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Clinical Significance of Aortic Knob Width and Calcification in Unstable Angina

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Background Chest radiography is a routine examination evaluating those patients with chest pain. There are few data about the correlation between aortic knob width, calcification and coronary atherosclerosis.

Methods and Results The aortic knob width was measured and the presence of aortic knob calcification was assessed via a chest posteroanterior view in 178 consecutive patients. The aortic knob width and calcification were compared to the risk factor and the extent of coronary artery disease. Patient's age (69.5±7.95 vs 61.1± 10.29 years, p=0.010), the prevalence of hypertension (65.9 vs 46.3%, p=0.024) and diabetes (43.2 vs 26.1%, p=0.033), the level of total cholesterol (196.8±63.21 vs 188.6±44.45 mg/dl, p=0.049) and the incidence of multivessel disease (65.9 vs 38.1%, p<0.001) were higher in patients with aortic knob calcification than in patients without calcification. The aortic knob width and the prevalence of aortic knob calcification were significantly correlated with the severity of coronary artery disease. Multivariate analysis demonstrated that aortic knob calcification and diabetes were independent factors for multi-vessel disease (p=0.018 and p=0.012).

Conclusions The observation of aortic knob on a chest radiograph can provide important predictive information of coronary atherosclerosis. (*Circ J* 2006; **70:** 1280–1283)

Key Words: Aorta; Atherosclerosis; Coronary artery disease

In routine clinical practice, all cardiovascular patients undergo chest radiography. Elderly patients usually have a more dilated and tortuous aorta. In cases of long-standing hypertension, aneurismal change of aorta and dilatation of aortic arch develop.

Sometimes it is difficult perform coronary angiography in patients with a dilated and tortuous aorta. In addition, such patients have severe coronary atherosclerotic lesions and coronary artery calcification.

Several reports have shown that calcification of the abdominal aorta predicts an increased incidence of cardiovascular events[1–4] However, there are few studies on the correlation between aortic knob width and calcification, and coronary atherosclerosis[5–7] We tested the usefulness of chest radiography in patients with unstable angina, particularly observation of the aortic knob, in assessing the severity of coronary artery disease (CAD).

Methods

Study Population

We studied 178 consecutive patients who underwent coronary angiography. The clinical diagnosis for each of them was unstable angina, which had a resting pain of less than 30 min or accelerating effort angina. We excluded patients who had more than a moderate degree of aortic valve disease, vasospastic angina proved through intracoronary ergonovine test, and had a severe concomitant kidney (serum creatinine ≥2.0 mg/dl) or liver disease. Moreover, we excluded patients whose chest X-ray was not properly centered, if there was any deviation of the trachea or shift of the mediastinum, and if there was any known disease in the aorta such as aortitis.

Data Collection

In the fasting state, coronary angiography was performed using the Judkins's method, which followed the puncture of a femoral artery or followed a radial artery approach. The severity of coronary atherosclerotic lesions was evaluated from at least 3 projections in all patients. Significant stenosis was defined as a diameter stenosis of 50% or greater.

After an overnight fast, a sample of blood was collected to measure routine chemistry including serum creatinine, total cholesterol, triglyceride, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, lipoprotein (a), and high-sensitivity (hs) C-reactive protein (CRP).

All patients had chest radiography in the posteroanterior (PA) view. An examiner who was unaware of the result of the patient's coronary angiography reviewed the chest radiography. The widest point of the ascending aortic knob was measured along the horizontal line from the point of the lateral edge of the trachea to the left lateral wall of the aortic knob (Fig 1). We noted the presence of calcification in the aortic knob.

