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ORIGINAL RESEARCH

Abdominal Aortic Calcification Detection Using Dual-Energy X-Ray Absorptiometry: Validation Study in Healthy Women Compared to Computed Tomography

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Abstract Abdominal aortic calcification (AAC) is an independent determinant of cardiovascular events. Computed tomography (CT) is currently the gold standard measure of AAC but is limited by high radiation exposure. Lateral dual-energy X-ray absorptiometry (DXA) has the potential to detect AAC at a fraction of the radiation dose. Our objective was to determine the accuracy of lateral-DXA in detecting AAC compared to CT in healthy women. Women from the TwinsUK registry aged 52–80 years ($n = 105$) underwent noncontrast CT and lateral-DXA imaging of the abdominal aorta at lumbar vertebrae L1–L4. Presence of calcium on CT was scored using the volume method. Lateral-DXA images were scored using the previously validated semiquantitative 24-point score and simplified 8-point score. Calcification was present in 81 % of women as determined by CT and 49 % with lateral-DXA. The mean volume score and the 24- and 8-point scores of AAC were 0.20 ± 0.41 cm^2, 2.39 ± 3.91 arbitrary units, and 1.47 ± 2.13 arbitrary units, respectively. There was moderate agreement between CT and 24-point lateral-DXA (Spearman's rank correlation coefficient $r = 0.58$, $P < 0.0001$). The sensitivity of lateral-DXA for detecting AAC was 56 % and specificity was 80 %. Sensitivity and specificity of lateral-DXA improved to 64 and 84 % when analysis was limited to calcium volumes $\geq$0.008 cm^3 as detected by CT. Lateral-DXA imaging may provide a useful alternative to CT in detecting AAC with minimal radiation exposure, which may be used with concurrent bone mineral density assessment.

Keywords Aorta · Calcification · CT · DXA

Conventional cardiovascular risk assessment is reliant on measurement of blood pressure, serum cholesterol levels, presence of diabetes mellitus, and smoking [1]. Although useful, approximately 20–30 % of cardiovascular events occur in individuals classified at low cardiovascular risk according to the above risk factors [2–4]. Several large epidemiological studies have found abdominal aortic calcification (AAC) to independently predict cardiovascular events after adjustment for conventional risk factors [5–8]. Reclassification of subjects according to calcium score improves risk prediction by 14–51 % [8–10]. Within the aorta, prevalence of calcification is higher in the abdominal compared to the thoracic aorta, increases with age, and correlates with coronary and extracoronary calcification [11, 12]. Accurate quantification of AAC is thus required for risk classification, to understand the epidemiology of calcification and to assess interventions to retard calcification.

Noncontrast computed tomography (CT) is currently the gold-standard method for quantifying aortic calcification and provides a volumetric calcium score [13]. However, this technique is limited by relatively high radiation exposure and cost [13]. Dual-energy X-ray absorptiometry (DXA) is

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traditionally used to quantify areal bone mineral density for the diagnosis of osteoporosis and prediction of risk fracture. Due to the anatomical position of the abdominal aorta anterior to the lumbar spine, it is possible to use lateral-DXA scans to detect AAC at a fraction of the radiation dose and cost [14, 15]. Previous studies investigating whether lateral-DXA imaging can detect calcification as detected by CT have reported good sensitivity and specificity [16, 17]. However, these studies were limited to patients with chronic kidney disease, a population known to have extensive vascular calcification and increased cardiovascular risk [18–20]. To our knowledge, this is the first study to examine the accuracy of lateral-DXA imaging to detect AAC compared to the gold-standard CT imaging in asymptomatic women.

Methods

A total of 105 consecutively consenting asymptomatic women were recruited from the UK Adult Twin Registry (TwinsUK) at St. Thomas' Hospital (London, UK). This cohort has similar characteristics to the general UK population [21]. All subjects underwent abdominal CT and lateral-DXA imaging to quantify AAC (Figs. 1 and 2). The study was approved by the St. Thomas' Hospital Research Ethics Committee, and written informed consent was obtained from all subjects.

