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Aortic calcification is associated with coronary artery calcification and is a potential surrogate marker for ischemic heart disease risk

A cross-sectional study

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Abstract

Coronary artery calcification, an established marker of atherosclerotic plaque burden associated with increased risk of coronary artery disease, is routinely evaluated using electron beam computerized tomography or multidetector computed tomography (CT). However, aortic calcification, which is also a risk factor for adverse cardiac events, is not frequently assessed, despite being easily detected via standard chest radiography. We therefore sought to clarify the association between aortic calcification and significant coronary artery calcification to determine the feasibility of performing chest radiography to evaluate the risk of future cardiovascular events.

Data from 682 consecutive patients who underwent cardiac CT scanning at our institution from May to September 2012 were included in this cross-sectional analysis. Electrocardiographic-gated CT was used to qualitatively evaluate calcification in 6 aortic segments. Cardiac contrast-ehnanced CT was performed to identify significant calcification of the coronary artery. Calcification was quantified by calculating the Agatston score, and the relationship between significant coronary artery calcification and calcification at each aortic site was evaluated.

Among the aortic sites, calcification was most commonly observed in the aortic arch (77.4% of patients). Significant coronary artery calcification was observed in 267 patients (39.1%). Calcification in the ascending aorta, aortic arch, descending aorta, abdominal aorta, and aortic valve were significantly associated with the presence of coronary artery calcification after adjustment for cardiovascular risk factors and statin use (odds ratios [95% confidence intervals] 4.21 [2.55, 6.93], 1.65 [1.01, 2.69], 2.14 [1.36, 3.36], 2.87 [1.83, 4.50], and 3.32 [2.02, 5.46], respectively). Mitral valve calcification was weakly but nonsignificantly associated with coronary artery calcification (odds ratio 1.84 [95% confidence interval 0.94, 3.62]). Calcification of each aortic segment assessed was significantly associated with Agatston score ≥ 100.

Aortic calcification was associated with coronary artery calcification. Calcification of the aortic arch, which can be readily detected by routine chest radiography, may be associated with coronary artery calcification and its assessment should therefore be considered to identify patients at increased risk of cardiovascular events. Further studies are warranted to confirm these findings.

Abbreviations: BMI = body mass index, CAD = coronary artery disease, CT = computed tomography, CV = cardiovascular, ECG = electrocardiographic.

Keywords: agatston score, aortic arch, coronary artery disease, ischemic heart disease, pathological calcification

1. Introduction

Ischemic heart disease is the leading cause of death globally and was responsible for more than 9 million deaths in 2016.[1] Coronary artery disease (CAD), the leading cardiovascular (CV) cause of death, is a form of ischemic heart disease characterized by blockage or narrowing (stenosis) of the arteries that supply blood to the heart. The primary pathologic process leading to CAD is atherosclerosis of the coronary arteries.[2] Coronary artery calcification, which initiates as microcalcifications that develop into larger calcium deposits, is an established independent risk factor for CAD; although it occurs early in the process of atherosclerosis, it is typically detectable through the use of imaging modalities only when it increases in quantity.[3–5]

Coronary artery calcification is most commonly evaluated using electrocardiographic (ECG)-gated cardiac electron beam

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computerized tomography or multidetector computed tomography (CT). The extent of calcification is presented as the coronary calcification score, or Agatston score,[6] and is associated with the atherosclerotic plaque burden. Coronary calcification scoring thus provides information on the patient's level of CV disease risk and can be used to guide decisions on interventions or prevention strategies for CAD.[7,8] For example, current guidelines recommend the use of calcification on CT as a criterion for eligibility for statin therapy, based on findings that symptomatic adults with extensive coronary artery calcification (Agatston score > 300) experience up to a 10-fold higher incidence of coronary events.[9,10] In contrast to coronary artery calcification, limited information is available on calcification of the aorta despite the fact that both events are associated with the development of major adverse CV events.[11–13] Furthermore, aortic calcification, which is routinely and easily detected via standard chest radiography, is an independent risk factor for CV morbidity and mortality[14,15] and may represent a surrogate marker of coronary artery calcification and, thus, of CAD.[16] In an analysis of patient data from the Heinz Nixdorf Recall Study, which was an unselected population-based evaluation of CV event prediction, 63.1% of participants had evidence of thoracic aortic calcification while 67.9% had coronary artery calcification.[17]

