

Conclusion: AKW and AKC, easily assessed with plain chest radiograph, are related to extensivity of LEAD.

Keywords: Atherosclerosis; aortic knob; lower extremity arterial disease; peripheral arterial disease; vascular calcification

INTRODUCTION

The chest radiograph is an easily acquired and cheap diagnostic tool which enables the clinician to assess cardiac and associated vascular structures. The aortic knob which is formed by arcus aorta and proximal descending aorta is usually evaluated visually for detecting aortic pathologies such as aneurysm and dissection. Previous studies reported that aortic knob width (AKW) is related to the extent of coronary artery disease (1). Similarly, aortic knob calcification (AKC) was shown to be associated with coronary artery complexity in patients with acute coronary syndrome (2).

Lower extremity arterial disease (LEAD) is a significant cause of morbidity and mortality. With the advances in percutaneous treatments, most of the patients with LEAD might be treated without the need for surgery. Conventionally, TASC II classification is not only used to define the extensivity of LEAD but also to choose the treatment modality. Conventionally, surgical treatment was proposed in patients with TASC C and D lesions due to superior patency rates (3). On the other hand endovascular treatment is the modality of choice in TASC A and B lesions. However, evaluation of TASC II classification depends on advanced imaging such as CT (Computed Tomography), MRI (Magnetic Resonance Imaging) or conventional angiography. Furthermore, these imaging modalities have several disadvantages such as nephropathy and they tend to be time-consuming. Therefore, aortic knob evaluation might help the clinician to predict the extensivity of LEAD without requirement for complex imaging modalities. We aimed to investigate the relationship between AKW, AKC, and extensivity of LEAD.

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MATERIAL and METHODS

Study Population

Data of 284 patients who underwent conventional or CT angiography for lower extremity artery disease (LEAD) between 2015 January and 2019 March were retrospectively evaluated. Patients with aortoiliac disease were included in the study. Patients with chest graph within 3 months were included. Patients whose chest graphs were not properly centered, graphs with tracheal deviation, evident mediastinal pathology or history of aortitis or previous aortic pathology were excluded. Patients with an eGFR (estimated glomerular filtration rate)<30 mL/min/1.73m^2 were excluded due to exaggerated calcification process in these patients. A total of 187 radiographs were assessed by an experienced cardiologist who is unaware of the severity of LEAD. AKW was measured from the point of the left lateral edge of the trachea to the left lateral wall of the aortic knob (Figure 1). AKC was noted. TASC II classification was used to assess the extensivity of the aortoiliac arterial disease (4). Demographics and risk factors of the patients were reviewed.

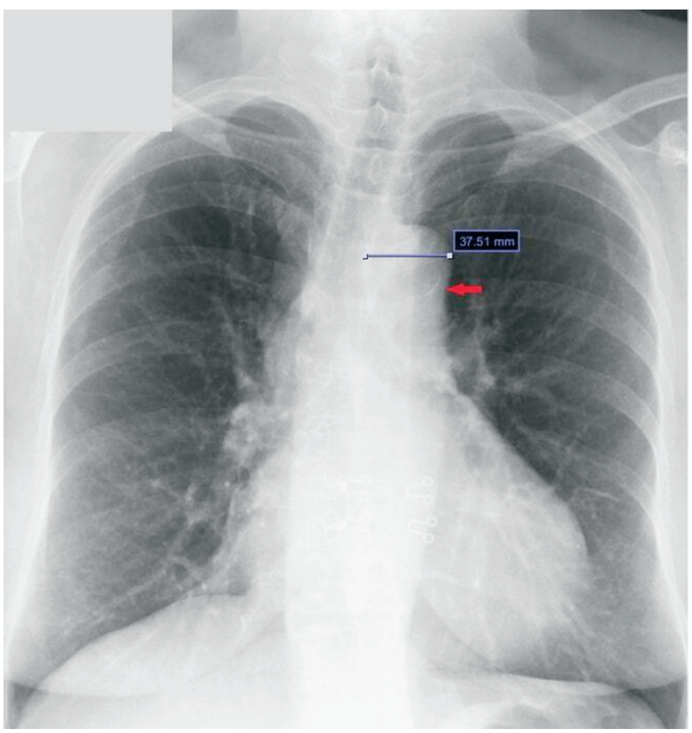

Figure 1. AKC (arrow) and measurement of AKW.

