Femoral neck and spine bone mineral density-Surrogate marker of aortic calcification in postmenopausal women

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Abstract

Objective: Osteoporosis and abdominal aortic calcification (AAC) are associated with increased morbidity and mortality in postmenopausal women. The aim of this study was to determine the accuracy of anterior-posterior (AP) dual-energy X-ray absorptiometry (DXA) compared with that of X-ray lateral lumbar radiography (LLR) in detecting and scoring AAC.

Methods: In this cross-sectional study conducted in 56 postmenopausal asymptomatic females aged 59.0±9.3 years and who never used medications to treat osteoporosis before, we determined femoral neck and lumbar spine bone mineral density (BMD) by AP DXA and AAC by X-ray LLR. We hypothesized that the subtracted femoral neck BMD (BMD_{FN}) from lumbar spine BMD (BMD_{LS}) presented as $\Delta BMD=BMD_{LS}-BMD_{FN}$ would have a diagnostic value in detecting abdominal vascular calcification.

Results: The mean BMD_{FN} was 0.744±0.184 g/cm^2, and the mean BMD_{LS} was 0.833±0.157 g/cm^2 ($p<0.0001$); the mean ΔBMD was 0.089±0.077 g/cm^2, and the mean AAC score was 2.182±1.982. Bivariate Pearson's correlation analysis revealed a significant positive correlation between AAC and ΔBMD ($r=0.449$, $p=0.0006$); by linear regression analysis, $R^2=0.2019$, and by multiple regression analysis, $\beta st=13.5244$ ($p<0.0001$). We found a sensitivity of 64.3% and specificity of 82.9% by receiver operating characteristic [ROC; area under the ROC curve (AUC=0.759)] in the prediction of AAC by ΔBMD.

Conclusion: This AP subtracting BMD DXA method provides a useful tool for detecting and scoring subclinical and extensive AAC in postmenopausal women using a simple, semiquantitative, and accurate scoring system with minimal radiation exposure and low cost.

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Keywords: aortic diseases, vascular calcification, osteoporosis, postmenopausal, absorptiometry DXA scan, femur neck, lumbar vertebrae

Introduction

Osteoporosis and atherosclerosis are associated with an increased morbidity and mortality in postmenopausal women (1). Calcification is a common feature of atherosclerotic plaques and is regulated in a way similar to bone mineralization (2). There are a lot of studies that have examined the association of atherosclerotic calcifications with bone mineral density (BMD) (1-4), but there is no study that examined the association between subtracted femoral neck BMD from lumbar spine BMD and vascular calcification. In addition, there is no study that confirmed the diagnostic value of that subtraction in aortic calcification detection.

The term osteoporosis is used to define a group of clinical disorders characterized by reduced bone mass or density without a defect in mineralization (5). Osteoporosis occurs when bones lose an excessive amount of their protein and mineral content (calcium). The bone is a tissue that is constantly being renewed in a two-stage process (resorption and formation) that occurs throughout life (6). After the mid-30s, bone mass is lost at a faster pace than it is formed, so BMD in the skeleton begins to slowly decline. Most cases of osteoporosis occur as an acceleration of this normal aging process, which is referred to as primary osteoporosis (7, 8).

The bone mineral loss is most often observed in older people and in women after menopause.

Women lose bone mineral mass more rapidly after menopause (usually around the age of 50 years), when they stop producing estrogen. Seven years after menopause, women can lose more than 20% of their bone mineral mass. Women are about five times more likely to develop osteoporosis than men (9). Vascular calcification and osteoporosis are common age-

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related processes (10). Abdominal aortic calcification (AAC) is displayed on routine lateral lumbar spine radiographs as dense calcium mineral deposits of the aorta that lies adjacent to the vertebrae (10). It means that vascular compromise due to aortic calcification may itself result in bone loss (10, 11). Atherosclerotic calcification has long been considered a late stage, unregulated sequel of the atherosclerotic process. Aortic calcification occurs more early with rapid progress and arterial narrowing (11). Recent studies implicated several possible metabolic linkages between aortic calcification and BMD loss, involving estrogen, vitamin D and K, lipid oxidation products, and osteoprotegerin (12-14).

The commonly used imaging modalities to assess bone mass and vascular calcification use the following imaging technologies of X-ray radiography: dual-energy X-ray absorptiometry (DXA) and lateral lumbar radiography (LLR). Data obtained from both the femur and anterior-posterior (AP) spine DXA scans are considered gold standards for diagnosing osteoporosis (3). DXA is used to assess the overall skeletal changes that often occur with age by measuring BMD. LLR detects calcified deposits in the aorta adjacent to each lumbar vertebra from L1 to L4 using the midline point of the intervertebral space below and above the vertebrae as the defined boundaries. Setiawati et al. (15) compared the following three methods in the detection and quantification of AAC: LLR, lateral spine DXA, and quantitative computed tomography (QCT). They considered lateral lumbar radiograph as the gold standard of AAC detection and scoring.

