

Does Atherosclerotic Aortic Plaque Detected by Telecardiography Indicate an Increased Risk of Coronary Artery Disease?

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ABSTRACT

Objective. The purpose of this study was to determine the cause of aortic arch calcification and to evaluate its prognostic value as an indicator of cardiovascular disease and its severity.

Methods and Results. The study was conducted prospectively among 1027 patients who underwent a coronary angiography in our hospital between April 2002 and September 2002 for suspected coronary artery disease. All chest x-rays were reviewed by a radiologist, who categorized aortic arch calcifications by their presence or absence. The patients were stratified according to age (≤ 50 , 51-64, and ≥ 65 years) to eliminate the influence of age on aortic arch calcification. Coronary lesions were considered either single-vessel or multivessel disease. Univariate analysis revealed significant correlation with age ($r = 0.37$; $P < .001$), presence of hypertension ($r = 0.14$; $P < .001$), smoking ($r = -0.10$; $P = .001$), presence of coronary artery disease ($r = 0.10$; $P = .001$), and the existence of multi-vessel disease ($r = 0.09$; $P = .006$). Multivariate analysis disclosed significant association with age and hypertension and no association with smoking, coronary artery disease, and other risk factors.

Conclusion. The aortic arch calcifications observed on plain chest x-rays are usually age related, and both aortic arch calcifications and coronary artery disease are strongly associated with age. The presence of aortic calcification on chest x-rays was not an indicator of the presence and extent of coronary artery disease.

INTRODUCTION

Atherosclerosis is a generalized disease that affects almost the entirety of the vascular system [Matsuma 1997]. Advanced age, male sex, estrogen level, smoking, hypertension, lipid profile, family history, diabetes, and obesity are among the

risk factors [Li 2002]. Calcium deposits in either the coronary or extra-coronary vascular bed may point to the presence of an atherosclerotic lesion and may be an indicator of subclinical cardiovascular disease [Iribarren 2000]. Chest x-ray examination is probably one of the least expensive, widely used noninvasive diagnostic tools in medicine, and there have been several studies examining the relation between the level of aortic arch calcification seen on chest x-rays and the presence of coronary artery disease. However, among the articles published, age as a factor has not been controlled for. In our study, we examined what might be associated with aortic arch calcification and evaluated its prognostic indications for the presence and the extent of coronary artery disease.

MATERIALS AND METHODS

The study was conducted prospectively among 1027 patients with suspected coronary artery disease who underwent a coronary angiography procedure in our hospital between April 2002 and September 2002. Patients with moderate to severe valvular heart disease, congenital heart disease, and idiopathic cardiomyopathies were excluded from the study. Data were collected for the presence of diabetes, hypertension, hyperlipidemia, smoking, peripheral arterial disease, and other related risk factors.

Diagnosis of hypertension was made in accordance with World Health Organization-International Society of Hypertension Guidelines [1999], and the American National Diabetes Association's criteria were used for the diagnosis of diabetes mellitus [1979]. Patients with blood cholesterol levels above 220 mg/dL or who were receiving antihyperlipidemic treatment were grouped as hypercholesterolemic patients. Smoking was considered a risk factor if the patient was a current smoker. Patients with absent distal pulses, previous history of, or operations related to, peripheral arterial disease, or symptoms highly suggestive of peripheral arterial disease were considered positive for peripheral vascular diseases.

Chest Radiography Analysis

The radiologist reviewed all plain chest x-rays. Roentgenograms were taken digitally by a Fuji FCR-5000 (Tokyo, Japan) from a distance of 180 cm, with the subject standing upright in a PA position during full inspiration.