Established CV risk factors including older age, male sex, increased serum low-density lipoprotein, smoking, hypertension, and diabetes have been associated with aortic valve calcification,[18–22] thus supporting the potential clinical value of evaluating calcification at sites other than the coronary artery to estimate the risk of developing ischemic heart disease and inform treatment decisions. For example, in a previous study in Japanese patients, calcification at vascular sites including the ascending aorta was significantly related to the need for coronary artery revascularization for stenosis.[23] However, while coronary artery calcification measurements are recommended for better risk stratification of patients at intermediate risk for CAD,[24] analysis of aortic calcification does not currently play a routine clinical role in this patient population and is not a standard aspect of the CV workup.[25] From this context, the aim of the present study was to clarify the relationship between aortic calcification and coronary artery calcification score, and to thus determine the feasibility of using routine chest radiography to evaluate the risk of ischemic heart disease in clinical settings.

2. Methods

2.1. Study population

In this cross-sectional study, we retrospectively examined medical record data from consecutive patients with suspected coronary heart disease who underwent cardiac CT scanning at our specialist cardiac secondary care facility from May to September 2012. Exclusion criteria were age < 20 years (20 years is the age of majority in Japan) and incomplete CT scan data. The sample size was determined by the number of eligible patients who underwent cardiac CT during the study period. ECG-gated coronary plain CT was used to qualitatively evaluate calcification of the ascending aorta, aortic arch, descending aorta (thoracic), abdominal aorta, aortic valve, and mitral valve by abdominal CT. Cardiac contrast-enhanced CT was performed to identify significant calcification of the coronary artery. These data were used to evaluate the relationship between significant coronary artery calcification and calcification at each aortic site. Ethical approval of the study protocol was provided by the institutional review board and ethics committee at our institution. The requirement for informed patient consent was waived for this retrospective analysis.

2.2. Cardiovascular risk factors

Data on CV risk factors were extracted from the patients' medical records. Blood pressure was measured in a seated position after at least a 5-min rest. The mean of 2 consecutive measurements was used in the analyses. Blood samples were obtained from participants by venipuncture after overnight fasting of at least 8 hours. Serum was obtained from blood samples by centrifugation and used in the assessment of lipid profiles and glucose levels using an automated enzymatic analyzer (FUJI DRI-CHEM 4000; Fujifilm, Tokyo, Japan). Diabetes was defined as fasting blood sugar ≥ 126 mg/dL or HbA1c ≥ 6.2%. Hypertension was defined as systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg. Dyslipidemia was defined as low-density lipoprotein ≥ 140 mg/dL, high-density lipoprotein < 40 mg/dL, and/or triglycerides ≥ 150 mg/dL. Smoking was defined as current smoking. Furthermore, hypertension, dyslipidemia, and diabetes were assumed to be present if medical records detailed that antihypertensive, lipid-lowering, or antidiabetic medication was prescribed, respectively. Weight and height data were collected for each patient, and body mass index (BMI) was calculated using the formula weight/height^2 (kg/m^2).

2.3. Scan protocols

All patients included in the study underwent ECG-gated cardiac multidetector CT using a 128-detector-row CT scanner (Brilliance iCT SP; Philips Healthcare, Best, The Netherlands). Individuals presenting with a baseline heart rate of >70 beats/min received an oral β-blocker (0.125 mg/kg landiolol hydrochloride; Ono Pharmaceutical, Osaka, Japan) 5 minutes before scanning started. Standard coronary CT angiography was performed with a 13-s intravenous infusion of Iopamiron 370 (240 mg/mL; Bayer HealthCare, Osaka, Japan). The acquisition parameters for calcification and cardiac CT imaging were as follows: detector collimation, 64 × 0.625 mm; tube rotation time, 270 ms; tube voltage, 120 kVp; tube current, 228.6 ± 57.5 mA (range, 100–370 mA); and volume CT dose index, 22.2 ± 5.5 mGy (range, 4.9–34.5 mGy). The calcium scoring protocol comprised prospective ECG-gating at 75% or 40% of the R–R interval, with collimation of 64 × 0.625 mm, gantry rotation time of 270 ms, standard cardiac filter, 2.5 mm slice thickness, and a tube voltage of 120 kV. The scan range was from the aortic arch to the diaphragm.