Our hypothesis was that the value of subtracted femoral neck BMD (BMD_{FN}) from lumbar spine BMD (BMD_{LS}) presented as $\Delta BMD=BMD_{LS}-BMD_{FN}$ would be the highest in those individuals with more vascular calcification of the abdominal aorta. The aims of this study were twofold: to find an association between AAC and femoral neck BMD, between AAC and spine BMD, and between AAC and ΔBMD; to determine the accuracy of the AP DXA scan in detecting and scoring AAC and to compare it with the AAC scoring evaluated by LLR.

Methods

Study populations

This cross-sectional study was conducted from October to December 2013. A total of 56 consecutively consenting asymptomatic women were recruited from ambulatory patients. None of the selected patients used medications to treat osteoporosis before. Fourteen women were smokers, 12 were with insulin-independent diabetes, and 30 were hypertensive. They had a mean age of 59.0±9.3 years, and their mean body mass index (BMI) was 27.7±3.65 kg/m^2.

Exclusion criteria were chronic renal disease, insulin-dependent diabetes, malignancy, rheumatoid arthritis, liver disease, or any chronic disease that might affect the skeleton. They signed an informed consent, and the Ethics Committee of our institution approved the study. The menopausal state was assessed by a self-administered questionnaire asking whether the menses had stopped. The women were classified as postmenopausal once they experienced at least 12 consecutive months of amenorrhea.

Demographic and clinical data were collected from the patient's chart and included age, weight, height, history of diabetes mellitus, smoking habit, hypertension, and the diseases mentioned above, which might affect the bone mass. BMD of the femoral neck and lumbar spine was assessed by DXA. LLR of the abdominal aorta was used to determine the overall AAC score.

BMD

DXA is an enhanced form of X-ray absorptiometry that is used to measure bone density. A DXA scanner is a machine that produces two X-ray beams, each with different energy levels. Measurement of bone density measuring is based on the difference between the two level beams. DXA is today's established standard for measuring BMD (16, 17).

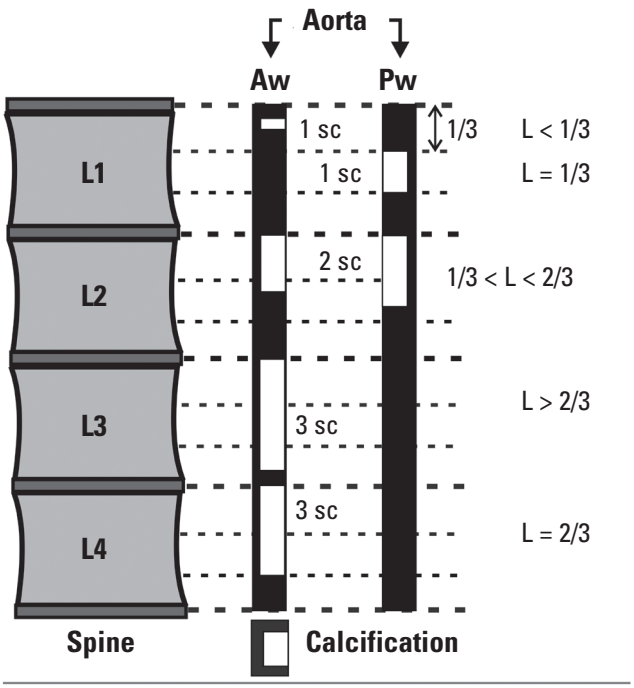
We conducted BMD testing using DXA by a Hologic QDR4500SL system (Hologic Inc., Bedford, MA, USA). BMD was measured by DXA in the lumbar spine and femoral neck. Two X-ray beams with differing energy were used for the measurement of BMD. BMD was determined based on the absorption of each beam by the bone after subtraction of the absorption of soft tissue. For assessment of the spine, the patient's legs were supported on a padded box to flatten the pelvis and lower the (lumbar) spine. For assessment of the femoral neck, the patient's foot was placed in a brace that rotates the hip inward. In both cases, the detector was slowly passed over the area generating images on a computer monitor (18).

Absolute BMD values and T-scores (number of SDs below BMD of a young reference group) of the lumbar spine and femoral neck were recorded as BMD (g/cm^2) and T-score (for femoral neck, total and L1 to L4 region). The World Health Organization (WHO) defined the following categories based on bone density in Caucasian females: normal bone, T-score greater than -1; osteopenia, T-score between -1 and -2.5; osteoporosis, T-score less than -2.5 (19).