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Table 1. Demographic Data of the Patients

	≤50 y	51-64 y	≥65 y	Total
No. (%)	266 (26)	447 (44)	314 (31)	1027
Sex, female (%)	66 (25)	169 (38)	105 (33)	340
Diabetes (%)	31 (12)	113 (25)	67 (21)	211
Hypertension (%)	76 (29)	215 (48)	174 (55)	465
Hyperlipidemia (%)	80 (30)	139 (31)	80 (25)	299
Smoking history (%)	183 (69)	244 (55)	117 (37)	544
Peripheral vascular disease (%)	17 (6)	34 (8)	32 (10)	83

Graphics were imprinted on film 24 × 36 cm in dimension for both the precalibrated parenchymal and bone doses. Aortic calcifications were assessed from these films. In cases where clear demonstrations of the lesion were not possible, brilliancy and contrast parameters were readjusted and the radiographs reassessed.

Coronary Angiography

Coronary angiographic studies were performed with Philips Integris H3000 cineangiographic equipment (GE Healthcare, Piscataway, NJ, USA) using Seldinger's technique. Coronary angiographic results were interpreted independently by investigators unaware of the chest x-ray readings. Stenosis of major coronary arteries beyond 50% of luminal diameter was considered critical. When the same condition was present in the left main coronary artery, the disease was regarded as 2-vessel disease. In our study, patients were categorized with either single-vessel or multi-vessel disease.

Statistical Analysis

All the numerical data are presented as mean ± standard deviation. The comparisons between patients with and without ascending aortic calcification were done with independent samples using the Student *t* test for the numerical data and chi-square test for the categorical data.

Comparisons of patients with or without aortic arch calcification on plain chest x-rays were conducted among 3 different

age groups (≤50, 51-64, ≥65 years) to eliminate the influence of age factor. Correlations of this calcification with various patient parameters were evaluated with Spearman linear regression analysis.

For multivariate analysis, dichotomous presence or absence of aortic arch calcification was used as the dependent factor and the 3 levels of age (≤50, 51-64, ≥65 years), presence of hypertension, hyperlipidemia, smoking, and coronary angiography were used as the independent factors. Backward likelihood ratio was used to eliminate independent variables. Statistical analyses were performed with a SPSS package (Chicago, IL, USA), and only *P* values <.05 were considered statistically significant.

RESULTS

The mean age of the 1027 patients participating in the study was 58 ± 10 years. Three hundred forty patients were women (mean age, 59 ± 10 years), and 687 patients were men (mean age 57 ± 11 years) (Table 1).

There were numerous factors associated with aortic arch calcification detected on chest x-ray. According to the univariate analysis, there was significant correlation for age ($r = 0.37$; $P < .001$), hypertension ($r = 0.14$; $P < .001$), smoking ($r = -0.10$; $P = .001$), coronary artery disease ($r = 0.10$; $P = .001$), and multi-vessel disease ($r = 0.09$; $P = .006$) (Table 2). According to the multivariate analysis, only the associations with age, hypertension, and coronary artery disease were significant (Table 3). The results of the comparisons of patients with and without aortic arch calcification detected on chest x-ray in 3 different age groups were as follows.