2.4. Analysis of calcification

Experienced scan reviewers, who were blinded to the clinical data of the participants and imaging reports, performed semiautomatic scoring of the calcifications. The scan sites representing the coronary arteries comprised the left main, left anterior descending, left circumflex, and right coronary arteries. The following aortic sites were assessed: aortic valve, ascending aorta (from the aortic valve to branching off of the brachiocephalic artery), aortic arch (including the origin of the aortic arch to the first 1 cm of the common carotid arteries, the vertebral arteries, and the subclavian arteries beyond the origin of the vertebral arteries), descending aorta (from left subclavian artery to aortic hiatus), and abdominal aorta (from aortic hiatus until bifurcation into left and right common iliac arteries). The mitral valve was also assessed.

Atherosclerotic calcifications were identified based on the presence of at least 2 contiguous pixels (1 mm^2) with an attenuation threshold of 130 Hounsfield units. Calcifications were scored using image reconstruction software (AZE VirtualPlace Fujin; AZE Ltd., Tokyo, Japan). Calcification of coronary arteries and aortic sites was quantified by calculating the Agatston score; a score ≥ 100 was considered to represent significant coronary artery calcification.[6]

2.5. Statistical methods

Continuous variables were assessed as mean ± standard deviation, and categorical variables as number (percentage). The