AAC

We performed LLR to determine AAC in the standing position using standard radiographic equipment (Shimadzu RADSpeed 324-DK, Nishinokyo-Kuwabarachou. Nakagyo-ku. Kyoto 604-8511, Japan). The film distance was 1 m, and the estimated radiation dose was no more than 15 mGy. AAC is often seen as linear thin-film tracks at the anterior or posterior wall of the abdominal aorta with a linear edge corresponding to the aortic wall beside lumbar vertebral segments L1 to L4.

We estimated the aortic score using a previously validated system (16-18). The measure for the unit AAC score is the linear length of aortic calcification compared with 1/3 of the aortic longitudinal wall projected near the vertebral segment beside it: score 0-no calcific deposits in front of the vertebra; score



Aw - anterior wall; Pw - posterior wall; sc - score;
L ≤ 1/3 (sc = 1), 1/3 < L < 2/3 (sc = 2),
L ≥ 2/3 (sc = 3). L - length of calcification.

Figure 1. Abdominal aorta calcification (AAC) scoring at the anterior and posterior walls of the abdominal aorta adjacent to vertebrae L1 to L4

1-small scattered calcify deposits filling less than 1/3 of the longitudinal wall of the aorta; score 2-1/3 or more but less than 2/3 of the longitudinal wall of the aorta calcified; score 3-2/3 or more of the wall calcified. The scores were summarized using the composite score for anterior and posterior wall severity (range score 0-3), where the scores of individual aortic segment calcifications, both for the anterior and posterior walls (max. 2×12) were summed (maximum score 24) (18, 20, 21). The scoring system of AAC is schematically depicted in Figure 1.

Two radiologists with more than 20 years' experience performed all the diagnostic procedures. Four observers performed an independent and blinded radiographic review assessing all radiographic parameters and the interpretation of final scoring. Interobserver reliability was determined using Cohen's kappa coefficient (κ). It was the highest across experience levels for AAC detection (κ=0.89) and AAC scoring (κ=0.96).

Statistical analysis

The data were analyzed using MedCalc for Windows, 13.0.6.0. (MedCalc Software, Ostend, Belgium). The results were expressed as mean±SD or percentage. The analysis of normality was performed with the Kolmogorov–Smirnov test. Student's t-test for paired data was used to compare the femoral neck BMD and lumbar spine BMD. Pearson's correlations were calculated to explore the relationship between femoral neck BMD, spine BMD, and ΔBMD and other variables, as appropriate. Simple linear regression analysis was performed to assess the associations between dependent and independent variables and to create the equation of linear regression. We conducted a multiple backward regression analysis to determine the effect on the dependent variable (AAC) of variations in one of the independent variables (femoral neck BMD, diabetes, hypertension, spine BMD, smoking, age, and BMI), while the other independent variables were fixed. All tests were two-sided. $p<0.05$ was considered to indicate a significant difference.

Table 1. Demographic characteristics of the patients

Characteristics	Mean±SD, n (%)	Range
Age, years	59.0±9.3	46-79
Height, cm	161.8±7.4	150-182
Weight, kg	72.6±10.5	50-101
BMI, kg/m^2	27.7±3.6	22.5-35.3
Hypertension	30 (53.6)	/
Diabetes	12 (21.4)	/
Smokers	14 (25.0)	/

Values are presented as mean±SD or number (%).
BMI - body mass index

Results

During the three-month period from October to December 2013, DXA and lateral lumbar X-ray radiography measurements and other demographic examinations were successfully conducted on 56 postmenopausal female participants aged 59.0±9.3 years and with BMI 27.7±3.6 kg/m^2. The demographic and clinical characteristics of the patients are presented in Table 1.

The mean BMD of the femoral neck was 0.744±0.184 g/cm^2 (D=0.0901, p>0.1), and the mean BMD of the lumbar spine was slightly greater at 0.833±0.157 g/cm^2 (D=0.1070, p>0.1). The results from the paired t-test between femoral neck and lumbar spine BMD were as follows: mean difference (-0.0896) and two-tailed probability (p<0.0001). The mean difference of lumbar spine and femoral neck BMD, presented as ΔBMD, was 0.089±0.077 g/cm^2. The mean aortic calcification was 2.182±1.982 (D=0.1131, p=0.0767). Fourteen (25.0%) patients were smokers, 12 (21.4%) were diabetics, and 30 (53.6%) were hypertensive; their mean BMI was 27.7±3.6 kg/m^2.