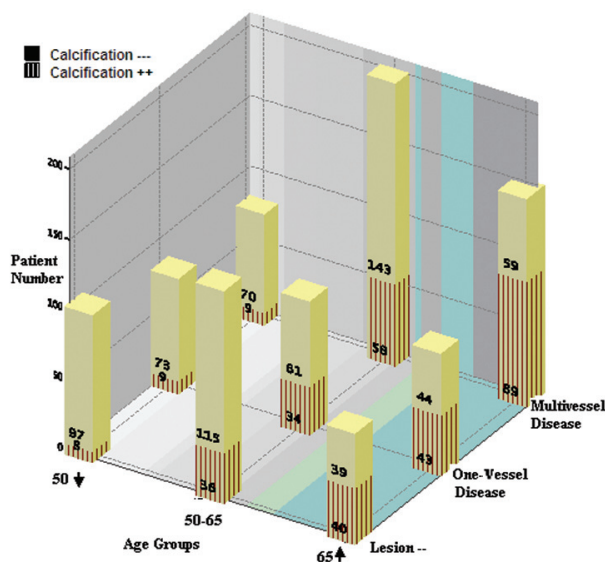
Table 2. Univariate Analysis

	<i>r</i>	<i>P</i>
Age	0.37	<.001
Sex	-0.06	.063
Hypertension	0.14	<.001
Diabetes	0.04	.244
Hyperlipidemia	-0.02	.469
Smoking history	-0.10	.001
Peripheral vascular disease	0.02	.515
Coronary artery disease	0.10	.001
Single-vessel disease	0.01	.736
Multiple-vessel disease	0.09	.006

Table 3. Logistic Regression Analysis of Factors Associated with Aortic Arch Calcification*

	$\beta \pm$ Standard Error	e^{β} (95% CI)	<i>P</i>
Age, y	1.084 ± 0.11	2.96 (2.38-3.67)	<.001
Hypertension	-0.395 ± 0.145	0.67 (0.51-0.89)	.006
Coronary artery disease	0.174 ± 0.085	1.19 (1.01-1.41)	.04
Constant	-1.955 ± 0.193		<.001

*Model $\chi^2 = 140.673$, $P < .001$; $df = 3$; $r^2 = 0.179$ (Nagelkerke R^2).



Correlation among age, coronary artery disease, and calcification in telecardiography.

Patients ≤50 Years Old

The mean age of patients with aortic arch calcification was 46 ± 5 , while that of patients without the calcification was 44 ± 5 ($P = .197$). The comparison for hypertension was similar (38% versus 28%; $P = .240$). No correlation was found for smoking, coronary artery disease, or other risk factors (Figure). There was also no demonstrable association with either single- or multivessel disease (Table 4).

Patients 51 to 64 Years Old

The mean age of patients with aortic arch calcification was 58 ± 4 , while that of patients without the calcification was 57 ± 4 ($P = .09$). For hypertension, the results were 55% versus 45% ($P = .120$) (Table 5). No statistically significant difference was observed for smoking, coronary artery disease, or the presence of single- or multivessel disease.

Patients 65 ≥ Years Old

The mean age of patients with aortic arch calcification was 70 ± 4 , while that of patients without the calcification was 70 ± 4 ($P = .212$). For hypertension, the results were 58% versus 52% ($P = .285$) (Table 6). No statistically significant difference was found for smoking, coronary artery disease, or the presence of single- or multivessel disease.

Sensitivity of aortic arch calcification for coronary artery disease was 59.5% and 79% for women and men, respectively. The specificity was 57% for women and 26% for men.

DISCUSSION

In this study, the age factor had the highest correlation with aortic calcification as seen on plain chest x-ray. Clustering by

age failed to demonstrate significant association between aortic arch calcification and coronary artery disease, and there has been no appreciable difference among patients with or without aortic arch calcification with regard to single- or multivessel disease.

In our study, the univariate analysis, age, hypertension, smoking, and the presence and extent of coronary artery disease had correlations with aortic arch calcification. All correlations were weak with the exception of age, which was modestly correlated. However, smoking was weakly but negatively correlated with the presence of aortic arch calcification, a correlation that needs explanation. We noticed that there was a modest negative correlation of smoking with age, which reflects the fact that people begin to quit smoking in their midlife years. This phenomenon, combined with the fact that smoking causes earlier myocardial infarction (ie, myocardial infarction occurs in younger patients), may explain this discrepancy of decreased aortic arch calcification in smoking patients.

Various studies on the subject present a significant association of aortic arch calcification on plain chest x-ray with age [Simon 1995; Khoury 1997; Matsuma 1997; Blackshear 1999; Agmon 2002], hypertension [Witteman 1990; Simon 1995; Parthenakis 1996; Khoury 1997; Blackshear 1999; Agmon 2002], diabetes [Parthenakis 1996; Blackshear 1999], male sex [Agmon 2002], smoking [Simon 1995; Blackshear 1999; Agmon 2002], and hyperlipidemia [Matsuma 1997]. Among all, the most prominent association was found with age. In our study, the strongest correlations with aortic arch calcification were also age and hypertension in multivariate analysis.

