Published in final edited form as:

Am J Cardiol. 2009 August 1; 104(3): 299–304. doi:10.1016/j.amjcard.2009.03.041.

Association of Coronary Aortic Calcium with Abdominal Aortic Calcium Detected on Lateral Dual Energy X-Ray Absorptiometry Spine Images

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Abstract

The association of abdominal aortic calcium (AAC) on lateral spine bone densitometry with coronary artery calcium (CAC) has not been reported. We studied 33 men and 73 women who had CAC scored with electron beam computed tomography at the 8th visit of the Rancho Bernardo study and lateral spine dual energy x-ray absorptiometry (DXA) images fully evaluable for AAC done at the 9th study visit. The association between CAC level and AAC tertile was assessed by ordinal logistic regression. The odds ratio of having a higher level of CAC score for those in the top tertile of AAC score (24-point scale score ≥ 5) was 6.42 (95% C.I. 2.28 – 18.1) and on an 8-point scale (score ≥ 3) was 3.38 (95% C.I. 1.26 – 9.07), compared to those with AAC scores in the bottom tertiles, adjusted for age, sex, systolic blood pressure, total and high density lipoprotein (HDL) cholesterol, smoking status, and diabetes. A 24-point AAC score of ≥ 5 had a sensitivity of 65% and a specificity of 70% to detect a high CAC score (≥ 400 units). An 8-point AAC score ≥ 3 had a sensitivity of 45% and a specificity of 78%. In conclusion, a high level of AAC on lateral spine DXA is strongly associated with coronary artery disease and may be commonly encountered since bone densitometry is indicated in all women age ≥ 65 and all men age ≥ 70 . Its presence should be reported to the patient's physician to identify and manage modifiable risk factors.

Keywords

Abdominal aortic calcium; Coronary artery calcium; Cardiovascular disease; Bone densitometry

Introduction

Abdominal aortic calcification (AAC) is associated with incident myocardial infarction or stroke,⁽¹⁾ but no study has reported the association of AAC on lateral spine dual energy X-ray absorptiometry (DXA) images with coronary artery calcium (CAC). The primary aim of this study was to assess the association between AAC scored on lateral spine DXA images intended for vertebral fracture assessment (VFA) using a validated 24-point semi-quantitative scale and coronary artery calcium detected with electron beam computed tomography (EBCT) in community-dwelling older men and women without known heart disease. The secondary aims

of this study were to assess the association between AAC scored on VFA images with a newer simplified 8-point semi-quantitative scale and CAC scored with EBCT, and to perform an exploratory analysis of the additional prediction of a high CAC level from the additional of AAC score on lateral spine DXA images combined with clinical risk factors compared to the prediction of CAC from clinical risk factors alone.

Methods

The Rancho Bernardo Study is an observational cohort study that enrolled 82% of white male and female adult residents residing in southern California in 1972. All data used for the analyses in this paper were collected with the approval of the Institutional Review Board of the University of California, San Diego, and all participants gave written-informed consent.

At the 8th study visit conducted from 2000 to 2002, 233 women and 200 men with no history of heart disease had coronary calcium scored with EBCT scans using an Imatron C-150 scanner (GE-Imatron, San Francisco, CA). Coronary artery calcium was quantified using the Agatston scale in the left main, left anterior descending, left circumflex, and other coronary vessels.(2) The total Agatston coronary artery calcium score was calculated as the sum of scores for each of these areas of the coronary vasculature.

An average 3.5 years later at the 9th study visit between 2003 and 2005, 107 men and 127 women had a lateral spine image obtained by DXA using a Hologic QDR 4500A densitometer with the participant in the lateral decubitus position for vertebral fracture assessment (VFA). These images were evaluated by one reader (J.T.S.) in late 2007 and early 2008 and scored for AAC using the previously validated semi-quantitative 24-point scale and a newer simplified 8-point scale. The reader was blinded to participants' EBCT coronary calcium scores and to all participant characteristics except age.