Fig. 1 Example of lateral dual-energy X-ray absorptiometric image. *Arrows* indicate calcification on the anterior and posterior walls of the aorta

CT Imaging

All subjects underwent a noncontrast CT scan as previously described [22]. Briefly, the scan was performed with a 64-slice CT helical scanner (Brilliance; Philips Medical Systems, Cleveland, OH). Five-millimeter transverse slices between the aortic arch and the aortic bifurcation were acquired. All images were viewed off-line using OsiriX© Medical Imaging Software (www.osirix-viewer.com). Analysis was performed on each cross-sectional slice separately, and aortic calcification was defined as any area within the aorta >1 mm^2 with attenuation ≥130 Hounsfield units (Fig. 2). Calcium was quantified in cubic centimeters using the volume score calculated as the product of voxel volume and the number of voxels for each cross-sectional slice; the total volume score was obtained by summing the score for all cross-sectional images.

Lateral-DXA Scan

Lateral-DXA images of the lateral lumbar spine (L1–L4) were obtained using a Hologic Discovery densitometer (Hologic, Bedford, MA) with participants in the lateral decubitus position. Quality-control scans were performed daily using a spine phantom. DXA images were scored using a 24-point and an 8-point method. For the 24-point method, the anterior and posterior aortic walls were divided according to the four lumbar segments (L1–L4). Each section was scored 0–3 according to whether there was no calcification, one-third or less of the aortic wall was calcified, calcification covered more than one-third but two-thirds or less of the aortic wall, or calcification covered greater than two-thirds of the aortic wall. The total score

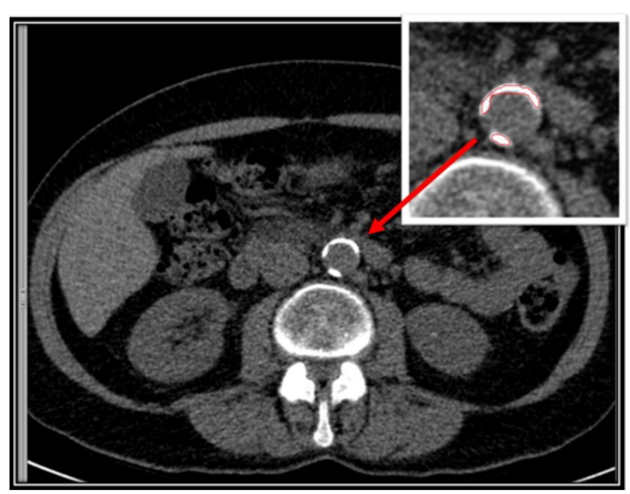

Fig. 2 Cross-sectional computed tomographic image of the abdominal aorta showing aortic calcification outlined by two regions of interest (*red arrow*), viewed off-line using OsiriX© Medical Imaging Software (www.osirix-viewer.com) (Color figure online)

ranged from 0 to 24 for the total aortic segment. For the 8-point score, the total lengths of the anterior and posterior aortic walls were considered for analysis. Each wall was scored 0–4 according to whether there was no calcification, the total length of calcification was the height of one vertebra or less, greater than that of one vertebra but equal to or less than that of two vertebrae, greater than that of two vertebrae but equal to or less than that of three vertebrae, or greater than the height of three vertebrae, as previously described [23, 24]. The total score ranged 0–8 for both the anterior and posterior aortic walls. All analyses were performed by M. C., blinded to calcification score as detected by CT at the time of analysis.

Statistical Analysis

Data analysis was performed using SPSS software (version 16.0; SPSS, Inc., Chicago, IL). Subject characteristics are presented as mean ± SD unless otherwise stated. Agreement between calcium scored using CT and lateral-DXA was determined using Spearman's rank correlation coefficient. We also calculated the sensitivity, specificity, and area under the curve for lateral-DXA, predicting aortic calcium as determined using CT for tertiles of volume scores which were >0, ≥0.008, and ≥0.08 cm^3.