Aortic arch calcification can be found in approximately 1.9% of men and 2.6% of women [Irribarren 2000]. The Framingham Study [Witteman 1990] demonstrates the incidence of calcific plaques of the thoracic aorta for patients between the ages of 40 and 44 as 8.5% for men and 3.9% for women. This incidence rises for patients 50 years of age or older, but the difference between sexes diminishes, equalizing by age 60. For patients age 70 or older, the prevalence of calcification of the thoracic aorta approaches a proportion almost as high as 80%.

The increment in cardiovascular risk factors accompanying advancing age is also preponderantly associated with an

Table 4. Data for Patients ≤50 Years of Age

	Aortic Plaque (n = 26)	No Aortic Plaque (n = 240)	P
Age, y	46 ± 5	44 ± 5	.197
Female (%)	6 (23)	60 (25)	.829
Hypertension (%)	10 (38)	66 (28)	.240
Diabetes (%)	2 (8)	29 (12)	.507
Hyperlipidemia (%)	7 (27)	73 (30)	.712
Smoking history (%)	19 (73)	164 (68)	.620
Peripheral vascular disease (%)	0 (0)	17 (7)	.161
Coronary artery disease (%)	18 (69)	143 (60)	.339
Single-vessel disease (%)	9 (35)	73 (30)	.660
Multiple-vessel disease (%)	9 (35)	70 (29)	.564

Table 5. Data for Patients 51-64 Years of Age

	Aortic Plaque (n = 128)	No Aortic Plaque (n = 319)	P
Age, y	58 ± 4	57 ± 4	.09
Female (%)	52 (41)	117 (37)	.436
Hypertension (%)	71 (55)	144 (45)	.120
Diabetes (%)	35 (27)	78 (24)	.525
Hyperlipidemia (%)	44 (34)	95 (30)	.343
Smoking history (%)	65 (51)	179 (56)	.306
Peripheral vascular disease (%)	12 (9)	22 (7)	.372
Coronary artery disease (%)	92 (72)	204 (64)	.109
Single-vessel disease (%)	34 (27)	61 (19)	.082
Multiple-vessel disease (%)	58 (45)	143 (45)	.926

elevation in the prevalence of aortic arch calcification. Among middle-aged men, significant correlation with systolic blood pressure, total cholesterol levels, smoking, diabetes, or obesity, which have been considered relative risk factors, has not been demonstrated; however, similar risk factors for the same age group were found statistically significant for women. Aortic arch calcification concomitant with advanced age exhibits a strong association with both coronary artery disease and intermittent claudication in women. Although women develop coronary artery disease at a much older age, the existence of aortic arch calcification in the presence of a cardiac risk factor facilitates a predisposition to coronary artery disease.

Functional changes of the cardiovascular system as well as other body systems occurring with aging may be misinterpreted to suggest that age is the major indicator of increased morbidity and mortality [Friesing 1998]. Most of the patients with atherosclerotic coronary disease are older than 65 years of age, and atherosclerotic coronary disease is a disorder for which the incidence and prevalence increase with age. Therefore, age may be considered an important risk factor [Maron 1998]. Similarly, calcification of the aortic arch is most often observed in elderly individuals older than 50 years of age [Steiner 1997].

Atherosclerosis is a generalized pathological process [Wittman 1990]. Chest radiography is one of the simple, noninvasive diagnostic tools for managing patients. Various studies have been conducted to disclose the relation between aortic arch calcification detected on plain chest x-rays and the extent of coronary artery disease [Wittman 1990; Iribarren 2000; Li 2002]. However, no significant association has been demonstrated. Both the work from Iribarren et al [2000] and the Framingham Study [Wittman 1990] were based on follow-ups and standard procedures, and participants were not evaluated thoroughly with respect to coronary artery disease. The diagnoses of coronary heart disease were made through nonspecific and noninvasive tests. Currently, the gold standard for the diagnosis of coronary artery disease is coronary angiography, without which reliable interpretation of the disease may not be possible [Friesing 1998].