Statistical Analysis

SPSS version 22.0 (IBM Corp. Armonk, NY, USA) was used for analysis. Kolmogorov-Smirnov test was used to test normality. Continuous data was expressed as mean ± standard deviation (SD) and categorical data was expressed as percentages. Differences between patient subgroups were tested using Student's T-test or Mann-Whitney U test. Categorical variables between groups were assessed with Chi-square test or Fisher's exact test, whichever was suitable. Logistic regression analysis (enter method) was used to identify the independent predictors of TASC II groups. Significant variables in univariate analysis were included in multivariate analysis. Receiver-operating characteristic (ROC) curve graphics were used to determine the cut off values of predictors for high TASC II class. A P-value < 0.05 was considered statistically significant.

RESULTS

AKC was observed in 79 (42.2%) of 187 patients. Patients with AKC were older compared to those without (63.7±9.4 vs 60.2±8.9; p:0.009). Smoking was more frequent in patients with AKC (65.8% vs 42.6%; p:0.002) whereas the frequency of coronary artery disease, hypertension (HT), dyslipidemia (DL), diabetes mellitus (DM) were similar. AKW was greater in patients with AKC (37.6±2.7 mm vs 36.7±2.4 mm; p: 0.013). Patients with AKC had higher TASC II class (2.8 ±0.9 vs 2.4±0.9; p:0.001)(Figure 2). Patients were divided into low (A,B)(n:81) and high (C,D) (n:106) TASC II groups. Male patients were more common in both groups albeit statistical difference (93.8% vs 82.1%; p:0.017).DM, HT and AKC were more common in high TASC II group [(41.5% vs 24.7%; p:0.016),(75.5% vs 33.3%: p:0.001),(53.8% vs 27.2%; p:0.001)]. AKW was greater in high TASC II group (38.0±2.5 mm vs 35.8±1.9 mm, p:0.001) (Figure 3). Characteristics of patients relation to AKC and TASC II were presented in Table 1. Male gender, DM, HT, AKW, and AKC were associated with high TASC II class in univariate regression analysis. HT [OR: 5,956 (2.800-12.671); p:0.001], AKW [OR: 1,583 (1.302-1.926); p:0.001] and AKC [OR: 2,540 (1.185-5.441); p: 0.017] were predictors for high TASC II class in multivariate logistic regression (Table 2). In ROC curve analysis, AKW greater than 36.5 had 72.6% sensitivity and 69.1% specificity [AUC: 0.766, p:0.01, 95% CI (0.698–0.834)] to predict high TASC II class (Figure 4).

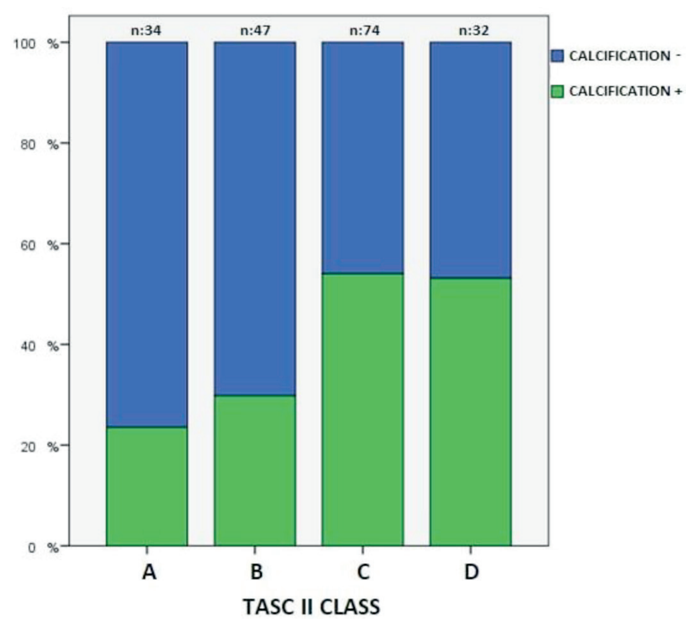

Figure 2. AKC of patients' relation to TASC II class.

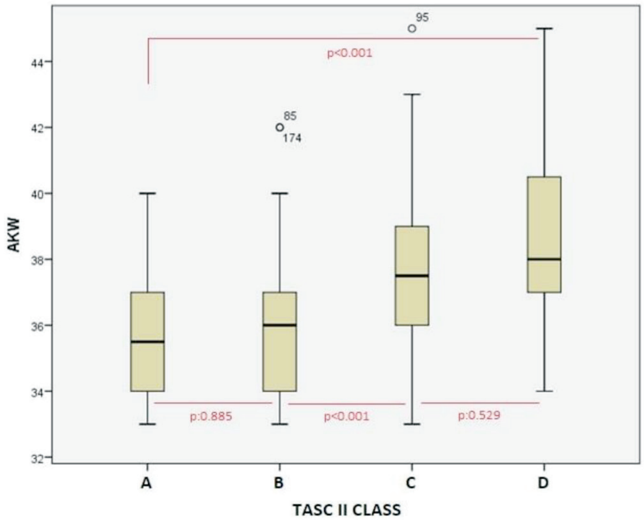

Figure 3. AKW of patients' relation to TASC II class.