Results

Characteristics of participants are listed in Table 1. Average age was 64.2 years (range 52–80). Of these women, 26 % were on treatment for hypertension, 22 % on statins, and 12 % on treatment for osteoporosis.

Table 1 Characteristics of the study population

Demographics	Total cohort (n = 105)
Age (years)	64.2 ± 7.4
Height (cm)	159.7 ± 16.4
Weight (kg)	68.6 ± 15.9
Systolic blood pressure (mm Hg)	128.8 ± 15.8
Diastolic blood pressure (mm Hg)	74.4 ± 8.8
Mean arterial pressure (mm Hg)	94.8 ± 10.1
Total cholesterol (mmol/L)	5.85 ± 1.11
HDL-cholesterol (mmol/L)	2.09 ± 0.53
LDL-cholesterol (mmol/L)	3.23 ± 1.00
Antihypertensive therapy (n)	27
Lipid-lowering therapy (n)	23
Diabetes therapy (n)	1
Osteoporosis therapy (n)	13
Current smoker (n)	8

Eighty-five subjects (81 %) had evidence of abdominal calcification by CT and 51 (49 %) by lateral-DXA. The mean volume score of AAC as detected by CT was 0.20 ± 0.41 cm^2. The mean 24- and 8-point scores from DXA images were 2.39 ± 3.91 arbitrary units (AUs) and 1.47 ± 2.13 AUs, respectively. The frequency distributions for the 24- and 8-point scores from lateral-DXA images are shown in Fig. 3. The 24- and 8-point scores were highly correlated (Spearman's rank correlation coefficient $r = 0.98$, $P < 0.0001$).

Considering CT as the gold-standard method for detecting the presence of AAC, agreement between lateral-DXA and CT scores and was moderately good (Spearman's rank correlation coefficient $r = 0.58$, $P < 0.0001$ for both 24- and 8-point scores, Fig. 4). Table 2 shows the sensitivity, specificity, and area under the curve for the lateral-DXA 24-point score predicting AAC as detected by CT. The lateral-DXA scan correctly detected AAC in 48/86 women (sensitivity 56 %), with false-positives in four subjects who did not have AAC (specificity 80 %); the area under curve was 0.68 for any AAC (Table 2). In order to investigate whether the accuracy of lateral-DXA changes with different degrees of aortic calcification CT, sensitivity and specificity were calculated for tertiles of volume score. For predicting AAC volume ≥0.008 and ≥0.08 cm^3 as detected by CT, most measures improved and the sensitivity, specificity, and area under the curve were 64 %, 84 %, and 0.74 and 71 %, 63 %, and 0.67, respectively (Table 2).

Discussion

Atherosclerotic disease is a systemic process affecting large and medium-sized arteries, with a long subclinical phase which underlies several clinical presentations such as myocardial infarction and stroke [25]. Advanced stages of atherosclerosis are characterized by calcification within atherosclerotic plaque [26], which, when assessed using noncontrast CT, independently predicts future cardiovascular events [5–10]. Calcification within the aorta is not confined to atherosclerotic plaque but may occur in the media of the wall [27]. In animal models, induced medial calcification is associated with increased arterial stiffness [28]. In humans, arterial stiffness predisposes to isolated systolic hypertension [29] and is an important predictor of cardiovascular events in healthy [30–32], hypertensive [33–35], and diabetic [36] populations. Several studies have shown aortic calcification to correlate with increased large artery stiffness [37–39]. Lateral-DXA imaging may therefore provide an important low-radiation tool for detecting patients at increased risk of large artery stiffening, isolated systolic hypertension, and cardiovascular events.