Statistical Analysis

Statistical analysis was performed with SPSS 11.0 for

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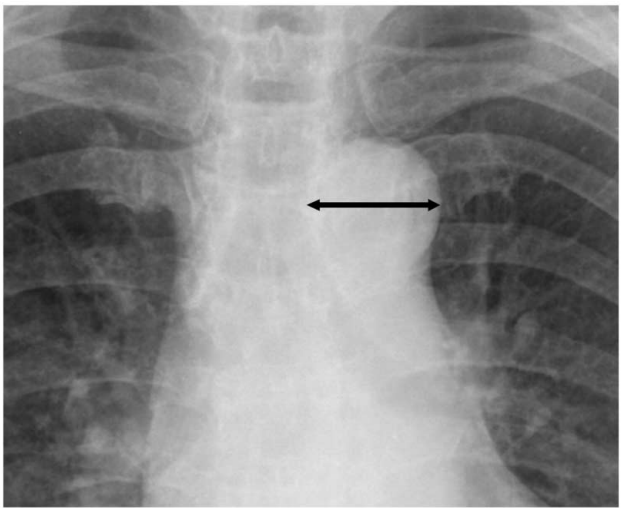

Fig 1. Method of aortic knob width measurement. The width of the aortic knob was measured from the point of the lateral edge of the trachea to the left lateral wall of the aortic knob.

Table 1 Comparison of Cardiovascular Risk Factors and Laboratory Findings According to the Presence or Absence of Aortic Knob Calcification

	Calcification (+) (n=44)	*Calcification (–) (n=134)*	*p value*
Age (years)	*69.5±7.95*	*61.1±10.29*	*0.010*
Male (%)	*18 (40.9)*	*77 (57.5)*	*0.056*
Smoker (%)	*8 (18.2)*	*62 (46.3)*	*0.001*
Hypertension (%)	*29 (65.9)*	*62 (46.3)*	*0.024*
Diabetes mellitus (%)	*19 (43.2)*	*35 (26.1)*	*0.033*
BMI (kg/m^2)	*24.6±3.28*	*24.6±3.32*	*0.973*
Monocyte (/mm^3)	*556.4±224.61*	*547.2±235.42*	*0.968*
Hemoglobin (g/dl)	*12.7±1.43*	*13.3±1.79*	*0.136*
hsCRP (mg/L)	*5.9±9.25*	*4.4±8.53*	*0.434*
Fibrinogen (mg/dl)	*328.8±84.39*	*287.9±81.05*	*0.230*
Total cholesterol (mg/dl)	*196.8±63.21*	*188.6±44.45*	*0.049*
Triglyceride (mg/dl)	*154.8±101.46*	*173.1±146.77*	*0.303*
HDL-cholesterol (mg/dl)	*47.9±11.29*	*45.2±10.66*	*0.413*
LDL-cholesterol (mg/dl)	*130.7±43.10*	*129.9±40.73*	*0.876*
Lipoprotein (a) (mg/dl)	*31.5±22.56*	*34.0±45.04*	*0.447*
BUN (mg/dl)	*18.9±7.57*	*16.4±5.94*	*0.099*
Creatinine (mg/dl)	*1.0±0.29*	*0.9±0.34*	*0.985*
Uric acid (mg/dl)	*5.4±2.11*	*5.5±1.69*	*0.274*
Multivessel disease (%)	*29 (65.9)*	*51 (38.1)*	*<0.001*

BMI, body mass index; hsCRP, high-sensitivity C-reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BUN, blood urea nitrogen.

Windows. All data are expressed as mean ± standard deviation. Patients' characteristics, according to the presence of aortic knob calcification, were compared by independent t-test and the χ^2 test. The aortic knob width was also compared with other risk factors and coronary atherosclerosis by 1-way ANOVA test. Multivariate analysis was conducted to determine the factors related to multivessel CAD. Statistical significance was set at $p<0.05$.

Results

The mean age of patients was 63.2±10.41 years and the numbers of male patients was 95 (53.4%). Overall, 44 patients (24.7%) had aortic knob calcification in the chest PA view.