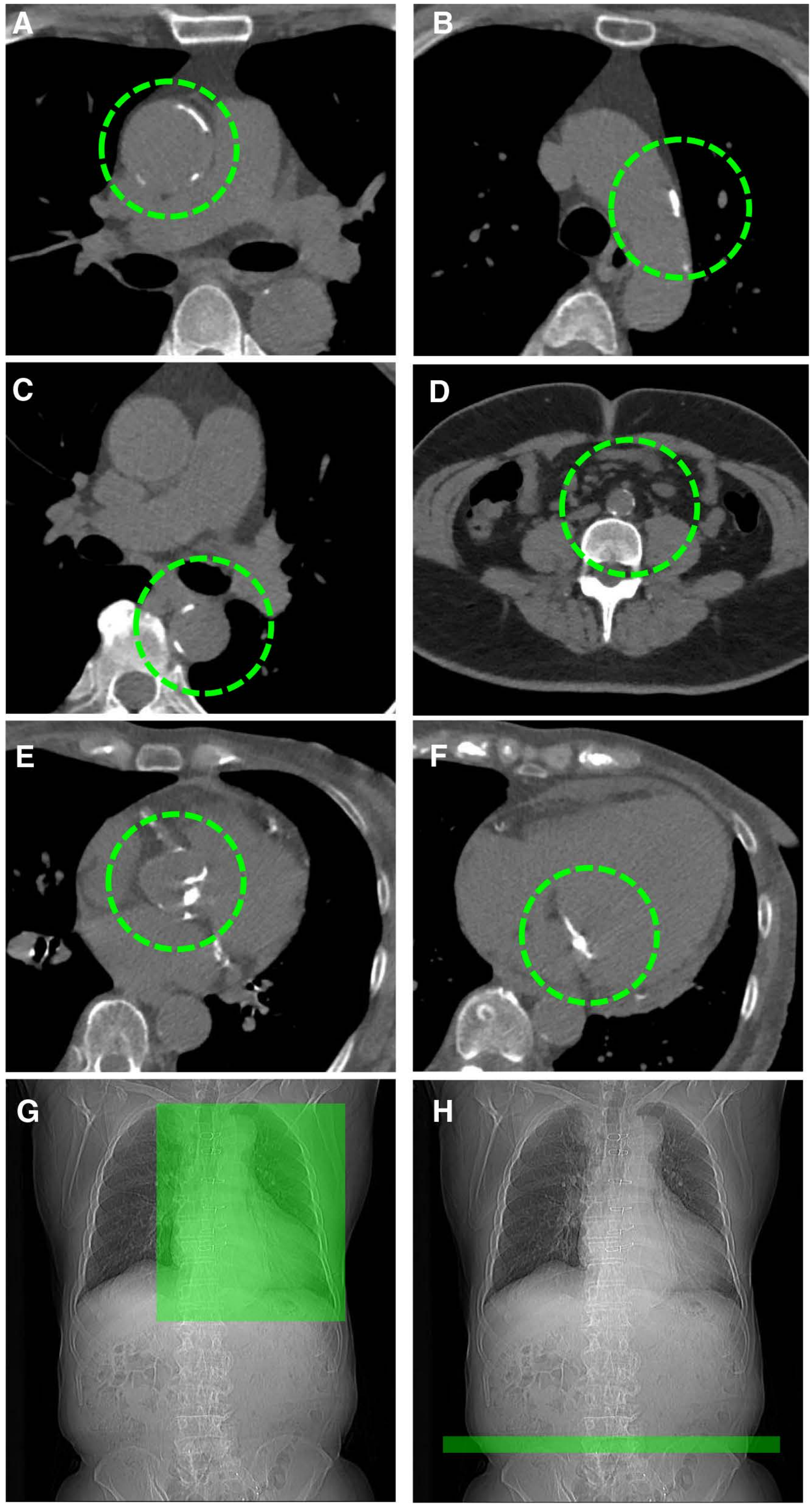

Figure 1. Representative images of the scanned vascular sites and imaging areas. (A) Ascending aorta; (B) aortic arch; (C) descending aorta; (D) abdominal aorta; (E) aortic valve; (F) mitral valve; (G) cardiac imaging area; (H) abdominal imaging area.

effects of all risk factors on significant coronary artery calcification were calculated using Pearson's chi-square test and univariate logistic regression analysis for each variable. Variables with a univariate significance level of ≤0.15 were entered into a multivariate logistic regression model. A nonparametric Wilcoxon rank-sum test was used to compare Agatston calcification score in patients with aortic segment calcification relative to patients with no segment calcification, stratified by aortic site. Univariable and multivariable logistic regression were used to analyze the association between aortic segment calcification

Table 1

Patient characteristics.

Characteristics	Study cohort (n = 682)
Age, years, mean (SD)	66.2 (12.3)
Median (IQR)	68 (59, 75)
Sex, male, n (%)	388 (56.9)
Height, cm, mean (SD)	159.8 (10.1)
Median (IQR)	160.0 (152.0, 167.1)
Weight, kg, mean (SD)	61.6 (12.5)
Median (IQR)	60.7 (52.5, 69.7)
Body mass index, kg/m^2, mean (SD)	24.0 (3.7)
Median (IQR)	23.5 (21.6, 25.8)
Atherosclerosis risk factors, n (%)	
Diabetes	135 (19.8)
Hypertension	389 (57.0)
Dyslipidemia	304 (44.6)
Smoking	160 (23.5)
Significant CAC*, n (%)	267 (39.1)
Statin, n (%)	481 (70.5)

CAC = coronary artery calcification; IQR = interquartile range; SD = standard deviation.
*Defined as Agatston score ≥ 100.

and coronary artery calcification. As a sensitivity analysis, the coronary artery calcification and Agatston score models were stratified by both sex and BMI quartile. A Hosmer–Lemeshow test was used to assess each model for goodness-of-fit. Values of $P < .05$ were considered statistically significant. All statistical analyses were performed using SPSS for Windows, version 11.0 (SPSS Inc., Chicago, IL, USA) and Stata version 16 (StataCorp, College Station, TX, USA). All available data were used in the analysis. Missing data were negligible, involving <2% of BMI data and <0.5% of hypertension, dyslipidemia, and smoking status data.