The present study shows a high prevalence of AAC in apparently healthy women, which is consistent with

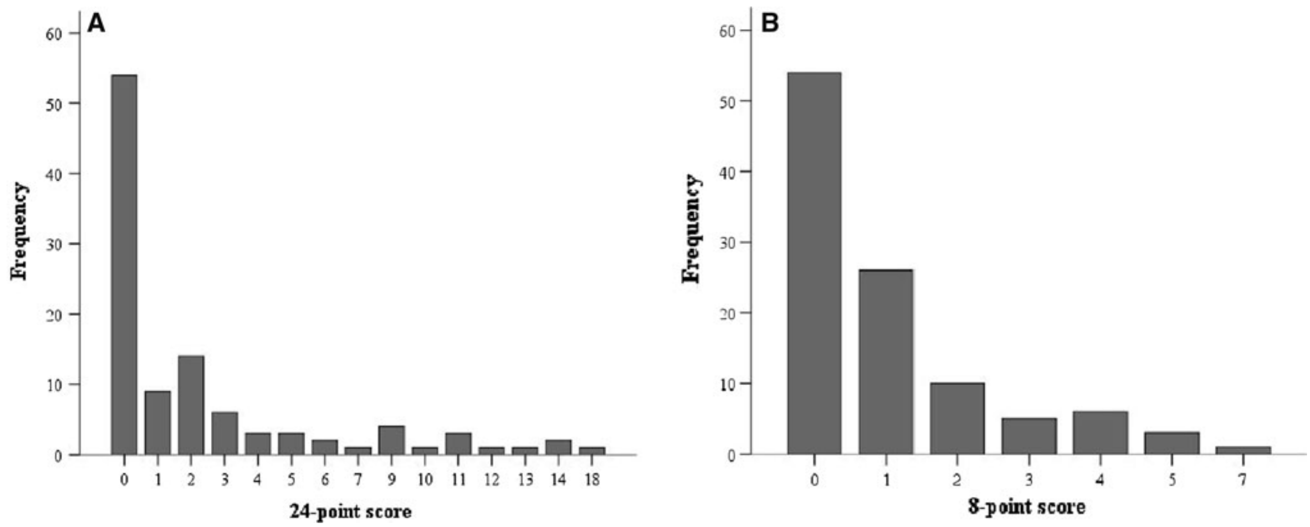

Fig. 3 Frequency distribution graphs of the 24-point score (**a**) and the 8-point score (**b**) from lateral dual-energy X-ray absorptiometric images

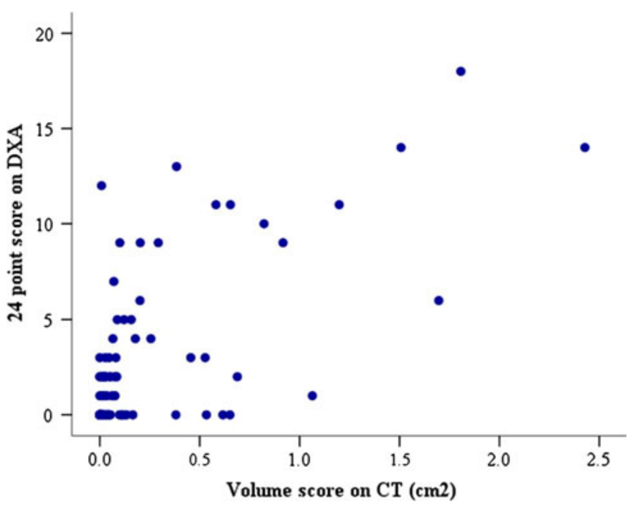

Fig. 4 Scatterplot of 24-point score from lateral dual-energy X-ray absorptiometry versus volume score from computed tomography

Table 2 Sensitivity, specificity, and area under the curve associated with lateral-DXA 24-point score predicting the presence of abdominal aortic calcification (AAC) as detected by CT for calcium volume scores >0, ≥0.008, and ≥0.08 cm^3