Details of both the AAC-24 and AAC-8 scales have been published.(3,4) Briefly, in the AAC-24 system, the anterior and posterior aortic walls were divided into four segments, corresponding to the areas in front of the lumbar vertebrae L1–L4. Aortic calcification scored as 0 if there was no calcification, as 1 if one-third or less of the aortic wall in that segment was calcified, as 2 if more than one-third but two-thirds or less of the aortic wall was calcified, or as 3 if more than two-thirds of the aortic wall was calcified. Scores could therefore range from 0 to 6 for each vertebral level, and the total score range was from 0 to 24.(3)

The AAC-8 scale has the same definition of aortic calcification as the AAC-24 scale, but uses a simplified scoring system. The AAC-8 score is the sum of the total length of calcification for each of the anterior and posterior aortic walls in front of vertebrae L1 to L4. A score of 0 is given if no calcification is seen, 1 if the aggregate length of calcification is $\leq$ to 1 vertebral height, 2 if that length is > 1 but ≤ 2 vertebral heights, 3 if that length is > 2 but ≤ 3 vertebral heights, and 4 if the aggregate length of calcification is > 3 vertebral heights.(4) The total score range is 0 to 8. In our experience, AAC-8 is faster and easier to score than AAC-24 and theoretically easier to implement in clinical practice.

Because these lateral images were obtained for vertebral fracture assessment and not for the purpose of AAC assessments, adequate space was present anterior to the lumbar spine to allow full visualization of the anterior abdominal aortic wall in 106 (45.3%). For the remainder, AAC was scored in the visible aortic wall segments and the unseen aortic wall segments were assumed not to be calcified (figure 1).

At the 8th study visit, participants had their blood pressure measured twice in a seated posture at rest, and blood samples drawn to measure fasting plasma glucose, triglycerides, and total,

HDL, and LDL cholesterol. Smoking status and physical exercise were assessed using standard questionnaires. A medical diagnosis of diabetes was assessed by self-report.

The distribution of total coronary artery calcium scores were highly left skewed, and therefore were modeled as ordinal levels using previously published cut-points (Agatston scores ≤ 10 , 11 to 100, 101 to 399, and ≥ 400).⁽⁵⁾ Participant characteristics were compared across CAC quartiles with chi-square statistics for categorical variables and one-way analyses of variance for continuous variables.

Primary analyses were performed on the 106 (73 women and 33 men) who had lateral DXA spine images fully evaluable for AAC. Ordinal logistic regression models were used first to assess the association between AAC 24-point scale tertile and CAC score adjusting for age and sex. Predictors in multivariable models included age, sex, cardiovascular risk factors (systolic blood pressure, total and HDL cholesterol, smoking status, prior diagnosis of diabetes) and other variables with a bivariate association with CAC at a p-value <0.2 (triglycerides, visceral to somatic fat ratio, and time interval between lateral DXA scan imaging and EBCT). Covariates unassociated with CAC in the full multivariable model (p-value >0.3) were dropped from the model one by one until the proportional odds assumption (by Chi-Square test) could no longer be rejected at the 0.10 p-value level. The final multivariable model included age, sex, systolic blood pressure, total and HDL cholesterol, smoking status, and the presence of diabetes. These same models were run to assess the association between AAC-8 point score and CAC score.

The degree to which AAC scored on lateral spine DXA images could detect those with the highest level of CAC (Agatston score ≥ 400) was assessed in two ways. First, receiver operating characteristics (ROC) curve analyses were also done to assess the sensitivity and specificity of AAC-24 and AAC-8 score at or above various cut-points to detect those with a medium to high level (Agatston score ≥ 100) or high level of coronary artery calcium (Agatston score ≥ 400). Second, ROC curves analyses were used to compare the areas under ROC curves in two prediction models to detect those with a high level of coronary calcium; AAC score plus clinical cardiovascular risk factors (age, sex, systolic blood pressure, total and HDL cholesterol, smoking status, and presence of diabetes), and clinical risk factors alone.

Since less than half the entire cohort had a lateral spine DXA image fully evaluable for AAC, secondary ordinal logistic regression analyses were repeated in the entire cohort ($n = 234$) to examine if the associations between the top tertile of AAC and CAC were still significant, adjusting for other covariates including a dummy dichotomous variable identifying those for whom the entire abdominal aorta was not visualized on the lateral spine DXA.