3. Results

3.1. Patients

Of 750 patients who underwent cardiac CT between May and November 2012, 2 were excluded because they were under 20 years old and 66 were excluded because complete scan data were lacking. The remaining 682 patients were eligible for this study and were included in the present analysis. Representative images of the scanning sites are shown in Figure 1. The characteristics of the patients included are shown in Table 1. The mean age (± standard deviation) of the study population was 66.2 (± 12.3) years, the mean BMI was 24.0 (± 3.7) kg/m^2, and 388 (56.9%) patients were male. The proportion of patients with atherosclerosis risk factors was 57.0%, 44.6%, 23.5%, and 19.8% for hypertension, dyslipidemia, smoking, and diabetes, respectively, and the proportion of current statin use was 70.5%. A total of 34 patients (5.0%) died by the end of study follow-up.

3.2. Calcification of the aorta

Regarding the distribution of calcification at each of the aortic sites, the largest proportion of patients (77.4%) had calcification in the aortic arch, followed by calcification in the abdominal aorta (74.0%) and descending aorta (61.6%) (Table 2). Significant coronary artery calcification, defined as an Agatston score ≥100, was observed in 267 patients (39.1%) (Table 1). The distribution of CV risk factors was stratified by the presence or absence of calcification at each aortic site. Of note, older age, dyslipidemia, diabetes, and presence of hypertension were significantly associated with the presence of calcification at all 6 sites (Table 2). An association between smoking and

Table 2

Patient risk factors by presence or absence of calcification at each aortic segment.

Aortic segment	With site calcification	Without site calcification	*P* value
Ascending aorta			
n (%)	282 (41.3)	400 (58.7)	
Age, years, mean (SD)	72.8 (8.9)	61.3 (12.1)	<.001
Median (IQR)	73 (68, 79)	63 (53, 70.5)	
Sex, male, n (%)	161 (57.1)	227 (56.8)	.929
BMI, kg/m^2, mean (SD)	24.2 (4.0)	23.8 (4.0)	.040
Median (IQR)	24.0 (21.7, 26.2)	23.3 (21.6, 25.5)	
Diabetes, n (%)	75 (26.6)	60 (15.0)	<.001
Hypertension, n (%)	210 (74.5)	179 (44.8)	<.001
Dyslipidemia, n (%)	147 (52.1)	157 (39.3)	.001
Smoking, n (%)	65 (23.0)	95 (23.8)	.790
Statin, n (%)	180 (63.8)	301 (75.3)	.001
Aortic arch			
n (%)	528 (77.4)	154 (22.6)	
Age, yr, mean (SD)	69.7 (9.9)	54.0 (11.8)	<.001
Median (IQR)	71 (64, 77)	53 (45, 62)	
Sex, male, n (%)	281 (53.2)	107 (69.5)	<.001
BMI, kg/m^2, mean (SD)	24.1 (3.7)	23.9 (3.4)	.938
Median (IQR)	23.5 (21.6, 25.9)	23.6 (21.8, 25.8)	
Diabetes, n (%)	125 (23.7)	10 (6.5)	<.001
Hypertension, n (%)	341 (64.6)	48 (31.2)	<.001
Dyslipidemia, n (%)	261 (49.4)	43 (27.9)	<.001
Smoking, n (%)	113 (21.4)	47 (30.5)	.018
Statin, n (%)	360 (68.2)	121 (78.6)	.013
Descending aorta			
n (%)	420 (61.6)	262 (38.4)	
Age, years, mean (SD)	71.5 (9.2)	57.5 (11.6)	<.001
Median (IQR)	72 (66, 78)	59 (48, 66)	
Sex, male, n (%)	220 (52.4)	168 (64.1)	.003
BMI, kg/m^2, mean (SD)	24.0 (3.6)	24.0 (3.8)	.889
Median (IQR)	23.5 (21.6, 25.8)	23.4 (21.7, 25.9)	
Diabetes, n (%)	108 (25.7)	27 (10.3)	<.001
Hypertension, n (%)	294 (70.0)	95 (36.3)	<.001
Dyslipidemia, n (%)	218 (51.9)	86 (32.8)	<.001
Smoking, n (%)	96 (22.9)	64 (24.4)	.642
Statin, n (%)	274 (65.2)	207 (79.0)	<.001
Abdominal aorta			
n (%)	505 (74.0)	177 (26.0)	
Age, years, mean (SD)	69.7 (10.2)	56.0 (12.0)	<.001
Median (IQR)	71 (63, 77)	57 (46, 65)	
Sex, male, n (%)	286 (56.6)	102 (57.6)	.818
BMI, kg/m^2, mean (SD)	24.2 (3.6)	23.7 (3.9)	.690
Median (IQR)	23.7 (21.7, 25.9)	23.3 (21.3, 25.6)	
Diabetes, n (%)	114 (22.6)	21 (11.9)	.002
Hypertension, n (%)	328 (65.0)	61 (34.5)	<.001
Dyslipidemia, n (%)	256 (50.7)	48 (27.1)	<.001
Smoking, n (%)	116 (23.0)	44 (24.9)	.568
Statin, n (%)	338 (66.9)	143 (80.8)	.001
Aortic valve			
n (%)	259 (38.0)	423 (62.0)	
Age, years, mean (SD)	73.3 (8.9)	61.8 (12.0)	<.001
Median (IQR)	74 (69, 79)	63 (54, 71)	
Sex, male, n (%)	140 (54.1)	248 (58.6)	.242
BMI, kg/m^2, mean (SD)	24.2 (3.8)	23.9 (3.6)	.353
Median (IQR)	23.8 (21.6, 25.9)	23.4 (21.6, 25.7)	
Diabetes, n (%)	67 (25.9)	68 (16.1)	.002
Hypertension, n (%)	186 (71.8)	203 (48.0)	<.001
Dyslipidemia, n (%)	144 (55.6)	160 (37.8)	<.001
Smoking, n (%)	59 (22.8)	101 (23.9)	.705
Statin, n (%)	165 (63.7)	316 (74.7)	.002
Mitral valve			
n (%)	107 (15.7)	575 (84.3)	
Age, years, mean (SD)	74.4 (8.7)	64.6 (12.2)	<.001
Median (IQR)	75 (70, 81)	66 (57, 73)	
Sex, male, n (%)	52 (48.6)	336 (58.4)	.059
BMI, kg/m^2, mean (SD)	24.2 (4.1)	24.0 (3.6)	.922
Median (IQR)	23.4 (21.3, 26.0)	23.6 (21.7, 25.8)	

