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Original Article

Extent of aortic arch calcification on chest radiographs is associated with coronary artery disease severity

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Abstract: Objective: Visible aortic arch calcification (AAC) on chest radiographs is putatively associated with cardiovascular outcomes. This retrospective study investigated a correlation between the semi-quantitative extent of AAC and cardiovascular disease severity. Methods: 305 consecutive patients presenting with chest pain who underwent coronary artery angiography and chest radiography during the same hospital stay were retrospectively enrolled. Radiologists blinded to the results of the coronary angiography graded the extent of AAC on a 4-point scale, grades 0-3. The severity of coronary artery disease was described by the number of diseased vessels and Gensini score. Results: AAC was graded as 0, 1, 2, and 3 in 182, 43, 51, and 29 patients, respectively. With increasing AAC grade, the patients tended to be older and coronary artery disease was more prevalent. The AAC grade significantly correlated with the number of affected coronary arteries, and the average Gensini score ($P < 0.001$, both). AAC grade 3 was an independent predictor for multivessel disease (OR 1.720, 95% CI, 1.184-2.498, $P = 0.004$) and high Gensini score (OR 1.529, 95% CI, 1.153-2.029, $P = 0.003$). Conclusion: The extent of AAC, semi-quantitatively determined by chest radiograph, correlated with the severity of coronary artery disease (number of diseased vessels and Gensini score). The highest AAC grade was an independent predictor of multivessel disease and high Gensini score.

Keywords: Aortic calcification, chest radiography, coronary artery disease

Introduction

Calcification can simultaneously affect multiple vascular beds such as the coronary, aortic, and carotid arteries. Studies of the coronary artery have shown that calcification is an independent predictor of cardiovascular events [1]. As known, the calcification across different vascular beds shares the same risk factor [2, 3]. Thus, there is increasingly more research interest focused on the association between calcification outside the coronary artery and rates of cardiovascular events.

Several reports have shown that patients with aortic arch calcification (AAC) have a higher incidence of coronary artery disease (CAD) and more complex lesions [4-7], but quantitative investigations are few or lacking. AAC can easily be detected on routine chest radiography, which is noninvasive and inexpensive. Research on the extent of AAC based on such images may provide more accurate information for clinical practice and expand the use of chest radiography for determining the likelihood of cardiovascular events. Herein, we assessed whether the extent of AAC as shown by radiography could reflect the severity of CAD.

Methods

The Institutional Review Board of our hospital approved this retrospective study, and waived the need for informed consent.

Study population

We retrospectively enrolled 305 consecutive patients with chest pain who had undergone coronary artery angiography and chest radiography within the same hospital stay between January and April 2015 at the Cardiology Department, Yuebei People's Hospital, Shaoguan, Guangdong Province, China. The exclusion criteria were kidney dysfunction (serum creatinine > 132 μmol/L) and history of aortic surgery.

Table 1. Clinical characteristics of the study population*

	Grade 0	Grade 1	Grade 2	Grade 3	*P*
Subjects, n	182	43	51	29	
Age, y	59.8 ± 10.7	63.9 ± 10.7	64.6 ± 10.5	65.2 ± 9.0	0.003
Male	132 (72.5%)	27 (62.8%)	34 (66.7%)	23 (79.3%)	0.386
Hypertension	102 (56.0%)	33 (76.7%)	32 (62.7%)	18 (62.1%)	0.094
Diabetes	28 (15.4%)	12 (27.9%)	14 (27.5%)	11 (37.9%)	0.013
Hyperlipidemia	84 (46.2%)	18 (41.9%)	30 (58.8%)	14 (48.3%)	0.349
Smoking	68 (37.4%)	15 (34.9%)	24 (47.1%)	14 (48.3%)	0.411
Coronary artery disease	114 (62.6%)	28 (65.1%)	41 (80.4%)	27 (93.1%)	0.002

*Reported as n (%), unless indicated otherwise.