Results

Among the 106 individuals with fully evaluable lateral spine DXA images for AAC, 73 (68.9%) were women; their mean age was 66.1 years (standard deviation 7.5 years). As shown in table 1, CAC was associated strongly with AAC score, age, sex, systolic blood pressure, HDL cholesterol, and visceral to somatic fat ratio, less so with total cholesterol, and not associated with LDL cholesterol, triglycerides, diastolic blood pressure, or smoking status.

As shown in table 2, those in the top tertile of AAC scored with the 24-point scale had about a 7-fold age- and sex-adjusted odds of having a higher level of coronary artery calcium, and those in the top tertile of AAC scored with the 8-point scale had about 4-fold higher odds. Multivariable adjustment for age, sex, systolic blood pressure, total and HDL cholesterol, smoking status, and presence of diabetes attenuated these associations only slightly (table 2).

ROC curves showed that an AAC-24 score of 5 or higher had a sensitivity and specificity of 65% and 70%, respectively, to detect those with a CAC score of 400 or higher (figure 2), and a sensitivity and specificity of 54% and 75% to detect those with a CAC score of 100 or higher. An AAC-8 score of 3 or higher had a sensitivity of 45% and a specificity of 78% to detect those with a CAC level of 400 or higher (figure 3). Employing an AAC-8 score cut-point of 2 raised the sensitivity to 75%, but lowered the specificity to 47%. AAC-24 and AAC-8 scores, respectively, of ≥ 10 and ≥ 4 had specificity of $>90\%$ for those with a CAC score of ≥ 400 .

The area under the ROC curve of a prediction model including both the covariates of the final multivariable model as clinical risk factors and AAC-24 point tertile was 0.86 (95% C.I. 0.75–0.96). The area under the ROC curve for a prediction model including those same clinical risk factors but omitting the AAC-24 tertile score appeared to be lower (0.81, 95% C.I. 0.68–0.954). This difference between the two models was of marginal significance (figure 4). The area under the ROC curve of a prediction model including clinical risk factors and AAC-8 point tertile was 0.82 (95% C.I. 0.76–0.96, p-value for difference from clinical risk factors alone 0.51).

For the entire cohort of 234 individuals, those in the highest tertile of AAC-24 point scale score had an adjusted increased odds of 4.11 (95% C.I. 2.07 – 8.15) of having a higher level of CAC on EBCT compared to those in the bottom tertile of AAC score, adjusted for age, sex, systolic blood pressure, total and HDL cholesterol, smoking status, the presence of diabetes, and whether or not the entire abdominal aorta was evaluable for AAC. Those in the highest tertile of AAC-8 scale score had a multivariable-adjusted increased odds of 3.89 (95% C.I. 1.93 – 7.84) of having a higher level of CAC on EBCT.

Discussion

In this cohort of community-dwelling men and women, AAC scored on lateral DXA scans intended for vertebral fracture assessment with a previously validated 24-point scale was highly correlated with CAC scored with EBCT. The AAC-8 scale did not perform as well as the AAC-24 point scale.

The association between AAC-24 on lateral DXA and CAC was of at least equal strength to the associations previously reported for CAC with IMT on carotid ultrasound (6) and with ankle-brachial index and CAC(7) in this cohort. An advantage of AAC scoring on lateral DXA compared to most other tests of subclinical cardiovascular disease is that lateral DXA imaging can be done easily at the point of service of a bone density test, which is currently recommended for all women age 65 and older and men age 70 and older,(8–10) and therefore would not require two separate patient visits. Lateral spine imaging with DXA has already been shown to be cost-effective for a large subset of women age 60 to 80 based purely on its utility for detection of prevalent vertebral fractures(11) and can be obtained with very little additional time and expense at the time of bone densitometry (median 2009 Medicare cost of \$31).(12) Although technicians obtaining the images have to be instructed beforehand to include adequate space anterior to the lumbar spine to allow AAC to be fully scored, a previous study has shown that when bone densitometry technicians are so instructed 90% of the images are fully scorable for AAC.(13)