(*Continued*)

Table 2

(*Continued*)

Aortic segment	With site calcification	Without site calcification	*P* value
Diabetes, n (%)	30 (28.0)	105 (18.3)	.021
Hypertension, n (%)	82 (76.6)	307 (53.4)	<.001
Dyslipidemia, n (%)	58 (54.2)	246 (42.8)	.033
Smoking, n (%)	20 (18.7)	140 (24.3)	.196
Statin, n (%)	64 (59.8)	417 (72.5)	.008

BMI = body mass index, IQR = interquartile range, SD = standard deviation.

calcification was observed only for the aortic arch, while male sex was associated with calcification at the aortic arch and descending aorta only.

3.3. Association between calcification of the coronary artery and aorta

In the analysis of the association between coronary artery calcification and aortic site calcification, median Agatston calcification score was found to be significantly higher in aortic sites with calcification compared with sites without calcification, across all 6 segments (Table 3). In the logistic regression analysis of coronary artery calcification and presence or absence of calcification in specific aortic segments, calcification in the ascending aorta, aortic arch, descending aorta, abdominal aorta, aortic valve, and mitral valve were associated with adjusted odds ratios and 95% confidence intervals (CI) of 4.21 (2.55, 6.93), 1.65 (1.01, 2.69), 2.14 (1.36, 3.36), 2.87 (1.83, 4.50), 3.32 (2.02, 5.46), and 1.84 (0.94, 3.62), respectively, after adjustment for variables including age, sex, BMI, diabetes, hypertension, dyslipidemia, smoking, and statin use (Table 4). A similar pattern of associations across aortic segments was observed when the analysis was stratified by sex, with female sex generally associated with larger odds of coronary artery calcification compared with male sex. Similarly, higher BMI quartiles also tended to be associated with greater odds of coronary artery calcification compared with lower BMI quartiles, although this varied with aortic segment (see Table 1, Supplemental Digital Content, http://links.lww.com/MD/G900, which presents logistic regression analysis of associations between coronary artery calcification and aortic segment calcification stratified by sex and BMI quartile).