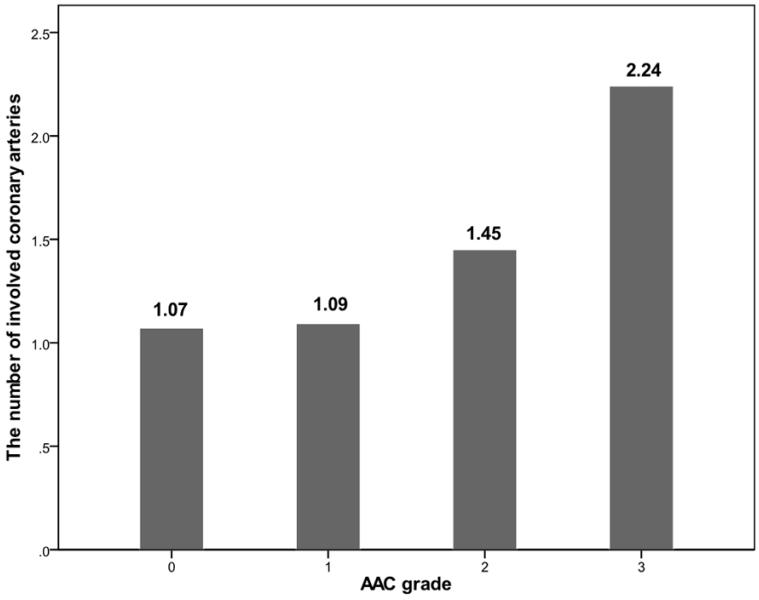

Figure 1. The average number of diseased vessels correlated with the AAC grade ($P < 0.001$). Comparisons among all pairs of groups revealed a significant differences between grade 3 and grade 0 ($P < 0.001$), grade 1 ($P < 0.001$), or grade 2 ($P = 0.001$), but there was no significant difference between grade 2 and grade 1 ($P = 0.084$), nor between grade 1 and grade 0 ($P = 0.899$).

The following data were recorded for each patient: age, gender, smoking history, hypertension, diabetes mellitus, and hyperlipidemia. Smoking history was defined as previous or current use of cigarettes. Hypertension was considered systolic pressure > 140 mmHg or diastolic pressure > 90 mmHg, or the use of antihypertensive drugs. Diabetes mellitus was recorded for the use of antidiabetic drugs, or a fasting venous blood glucose level > 7.0 mmol/L, or random venous blood glucose level > 11.1 mmol/L. Hyperlipidemia was defined as total cholesterol concentration > 5.17 mmol/L or low-density lipoprotein content > 3.11 mmol/L.

We used anteroposterior chest radiographs to assess AAC. For those patients who had undergone several chest radiography tests, we chose the one closest in time to the coronary angiography procedure. Radiologists were blinded to the results of the coronary angiography. A semi-quantitative method was used to assess the extent of AAC, as follows: grade 0, no visible calcification; grade 1, small spots, or a single thin area of calcification; grade 2, one or more areas of thick calcification; grade 3, circumferential calcification [8].

Coronary angiographs were reviewed by a well-trained physician who was blinded to the results of the chest radiograph. CAD was defined as the presence of stenosis with a diameter reduction of ≥ 50% in the affected coronary arteries. The number of diseased vessels was recorded. Multivessel disease was defined as substantial stenosis of ≥ 3 coronary arteries. The Gensini score was split into thirds and calculated based on coronary angiography results, as reported earlier [9]. Based on 3 distributions of the results, a high Gensini score was defined as a value in the upper third (≥ 40), and a low score was defined as a value in the middle or lowest third (< 40).

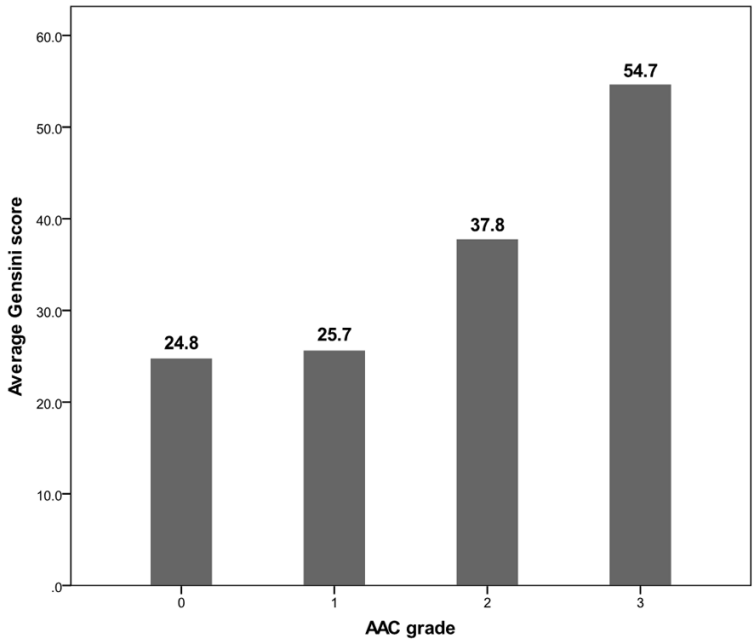

Figure 2. Average Gensini score increased with rise in AAC grade ($P < 0.001$). There were significant difference between grade 3 and grade 0 ($P < 0.001$), grade 1 ($P < 0.001$), and grade 2 ($P = 0.02$). However, grades 2 and 1 ($P = 0.06$), and grades 1 and 0 ($P = 0.870$), were statistically similar.