AAC scored on lateral spine radiographs has been shown to predict incident coronary heart disease,(14,15) CVD mortality,(14) congestive heart failure,(16) and stroke.(17) Previous studies have shown that AAC scores on lateral DXA images have very good agreement with AAC scores on lateral spine radiographs(4,13), and may predict incident stroke or myocardial infarction independent of other clinical cardiovascular disease risk factors.(1) For those at intermediate risk of coronary heart disease based on clinical risk factor scores (such as Framingham Point Score), documentation of a high level of AAC on lateral spine radiographs

or lateral spine DXA images may indicate a sufficiently high level of risk to justify more aggressive treatment of dyslipidemia and hypertension. Although coronary artery calcium score on EBCT is more predictive of incident coronary heart disease than other measures of subclinical CVD, including AAC, EBCT has not gained widespread acceptance as a screening test for subclinical cardiovascular disease, in part because of its expense and radiation exposure. (18,19)

Because the findings of this study do not confirm that AAC scored with the 24- point scale on lateral DXA images adds predictive value to clinical risk factors alone for predicting who is likely to have a high level of CAC on EBCT, larger studies with greater statistical power are needed to investigate this. Studies would be particularly useful to men and women judged to be at intermediate cardiovascular risk based on standard CVD risk factors, and to estimate the degree to which documentation of AAC in clinical practice could alter management of modifiable CVD risk factors and, ultimately, the effect of its use on CVD morbidity and mortality. In the meantime, practitioners whose patients who are shown incidentally to have a high level of AAC on lateral DXA images are urged to re-evaluate management of these patients' modifiable risk factors.

This study has several limitations. Over half of the participants did not have a lateral DXA image fully evaluable for AAC. Nevertheless, this small study still showed a strong association between a high level of AAC and a high CAC score, even when those with a lateral DXA image not fully evaluable for AAC were included. There was a 3- to 4-year interval between the EBCT scans and subsequent DXA imaging, which likely caused a conservative bias toward the null. The study population was almost entirely Caucasian, so these results may not apply to other populations.

This study has important strengths. This is the first study to report the association between AAC score on lateral DXA images and CAC score on EBCT, showing that AAC on lateral DXA is strongly associated with coronary artery plaque burden and may have a role to play in identifying individuals at high risk of CVD. Comprehensive assessment of other clinical cardiovascular disease risk factors was available for all participants, allowing examination of the independence of the AAC and CAC association. The DXA images for ACC were assessed by one investigator, who was blinded to all covariate data except age.

Acknowledgments

The Rancho Bernardo Study was funded by the National Institutes of Health/National Institute on Aging grants AG07181 and AG028507 and the National Institute of Diabetes and Digestive and Kidney Diseases, grant DK31801.

Funding: The Rancho Bernardo Study was funded by the National Institutes of Health/National Institute on Aging grants AG07181 and AG028507 and the National Institute of Diabetes and Digestive and Kidney Diseases, grant DK31801.

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Figure 1.
Lateral Spine Dual Energy X-Ray Absorptiometry Images Not Fully Evaluable (Left Panel)
and Fully Evaluable (Right Panel) for Abdominal Aortic Calcium

Figure 2.
Sensitivity and Specificity of Abdominal Aortic Calcium-24 Score Cut-Point for Coronary Artery Calcium (Agatston Score ≥ 100 or ≥ 400)

Figure 3.
Sensitivity and Specificity of Abdominal Aortic Calcium-8 Score Cut-Point for Coronary Artery Calcium (Agatston Score ≥ 100 or ≥ 400)

Figure 4.