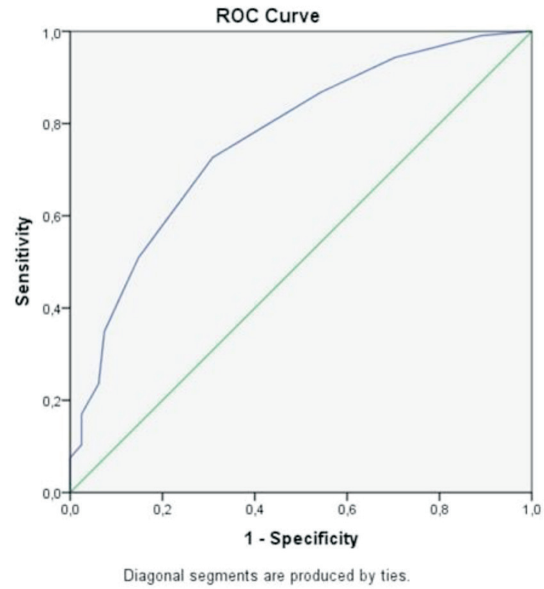

Figure 4. ROC curve of AKW for predicting high TASC II class. AKC, aortic knob calcification; AKW, aortic knob width; ROC, receiver operating characteristics

Table 1. Baseline characteristics of patients relation to aortic knob calcification and TASC II groups.

	Calcification (-) n=108	Calcification (+) n= 79	p	TASC A-B n=81	TASC C-D n= 106	p
Sex (male), n (%)	96 (88.9)	67 (84.8)	0.410	76 (93.8)	87 (82.1)	0.017
Age (years)	60.2±8.9	63.7±9.4	0.009	61.3±8.8	61.9±9.6	0.623
Body mass index (kg/m^2)	27.2±3.9	26.5±3.5	0.196	27.5±4.1	26.6±3.3	0.111
Smoking, n (%)	46 (42.6)	52 (65.8)	0.002	38 (46.9)	60 (56.6)	0.189
DM, n (%)	31 (28.7)	33 (41.8)	0.063	20 (24.7)	44 (41.5)	0.016
HT, n (%)	56 (51.9)	51 (64.6)	0.083	27 (33.3)	80 (75.5)	0.001
CAD, n (%)	25 (23.1)	22 (27.8)	0.464	17 (21.0)	30 (28.3)	0.253
eGFR (mL/min/1.73m^2)	100.6±27.7	93.8±28.2	0.116	97.0±25.9	98.0±29.6	0.818
Total Cholesterol (mg/dl)	207.5±48.8	206.2±69.7	0.924	206.5±49.8	207.5±63.7	0.944
LDL-C (mg/dl)	129.1±36.9	126.9±46.5	0.825	124.6±33.9	131.2±45.5	0.486
HDL-C (mg/dl)	40.1±10.5	42.7±11.2	0.320	40.8±7.1	41.5 ±13.1	0.776
AKW (mm)	36.7±2.4	37.6±2.7	0.013	35.8±1.9	38.0±2.5	0.001
TASC II class	2.4±0.9	2.8 ±0.9	0.001	1.6±0.5	3.3 ±0.5	
AKC, n (%)				22 (27.2)	57(53.8)	0.001

DM, diabetes mellitus; HT, hypertension; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; AKW, aortic knob width; AKC, aortic knob calcification

Table 2. Logistic regression analysis of high TASC II class						
	Univarite Analysis			Multivariate Analysis		
	OR	95% CI	p	OR	95% CI	p
Sex (male)	3.320	1.183-9.318	0.023	0.411	0.122-1.382	0.151
Age (years)	1.008	0.977-1.040	0.625			
Body mass index (kg/m^2)	0.937	0.866-1.013	0.103			
Smoking	0.678	0.379-1.212	0.189			
DM	2.165	1.146-4.088	0.017	1.556	0.700-3.461	0.278
HT	6.154	3.246-11.667	0.001	5.956	2.800-12.671	0.001
CAD	0.673	0.340-1.330	0.255			
eGFR (mL/min/1.73m^2)	1.001	0.990-1.012	0.816			
Total Cholesterol (mg/dl)	1.000	0.992-1.008	0.943			
LDL-C (mg/dl)	1.004	0.993-1.016	0.482			
HDL-C (mg/dl)	1.006	0.964-1.049	0.785			
AKW	1.601	1.348-1.902	0.001	1.583	1.302-1.926	0.001
AKC	3.120	1.677-5.804	0.001	2.540	1.185-5.441	0.017