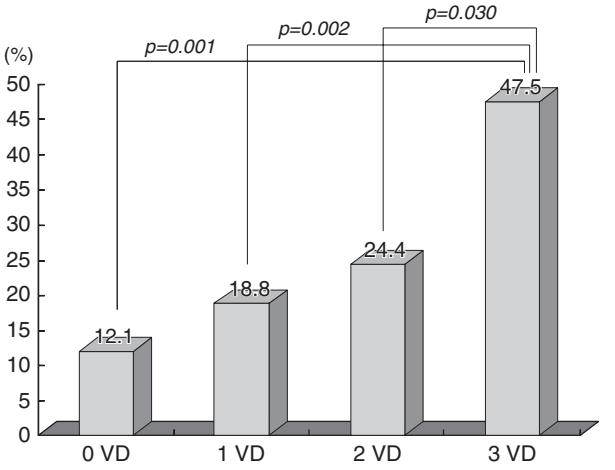

Fig 2. Prevalence of aortic knob calcification was proportional to the number of involved coronary arteries. Aortic knob calcification was revealed in 4 out of 33 (12.1%) patients with insignificant coronary stenosis, 12 out of 64 (18.8%) patients with single vessel disease, 10 out of 41 (24.4%) patients with 2-vessel disease, and 19 out of 40 (47.5%) patients with 3-vessel disease. VD, vessel disease.

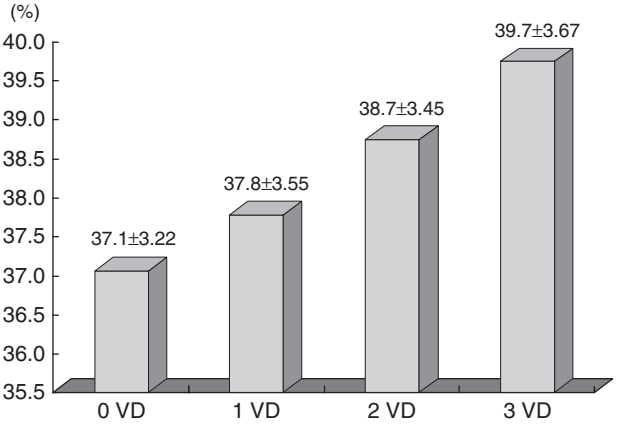

Fig 3. Width of the aortic knob was relatively correlated with the number of involved coronary arteries (p=0.030 by ANOVA test). A Post-Hoc test revealed a significant difference between the aortic knob width and the 0-, 1-, 2-vessel disease group and 3-vessel disease group. VD, vessel disease.

Aortic knob calcification was observed more commonly in elderly patients, non-smokers, those with hypertension, and in patients with diabetes (Table 1). The level of total cholesterol was 196.8±63.21 mg/dl in patients with aortic knob calcification and 188.6±44.45 mg/dl in those without calcification (p=0.049). There was no significant difference between the 2 groups in terms of other lipid profile, serum creatinine, hsCRP, and fibrinogen levels.

The prevalence of aortic knob calcification increased in proportion to the extent of significant coronary stenosis. Aortic knob calcification was revealed in 4 of 33 (12.1%) patients with insignificant coronary stenosis, 12 of 64 (18.8%) patients with 1-vessel disease, 10 of 41 (24.4%) patients with 2-vessel disease, and in 19 of 40 (47.5%) patients with 3-vessel disease (Fig 2). The patients with 3-vessel disease had a significantly higher incidence rate of aortic knob calcification than the patients with 0-, 1-, and 2-vessel disease. However, there was no significant dif-

Table 2 Multiple Regression Analysis for the Prediction of Multivessel Coronary Disease

Variable	*Odds ratio*	*95% Confidence interval*	*p value*
Diabetes	*2.655*	*1.243–5.672*	*0.012*
Aortic knob calcification	*2.765*	*1.189–6.432*	*0.018*
Serum creatinine	*2.772*	*0.914–8.410*	*0.072*
LDL-cholesterol	*1.008*	*0.999–1.017*	*0.086*
Age	*1.023*	*0.981–1.066*	*0.296*
Aortic knob width	*1.036*	*0.960–1.117*	*0.363*
Smoking	*0.622*	*0.222–1.745*	*0.367*
hsCRP	*1.009*	*0.969–1.050*	*0.665*
Male gender	*1.178*	*0.566–2.349*	*0.771*

Abbreviations see in Table 1.

ference in the incidence rate of aortic knob calcification among the patients with 0-, 1-, 2-vessel disease. An increased trend in aortic knob width was observed according to the severity of CAD (Fig 3). An ANOVA test showed the significant difference of aortic knob width between the groups of patients with CAD (p=0.030). A post-hoc test using the Duncan test revealed a significant difference between the 0-, 1-, 2-vessel disease and the 3-vessel disease.