Comparison of Abdominal Aortic Calcium-24 plus Clinical Risk Factors* vs Clinical Risk Factors* Alone to Detect Those with a High Level of Coronary Artery Calcium (Agatston Score ≥ 400)

*Clinical risk factors: age, sex, systolic blood pressure, total and HDL cholesterol, smoking status, and a diagnosis of diabetes

p-value for difference: 0.094

Table 1
Bivariate Associations of Predictors with Coronary Artery Calcium (N=106)

Variable	Coronary Artery Calcium Score			P-Value
	0 (n=42) 61.8 (5.7)	1-99 (n=21) 67.8 (7.0)	100-399 (n=23) 69.5 (7.9)	
Age, years (Standard Deviation)				<0.01*
Female/Male	93% / 7%	62% / 38%	57% / 43%	40% / 60% <0.01**
Time Lapse EBCT to Lateral DXA (years) (Standard Deviation)	4.0 (0.8)	3.3 (1.0)	3.1 (1.2)	3.2 (0.7) <0.01*
Systolic BP, (mmHg) (Standard Deviation)	121.8 (15.5)	131.6 (16.1)	132.8 (13.0)	136.2 (20.0) <0.01*
Diastolic BP, (mmHg) (Standard Deviation)	74.5 (7.3)	77.4 (8.0)	74.7 (7.0)	78.8 (10.0) 0.16*
Total Cholesterol (mg/dl) (Standard Deviation)	217.1 (35.5)	206.2 (27.3)	193.7 (34.3)	206.6 (31.4) 0.06*
LDL Cholesterol (mg/dl) (Standard Deviation)	123.7 (33.2)	119.7 (24.9)	108.3 (24.7)	123.8 (32.8) 0.22*
HDL Cholesterol (mg/dl) (Standard Deviation)	65.3 (16.9)	64.3 (15.2)	54.9 (18.4)	53.7 (17.6) 0.02*
Triglycerides (mg/dl) (Standard Deviation)	140.4 (68.3)	111.6 (43.5)	152.1 (84.6)	145.1 (49.4) 0.19*
Creatinine, (mg/dl) (Standard Deviation)	0.81 (0.17)	1.23 (1.58)	0.93 (0.27)	0.94 (0.18) 0.21*
Smoking Status (Never vs. Past-Current)	48% / 52%	38% / 62%	48% / 52%	35% / 65% 0.73**
Diabetes Diagnosis	0%	4.8%	4.4%	10% 0.28
Visceral to Somatic Fat Ratio	0.39 (0.21)	0.75 (0.53)	0.56 (0.31)	0.66 (0.39) <0.01*
Exercise or Labor (3 times per week)	76%	81%	83%	80% 0.93**
Strenuous Exercise (3 times per week)	40%	14%	35%	30% 0.21**
AAC-24 Tertiles: Bottom Middle Top	48% 33% 19%	43% 19% 38%	13% 44% 43%	15% 20% 65% p-value <0.01**
AAC-8 Tertiles: Bottom Middle Top	52% 36% 12%	48% 28% 24%	35% 26% 39%	25% 30% 45% p-value 0.09**

Abbreviations: EBCT-electron beam computed tomography; DXA- dual energy x-ray absorptiometry BP-blood pressure; AAC-abdominal aortic calcium

Table 2

Age- and Multivariable-Adjusted Associations of Abdominal Aortic Calcium (AAC) and Coronary Artery Calcium (CAC)

AAC Tertile	AAC-24		AAC-8	
	Age- and Sex-Adjusted OR (95% C.I.) [^]	Multivariable-Adjusted [*] OR (95% C.I.) ^{*^}	Age- and Sex-Adjusted OR (95% C.I.) [#]	Multivariable-Adjusted [*] OR (95% C.I.) ^{##}
1	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
2	2.50 (0.89 – 7.02)	2.49 (0.88 – 7.16)	1.93 (0.77 – 4.88)	1.72 (0.64 – 4.60)
3	7.12 (2.63 – 12.3)	6.42 (2.28 – 18.1)	3.92 (1.50 – 10.2)	3.38 (1.26 – 9.07)

^{*} Adjusted for age, sex, systolic blood pressure, total and HDL cholesterol, smoking status, and presence of diabetes

Chi-Square Tests for Proportionality of Odds Assumption:

[^] 29.33, p-value = 0.14

^{^^} 14.27, p-value = 0.28

[#] 22.00, p-value = 0.46

^{##} 11.47, p-value = 0.49