In the analysis of coronary artery calcification with an Agatston score ≥ 100, calcification in the aortic arch again showed a significant association of 2.86 times the odds (CI: 1.52, 5.37) of having an Agatston score ≥ 100, compared with no ascending aorta calcification, after adjustment for all CV risk factors (Table 5). The corresponding odds ratios and 95% CIs for the ascending aorta, descending aorta, abdominal aorta, aortic valve, and mitral valve were 3.96 (2.66, 5.87), 3.51 (2.17, 5.66), 3.60 (2.00, 6.47), 3.15 (2.13, 4.67), and 1.88 (1.15, 3.08), respectively. Stratification of patients by presence/absence of calcification in the aortic arch showed that 77% (404/528) of patients with calcification at this site also had significant coronary artery calcification, and almost half (252/528) had an Agatston score of ≥ 100. Consistent with the sex-stratified adjusted modeling of coronary artery calcification, female sex was associated with increased odds of having an Agatston score ≥ 100 across most aortic segments, with the exception of mitral valve calcification, which was significant in males (OR 2.31; 95% CI 1.09, 4.87) but not in females (OR 1.60; 95% CI 0.78, 3.26) (see Table 2, Supplemental Digital Content, http://links.lww.com/MD/G900, which presents logistic regression analysis of associations between Agatston score ≥ 100 and aortic segment calcification stratified by sex and BMI quartile). The patterns of associations were more mixed when the modeling was stratified by BMI quartile compared with other factors.

4. Discussion

In this analysis of retrospective data from our institution, a significant relationship was demonstrated between calcification of the aortic arch and significant coronary artery calcification (Agatston score of ≥ 100 points), placing these patients in a high-risk group for ischemic heart disease. In a previous study of Japanese patients with suspected ischemic heart disease who underwent multidetector CT to diagnose coronary artery stenosis, calcification of the ascending aorta was shown to be an independent risk factor for significant coronary artery calcification.[23] In patients with acute coronary syndrome, the extent of calcification in the aortic arch was found to have a positive association with the severity of CAD[26,27] and has also been proposed in previous studies as a surrogate marker of atherosclerosis, associated with an increased risk of major CV events.[13,15,28] Of note, several of these previous studies assessed calcification by standard chest radiography, which is not considered a quantitative method and may lead to underestimation of the true extent of calcium deposition in the aortic arch. However, the quantification of aortic calcification using CT imaging methods, as utilized in the present analysis, can also vary considerably because of the absence of standardized acquisition protocols, limiting the applicability of Agatston scoring.[29] Nevertheless, calcification of the aortic arch in particular can be readily quantified using plain chest radiography,[14,15] which has been shown to be a cost-effective and reliable method of assessment that correlates positively with coronary artery calcification assessed by CT.[30]

Previous studies have shown that the extent of coronary artery calcification is associated with CV risk factors including hypertension and diabetes.[31] However, few studies to date have

Table 3

Comparison of Agatston calcification scores by aortic segment.

	Agatston calcification score median (interquartile range)		
Aortic segment	With site calcification	Without site calcification	*P* value (rank-sum)
Ascending aorta	286.2 (54.0, 818.8)	1.0 (0.0, 65.9)	<.0001
Aortic arch	86.6 (1.0, 498.6)	0.0 (0.0, 13.1)	<.0001
Descending aorta	183.8 (14.2, 596.5)	0.0 (0.0, 23.5)	<.0001
Abdominal aorta	97.9 (5.6, 519.2)	0.0 (0.0, 8.4)	<.0001
Aortic valve	254.7 (48.7, 854.5)	3.9 (0.00, 93.2)	<.0001
Mitral valve	407.7 (40.1, 1388.0)	23.1 (0.0, 230.7)	<.0001

Table 4

Associations between coronary artery calcification and aortic segment calcification–logistic regression.