In the study by Li et al [2002], no information was available concerning the extent and magnitude of the coronary system's involvement. Also, the design of their study made no attempt to eliminate the effect of spurious factors, age in this case, that may lead to the derivation of unreliable results from the interpretation of the relation between aortic arch calcification and coronary artery disease. In our case, we have partitioned our study group according to age, and these subgroups constitute the milieu in miniature in which we can test our factors of interest independent of the age factor ($r = 0.120$; $P < .001$). These results do not indicate that surgeons should begin arranging patients by age subgroups and admitting them as a whole. Statistical analysis demonstrates significant correlation among aortic arch calcification and coronary artery disease; whereas when the same study was adjusted for the age factor by age subgrouping, no correlation could be found.

The study of Yun et al [2006] found that the observation of an aortic knob on chest radiography can provide important predictive information for coronary atherosclerosis. Their study consisted of 178 patients. We found that a calcification of the aorta seen on plain chest x-ray is mainly age related and provides no value concerning either the extent or prognosis of coronary artery disease in 1027 patients. If Yun et al increase the patient number, we believe they would find the same result [Yun 2006]. Their study showed that aortic knob calcification correlated with old age, hypertension, diabetes, and a high level of total cholesterol. We found that calcification correlated with only old age and hypertension.

Taniguchi et al [2004], Takasu et al [2003], and Yamamoto et al [2003] found that magnetic resonance imaging evaluation, electron beam computed tomography, and thoracic aortic calcium screening tests reveal the angiographic extent and severity of coronary artery disease and add incremental diagnostic value to the coronary artery calcium score, but these studies had fewer than 100 patients. The specificity and sensitivity of electron beam computed tomography, magnetic resonance imaging, and thoracic aortic screening tests are higher than with plain chest x-ray, but in routine clinical practice, x-ray scans are easy and accessible. Therefore, we recommend checking for calcification by x-ray, and our report has found that calcification and older age are correlated.

Table 6. Data for Patients ≥65 Years of Age

	Aortic Plaque (n = 172)	No Aortic Plaque (n = 142)	P
Age, y	70 ± 4	70 ± 4	.212
Female (%)	63 (37)	42 (30)	.187
Hypertension (%)	100 (58)	74 (52)	.285
Diabetes (%)	37 (22)	30 (21)	.934
Hyperlipidemia (%)	39 (23)	41 (29)	.210
Smoking history (%)	65 (38)	52 (37)	.831
Peripheral vascular disease (%)	17 (10)	15 (11)	0.843
Coronary artery disease (%)	132 (77)	103 (73)	0.392
Single-vessel disease (%)	43 (25)	44 (31)	.238
Multiple-vessel disease (%)	89 (52)	59 (36)	.072

Sekoranja et al [2004] and Rohani et al [2005] found that the detection of atherosclerotic plaques is a useful marker of significant coronary artery disease. However, these studies had only 60 patients. Specificity and sensitivity of this technique is also higher than with chest x-ray.

We conclude, therefore, that these 2 events are not interrelated, but they are strongly correlated, with age factor existing as an epiphenomena. The calcification of the aortic arch as seen from the chest x-ray has a significant association with the age factor and has no appreciable relation with coronary artery disease; and it does not have any prognostic value regarding the extent of the pathology.

In conclusion, aortic arch calcification detected by plain chest x-ray is mainly an age-related condition. Both this lesion and coronary artery disease are strongly associated with age. Therefore, the presence of aortic calcification on chest x-ray has no value concerning either the extent or prognosis of coronary artery disease.

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