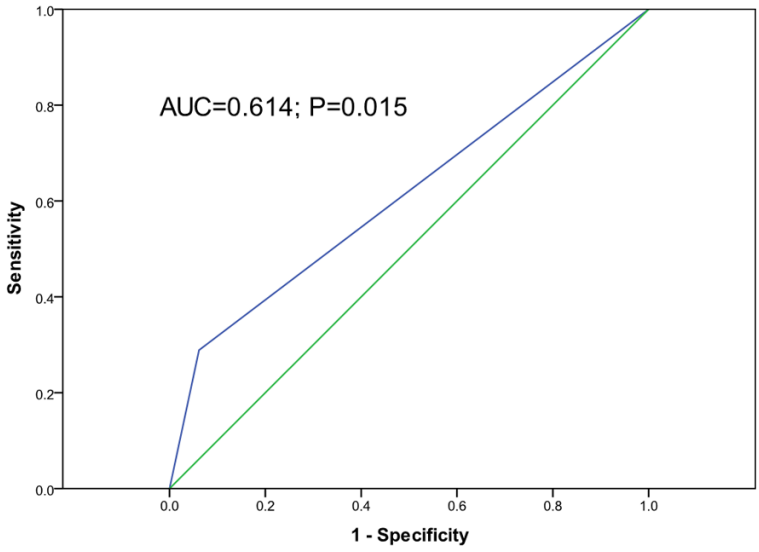

Figure 3. The ROC curve analysis of AAC grade 3 for predicting multivessel disease.

Statistical analysis

Statistical analysis was performed via SPSS 19.0 for Windows (SPSS, Chicago, IL, USA). Continuous variables were defined as mean ± standard deviation; categorical variables as numbers and percentages. Differences among multiple groups were analyzed by the Kruskal-Wallis H test for continuous variables and the chi-squared test for categorical variables. Multivariate logistic analysis was conducted to determine the independent predictors of multivessel disease and a high Gensini score. Receiver-operating characteristic (ROC) curve analysis was performed to evaluate the predicting value of AAC grade 3 for multivessel disease. Statistical significance was set at $P < 0.05$.

Results

In our study, 210 patients received a diagnosis of CAD (**Table 1**). The extent of calcification visible on chest radiographs was given an AAC grade score. There were 182, 43, 51, and 29 patients given scores of grade 0, 1, 2, and 3, respectively. With each increase in AAC grade, patients were older ($P = 0.003$) and CAD more prevalent ($P = 0.002$).

The patients with AAC grade 3 had more diseased vessels and higher Gensini score than did the patients with grade 0, 1, or 2 (**Figures 1**, **2**). The results of ROC analysis indicated that only AAC grade 3 successfully predicted multivessel disease in patients, with specificity 0.938 and sensitivity 0.289 (**Figure 3**).

Univariate analysis revealed that multivessel disease was associated with age and AAC grade 3 (**Table 2**). A high Gensini score was associated with age, hyperlipidemia, and AAC grade 3 (**Table 3**). Multivariate analysis results implied that AAC grade 3 could serve as an independent predictor for multivessel disease (OR 1.720, 95% CI,

Table 2. Results of the multivariate analysis conducted to assess the predictors of multivessel disease

		P	OR (95% CI)
Age		0.031	1.040 (1.004-1.078)
Gender		0.046	2.430 (1.016-5.814)
Hypertension		0.432	1.344 (0.643-2.807)
Diabetes		0.476	1.328 (0.608-2.903)
Hyperlipidemia		0.363	1.385 (0.687-2.794)
Smoking		0.182	0.610 (0.295-1.260)
AAC	Grade 1	0.497	0.670 (0.211-2.129)
	Grade 2	0.943	1.018 (0.628-1.650)
	Grade 3	0.004	1.720 (1.184-2.498)

Table 3. Multivariate analysis to assess the predictors of high Gensini score

		P	OR (95% CI)
Age		0.035	1.028 (1.002-1.054)
Gender		0.071	1.705 (0.955-3.045)
Hypertension		0.988	0.996 (0.588-1.686)
Diabetes		0.491	1.234 (0.678-2.248)
Hyperlipidemia		0.011	1.952 (1.166-3.267)
Smoking		0.483	0.832 (0.497-1.391)
AAC	Grade 1	0.664	1.180 (0.559-2.490)
	Grade 2	0.218	1.237 (0.882-1.735)
	Grade 3	0.003	1.529 (1.153-2.029)

1.184-2.498, $P = 0.004$) and a high Gensini score (OR 1.529, 95% CI, 1.153-2.029, $P = 0.003$).