	Unadjusted analysis		Adjusted* analysis	
Aortic segment	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Ascending aorta	7.63 (5.40, 10.79)	<.001	4.21 (2.55, 6.93)	<.001
Aortic arch	8.46 (4.84, 14.80)	<.001	1.65 (1.01, 2.69)†	.045
Descending aorta	8.73 (5.78, 13.19)	<.001	2.14 (1.36, 3.36)	.001
Abdominal aorta	9.23 (5.43, 15.67)	<.001	2.87 (1.83, 4.50)	<.001
Aortic valve	6.04 (4.30, 8.49)	<.001	3.32 (2.02, 5.46)	<.001
Mitral valve	3.81 (2.46, 5.90)	<.001	1.84 (0.94, 3.62)	.077

*Adjusted for age, sex, body mass index, diabetes, hypertension, dyslipidemia, smoking, and statin use.
†Hypertension excluded from the adjusted model secondary to collinearity.
CI = confidence interval.

Table 5

Associations between Agatston score ≥ 100 and aortic segment calcification–logistic regression.

	Unadjusted analysis		Adjusted* analysis	
Aortic segment	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Ascending aorta	7.81 (5.55, 11.00)	<.001	3.96 (2.66, 5.87)	<.001
Aortic arch	8.77 (5.02, 15.33)	<.001	2.86 (1.52, 5.37)	.001
Descending aorta	9.15 (6.07, 13.80)	<.001	3.51 (2.17, 5.66)	<.001
Abdominal aorta	9.64 (5.68, 16.35)	<.001	3.60 (2.00, 6.47)	<.001
Aortic valve	5.84 (4.18, 8.16)	<.001	3.15 (2.13, 4.67)	<.001
Mitral valve	3.93 (2.55, 6.06)	<.001	1.88 (1.15, 3.08)	.011

*Adjusted for age, sex, body mass index, diabetes, hypertension, dyslipidemia, smoking, and statin use.
CI = confidence interval.

directly explored the association between established risk factors and calcification of vascular sites other than the coronary arteries. Furthermore, the majority of studies on the correlation between aortic calcification and CV risk factors have been limited to Western populations, in whom the absolute risk of CAD is higher than that in East Asian populations, particularly Japan.[32] Data from the Framingham study showed that the presence of calcification in the aortic arch was associated with high blood pressure and, to a lesser extent, with high serum cholesterol levels.[33] More recently, aortic arch calcification has been associated with diabetes and renal dysfunction, among other risk factors, in addition to being shown to accurately represent the magnitude of calcification throughout the entire aorta.[14,34]

Clinical implications of the results from the present study include the need for careful investigation of ischemic heart disease in patients with evidence of calcification in the aortic arch, detected via routine chest radiography, as these patients are highly likely to have significant coronary artery calcification. Although the present study evaluated aortic calcification using CT scanning methodology, standard chest radiography is less expensive, widely available, and does not involve exposure to substantial levels of radiation. Furthermore, there is evidence for an association between such semiquantitative, radiographic methods and more sophisticated and quantitative methods to assess the extent of CV calcification.[35] Further studies are needed to clarify the relationships between CV risk factors and calcification in the coronary artery and aortic sites in a population with a lower risk of CAD, which would elucidate the underlying mechanisms of atherosclerotic disease in Japanese patients.

This study has some limitations, including the single-center design and relatively small sample size. The latter, in particular the variability and small numbers in some groups in the stratified analyses, is likely to underlie some of the wide 95% CIs observed in the study. There is also the possibility of residual confounding, with some adjustment variables categorized as binary variables (e.g., hypertension and dyslipidemia) rather than as continuous values. Furthermore, as mentioned previously, quantification of aortic calcification in particular can vary considerably, limiting the applicability of Agatston scoring. The retrospective nature of the study meant that certain information such as aortic root calcification scoring and previous smoking history that may have further strengthened the analyses was not available. The inclusion of only Japanese patients may also restrict the wider generalizability of the study. Larger multicenter studies will be of benefit to further explore the findings of this study.

5. Conclusions

The findings of the current retrospective analysis reveal that significant coronary artery calcification is more likely to be present in patients with aortic calcification, particularly in the aortic arch. Where calcification in the aortic arch is detected on standard chest radiography, further investigation is therefore recommended. Prospective studies with larger sample sizes are warranted to confirm these findings.

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