CT score	Sensitivity (%)	Specificity (%)	Area under curve (95 % CI)
AAC >0	56	80	0.68 (0.55–0.80)
AAC ≥0.008 cm^3	64	84	0.74 (0.65–0.84)
AAC ≥0.08 cm^3	71	63	0.67 (0.56–0.78)

histological observations [25]. Furthermore, we found a good correlation of 0.58 between AAC detected by lateral-DXA compared to that detected by CT (Fig. 4). Previous studies comparing lateral-DXA to CT imaging of AAC were limited to patients with chronic kidney disease. These studies reported intraclass correlation coefficients between 0.52 and 0.58 using the 24-point scoring system [16, 17]. However, chronic kidney disease patients present with extensive aortic calcification and are already classified at high cardiovascular risk [18–20]. In asymptomatic individuals, lateral-DXA imaging of AAC compares well to radiographic imaging, with a reported correlation of 0.80–0.82 [15, 24]. The higher correlation between AAC detected using lateral-DXA and radiographic imaging to that detected by lateral-DXA and CT is likely due to reduced sensitivity of radiographs compared to the gold-standard CT in detecting aortic calcification. In the present study, the accuracy of lateral-DXA imaging improved when analysis was limited to women with a higher degree of aortic calcification. Cardiovascular disease remains the leading cause of death in women, with approximately 30 % of cardiovascular events unexplained by conventional risk factors [23]. Stepwise increase in AAC corresponds with increased cardiovascular risk as detected by radiographs [6–8] and confirmed by CT [40]. Risk stratification is improved by addition of an extracoronary calcium score [9]; lateral-DXA scans therefore provide a low-radiation method (0.001 mSv for DXA compared to 8 mSv for abdominal CT [41]) with high sensitivity and specificity to detect extensive aortic calcification in asymptomatic women.

In the present study, AAC detected using lateral-DXA was measured using two methods, the 8- and 24-point scores. In the Framingham cohort, the 24-point score applied to radiographic images is an important predictor of cardiovascular events [8]. We found a strong correlation between the two 24-point scoring methods and a simplified 8-point score ($r = 0.98$, $P < 0.0001$). This suggests that this simplified scale may provide a quick, accurate tool for assessment of AAC. Our findings are consistent with previous studies that have shown the correlation between the two methods to be 0.95 [24] with good reproducibility of the 8-point score [15–17]. Future studies are needed to determine the predictive value of the 8-point score for cardiovascular events, although secondary analysis from initial limited data supports AAC as detected by lateral-DXA to be a predictor of cardiovascular events [42–44].

Study Limitations

This study is limited to female twins from the TwinsUK cohort and cannot be extended to men. However, this cohort is comparable to women in the general UK population for disease and lifestyle characteristics [21]. Furthermore, the all-cause and cardiovascular mortality of twins are comparable to rates in the general population [45]. Although the inter- and intrarater variabilities were not tested in this study, previous studies have reported high intraclass correlations of 0.83–0.88 for the 8-point score [15, 16] and 0.91–0.93 for the 24-point score [16] and a high interrater correlation of 0.89 for the 24-point score [24]. Relatively high slice thickness (5 mm) was used for the CT imaging protocol. However, since CT was more sensitive than DXA at detecting calcification, a thinner slice would not be likely to improve the correlation. Due to the limitation of current imaging techniques, we were unable to distinguish between intimal and medial aortic calcification. It is possible that lateral-DXA and CT differ in their sensitivity to detect medial and intimal calcification, with lateral-DXA scans being better for both medial and intimal calcification and CT possibly only picking up the latter. Future prospective and interventional studies will be required to define the clinical implications of aortic calcification as detected by lateral-DXA.

In conclusion, lateral-DXA imaging provides a useful tool for detecting subclinical AAC compared to CT using a simple semiquantitative scoring system, with minimal radiation exposure and low cost.

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