DM, diabetes mellitus; HT, hypertension; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; AKW, aortic knob width; AKC, aortic knob calcification

DISCUSSION

To our best knowledge, this is the first study which demonstrated that AKW and AKC are associated with severity of LEAD. A simple chest graph prior to further imaging may aid the clinician to predict the severity of LEAD.

Calcification is a complex process of biomineralization of intima and media layers which resembles osteogenesis. Although several signaling molecules were identified regulating calcification exact pathogenesis still remains elusive (5). Classical risk factors for atherosclerosis including smoking, age and HT were consistent predictors of vascular calcification (6). Furthermore, a twin study suggested genetic factors seem to have a significant role in aortic calcification and stiffness (7).

There has been a historical interest in the relationship between aortic calcification and extensivity of atherosclerotic disease (8). Several studies concluded that AKC might be a part of the general vascular atherosclerotic process and associated with coronary artery disease (9,10,11). Later studies showed a clear link between AKC and multivessel involvement in patients with unstable angina (1). Korkmaz L et al. found that AKC is a predictor of coronary artery disease complexity assessed with SYNTAX score (2). In addition to the close relationship between AKC and coronary artery disease, the involvement of carotid arteries and intracranial arteries were demonstrated (12,13). Aortic calcification was associated with the development of intermittent claudication (14). Compatible with the previous study we found that AKC is related to extensivity of LEAD.

Pulsatile stress and conventional risk factors cause dynamic a change in aortic wall and geometry with subsequent dilatation and tortuosity. Thus aortic dilation is a measure of the target organ damage and was shown to be associated with arterial stiffness (15). In a necropsy study, 91 human aortas were assessed regarding the cause of death. Aortic diameter in all segments was larger in subjects who died due to cardiovascular causes (16). Although ascending aorta dilatation is less studied, atherosclerosis and link between abdominal aorta dilatation is clearly demonstrated (17). Recently, Ozdemir B et al. showed increased ascending aorta diameter in patients with coronary artery disease compared to those without (18). Cardio-ankle vascular index (CAVI) and pulse wave velocity (PWV) are quantitative measures of vascular function. AKW and AKC are shown to be associated with CAVI (19,20). Another study found that PWV is closely related to the presence of AKC (21). A previous study prospectively evaluated the change of aortic calcification burden from the level of the aortic arch to the level of iliac bifurcation with CT. The study suggested that annual change in aortic calcification was positively and significantly associated with arterial stiffness progression (22). Furthermore, two studies confirmed that AKW is independently predictive of invasively measured aortic pulse pressure which is a measure of vascular stiffness (23,24). Therefore both AKW and AKC seem to be useful for evaluating vascular stiffness and functions.

A previous study showed that aortic stiffness contributes to aortic calcification and it is related to more severe atherosclerotic disease in patients with PAD (peripheral arterial disease) (25). Another study revealed that the severity of lower limb perfusion impairment is related to central aortic pressure measured with augmentation index (26). Aortic arch and descending aorta calcification were associated with enlarged, unfolded, less tapered and more tortuous aorta. Additionally, calcification was positively associated with the size of the aortic arch and descending aorta (27). Compatible with this study we found greater AKW in patients with AKC. Nevertheless, AKW and AKC seem to be surrogate markers for predicting extensivity of atherosclerotic involvement not only in coronary arteries but also in lower extremity arteries.

Limitations

The small number of patients and retrospective nature of the study are the main limitations. Central hemodynamics such as pulse pressure might further contribute to the study, unfortunately, these parameters were not routinely recorded in patients with LEAD during conventional angiography. Calcium scoring with CT might be more useful due to quantitative evaluation of calcium burden, however, majority of patients in our practice were scheduled for conventional angiography depending on clinical assessment or Doppler ultrasound evaluation.

CONCLUSION

AKW and AKC, easily assessed with plain chest radiograph, are related to extensivity of lower extremity arterial disease.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports

Ethical approval: There is no need for ethical consent since the study is designed retrospectively

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