Multivariate analysis showed that aortic knob calcification and diabetes were independent factors affecting multivessel CAD (p=0.018 and p=0.012) (Table 2).

Discussion

This is the first clinical study which indicating that aortic knob calcification and width confirmed on routine chest X-rays are useful predictors of multivessel coronary lesions in patients with unstable angina.

Atherosclerosis is one of the leading causes of death and disability in the developed world. Atherosclerosis of the coronary arteries commonly causes myocardial infarction and angina pectoris. In contrast, ectasia and the development of aneurysmal disease frequently occur in the aorta. Atherosclerosis is a focal disease within a given arterial bed, but within the patient, it is a systemic disease. These concepts were first published by DeBakey et al in 1957[8] They reported the concept of a segmental nature of atherosclerotic vascular occlusive disease, and they have subsequently published several articles on the subject of systemic patterns of atherosclerosis[9,10] Thus, patients who suffer ischemic stroke or peripheral artery disease have a higher incidence of concomitant CAD, which may explain our results involving the simultaneous involvement of aorta and coronary arteries.

Recently, there has been great interest in vascular calcification in terms of risk factors and subsequent outcomes. Calcium deposits in the coronary artery and extracoronary arterial beds indicate the extent of atherosclerotic lesions, and may be markers of subclinical cardiovascular disease[11–13] Studies of the coronary arteries using electron-beam computed tomography (EBCT) demonstrate an association between calcification and cardiovascular events[14–18]

In their population-based study, Iribarren et al reported that aortic arch calcification on chest radiography was independently related to the risk of CAD[5] They showed that men with aortic arch calcification have a 1.27-fold higher risk of developing coronary heart disease, and women have a 1.22-fold higher risk. The present study confirms this in patients with angiographically proven CAD, which is in addition to calcification. Aortic knob width is also a worthy predictor of coronary disease.

Although the precise mechanism of vascular calcification is yet to be elucidated, it most likely involves some elements of bone metabolism. Briefly, an active model has been suggested, which incorporates analogous cell types and cytokines, such as osteoprotegerin, with those involved in bone remodeling[19] Previous studies revealed that calcification of the aorta was associated with atherosclerotic risk factors such as old age[1,20] postmenopausal women[1,5] diabetes[20,21] hypertension[5,22] smoking[5,23] renal failure[20,24] and peripheral artery disease[21] and associated with serum markers, such as cholesterol[1,5,25] and CRP[26] The present study showed that aortic knob calcification correlated with old age, hypertension, diabetes, and a high level of total cholesterol, which was similar to the results obtained in previous studies. However, in contrast to previous studies, the present study revealed that the percentage of smokers was significantly lower in the aortic knob calcification group than in the non-calcification group. These results are explained by the difference in the study population; that is, the present study had a higher proportion of non-smoker females than the other epidemiologic series. In fact, aortic calcification is significantly associated with female gender, especially postmenopausal women[1,5] The present study had a lower incidence of smoking in the population (2.4%). Further studies are needed to confirm the relationship of smoking and aortic knob calcification.

Study Limitations

Our analysis was limited by the study population because it included only those patients pre-selected to undergo coronary angiography. Also, we retrospectively analyzed the data, and the number of patients examined was low. As non-invasive tools for the diagnosis of CAD have been developed, a population-based prospective study with more patients can be performed. Therefore, an epidemiologic study is required to confirm the results. We could not confirm the presence of aortic arch calcification using other methods such as EBCT. Chest radiography is the simplest method to use, but the accuracy and reproducibility were not tested. Presently, no modality has been accepted as the gold standard for measuring aortic calcification, and consequently there are few assessments for the sensitivity and specificity of these techniques. Further study is necessary.

In conclusion, aortic knob dilatation and calcification are closely related to significant coronary artery stenosis in patients with unstable angina; and aortic knob calcification is a reliable predictor for multivessel CAD. These preliminary findings may enhance the use of chest radiography as a screening method and, if confirmed, can assist risk stratification in patients suspected of having CAD.

Acknowledgments

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