Discussion

In this retrospective investigation of 305 patients, we semi-quantitatively assessed the extent of AAC on an increasing 4-point graded scale to examine an association with CAD severity. Our findings showed that AAC grade was positively associated with the number of affected coronary arteries and the Gensini score. AAC grade 3 (the highest) predicted multivessel diseases and high Gensini score independently of traditional risk factors.

Calcification is a characteristic of advanced atherosclerosis [10]. The extent of calcification provides an additional predictor of cardiovascular events. The calcium score from electron-beam computed tomography is reportedly associated with the severity of atherosclerotic plaque disease and mortality [11, 12]. There is also evidence that the degree of abdominal aortic artery calcification is a risk factor for adverse cardiovascular outcomes [13-15].

Chest radiography is a routine clinical examination for patients with chest pain, and it can clearly detect calcification of the aortic arch. However, most studies have not quantified the degree of calcification of the aortic arch on chest radiographic images. Hashimoto et al. [8] proposed a four-point grading method to assess the extent of calcification. In addition, higher AAC grades were associated with an increased incidence of cardiovascular events [16]. Bannas et al. [17] reported that the 4-point AAC grade positively correlated with the coronary artery calcium score determined by computed tomography. Nevertheless, whether AAC grade is associated with the severity of coronary artery lesions needs to be investigated further.

In our present study, the number of affected coronary arteries and the average Gensini score increased with the increase in AAC grade. The patients with AAC grade 3 had considerably more diseased vessels and a higher average Gensini score than did the patients with AAC grades 0, 1, or 2. However, there was no significant difference between AAC grades 0 and 1. We speculate that study population inclusion bias could have led to this result-patients with chest pain were enrolled, 68.9% of whom were diagnosed with CAD by coronary angiography, and on average, even the patients with AAC grade 0 had more than one coronary artery with pathological changes. Most previous studies consisted of a population selected at health checkups or as outpatients [4, 16].

In our study, the multivariate analysis results revealed that AAC grade 3 was a viable independent predictor of multivessel disease and a high Gensini score. This finding is partly consistent with that of a previous study, in which AAC grade 3 was reported to be strongly associated with a coronary artery calcium score > 400 [17]. Our result suggests that only severe calcification in the aortic arch could reliably imply clinical CAD severity.

In our investigation, there were more male patients in the non-calcification group (grade 0; 72.5%) than in the group with calcification

(grades 1-3; 68.3%), although these were statistically comparable (P = 0.425). The association between aortic calcification and gender is controversial. For example, Allison et al. [18] reported that the prevalence of calcification was greater in men patients, whereas Takasu et al. [3] discovered the opposite tendency. The discrepancy may be due to the different ages of the populations in these studies. Iribarren et al. [4] found a significant gender-based difference in aortic calcification in patients older than 65 years, but in the younger group the genders were similar.

In our study, the predictive specificity of AAC grade 3 for multivessel disease was 0.938. This high specificity guarantees that chest radiography is feasible for stratifying risk. Thus, we conclude that grade 3 AAC on chest radiography could help direct therapy for patients with chest pain, especially for patients whose clinical condition contraindicates coronary angiography or for whom the cost of coronary angiography is prohibitive. We also acknowledge the low sensitivity of AAC grade 3, which warrants the need for confirmation by other tests.

Study limitations

The application of AAC grades has previously been reported as a reliable and reproducible method [8, 17]. In our study, the accuracy and reproducibility of AAC grades were not tested. However, we demonstrated that only severe calcification in the aortic arch had clinical implication. According to our experience, it is relatively easy to distinguish AAC grade 3 on a chest radiograph. As the patients in the present study presented with chest pain and were preparing to undergo coronary angiography, the association we found between AAC grade and the severity of coronary artery lesions cannot be extrapolated to other population groups. Since chest radiography is a common test used both in clinical practice and for health checkups, more studies based on populations without unique characteristics are required to confirm the association.

Conclusion

We demonstrated that the AAC grade, as determined by chest radiographic images of patients with chest pain, correlated positively with the severity of CAD, and AAC grade 3 was an independent predictor of multivessel disease and a high Gensini score. We presume that our findings can expand the use of chest radiography.

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Disclosure of conflict of interest

None.

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