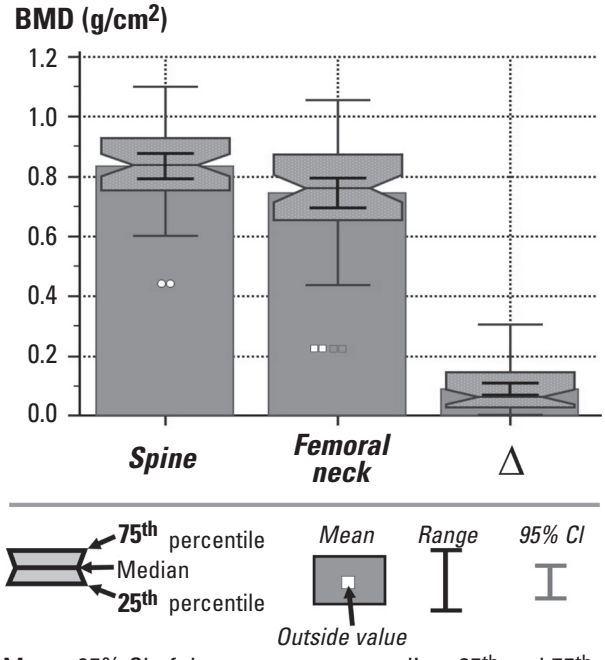
The notched box-and-whisker bars for the tissue biomarkers of BMD are presented in Figure 2.

Table 2 shows the positive value of Pearson product–moment correlation coefficient (r) as the measure of the strength of linear dependence between two variables (one in the measured tissue markers in the top horizontal row and one in the demographic and tissue markers in the vertical column) indicated a significant positive correlation between the following: aortic calcification and hypertension (r=0.268, p=0.047), aortic calcification and smoking (r=0.352, p=0.008), aortic calcification and

Table 2. Bivariate Pearson's correlation analysis of demographic characteristic with BMD and aortic calcification

	BMD FN, g/cm^2		BMD spine, g/cm^2		ΔBMD, g/cm^2		Aortic calcification	
	R	*P*	*R*	*P*	*R*	*P*	*R*	*P*
Age, years	-0.325	0.015	-0.356	0.007	0.197	0.149	0.118	0.391
BMI, kg/m^2	0.291	0.031	0.204	0.135	0.278	0.041	0.135	0.324
Hypertension	-0.062	0.654	-0.039	0.775	0.032	0.817	0.268	0.047
Diabetes	0.235	0.084	0.231	0.091	0.081	0.556	0.116	0.398
Smokers	-0.286	0.034	-0.323	0.016	0.187	0.171	0.352	0.008
BMD FN, g/cm^2	/	/	0.214	0.116	0.131	0.324	-0.241	0.076
BMD spine, g/cm^2	0.214	0.116	/	/	0.235	0.084	-0.178	0.193
ΔBMD, g/cm^2	0.131	0.324	0.235	0.084	/	/	0.449	0.0006
Aortic calcification	-0.241	0.076	-0.178	0.193	0.449	0.0006	/	/

The results of the bivariate Pearson's correlation analysis of demographic characteristic with BMD and aortic calcification are presented as (r) indices and (p) values. Values are presented as mean±SD. BMD - bone mineral density; BMI - body mass index; FN - femoral neck



Mean, 95% CI of the mean, range, median, 25th and 75th percentiles present lumbar spine. BMD - femoral neck BMD and lumbar spine minus femoral neck MD (Δ). BMD - bone mineral density; CI - confidence interval.

Figure 2. Box plots of the mean, range, median, and 25th and 75th percentiles for tissue biomarkers

ΔBMD (r=0.449, p=0.0006), ΔBMD and BMI (r=0.278, p=0.041), and BMI and femoral neck BMD (r=0.291, p=0.031). Pearson's correlations revealed a significant inverse correlation between the following: age and both femoral neck and lumbar spine BMD (r=-0.325, p=0.015 and r=-0.356, p=0.007 respectively), femoral neck BMD and smoking (r=-0.286, p=0.034), and lumbar spine BMD and smoking (r=-0.323, p=0.016).

The results of linear regression, which are an approach for modeling the relationship between a scalar dependent variable Y (aortic calcification) and an explanatory variable denoted X (ΔBMD, g/cm^2) were presented as follows: coefficient of determination R^2=0.2019, regression parameter b_0=1.151, regression parameter b_1=11.5049, and equation of simple linear regression y=1.1510+11.5049 X. The coefficient of determination R^2 (0.2019) showed that 20.19% of the total variability was explained with the linear relation between aortic calcification and ΔBMD or that 20.19% from aortic calcification was dependent on ΔBMD. Only 20.19% of the changes in aortic calcification were the result of ΔBMD value changes, and the remaining from the total variability between them were not explained (79.81% of aortic calcifications were dependent on other factors, which were not covered with the regression model). This model was used as a criterion for the best regression equation choice, so the greater its value will be, the better the model of approximation will be. The regression parameter b_0=1.151 showed the expected theoretical value of aortic calcification in case ΔBMD would have a value equal to zero. This parameter also showed the point of the y-axis (dependent variable axis, aortic calcification) through which the regression line passed. The regression parameter b_1=11.5049 signified that with each increase of one unit (g/cm^2) in ΔBMD, the aortic calcification score increased by 11.5049. The equation of simple linear regression showed the average coordination of aortic calcification and ΔBMD variations. With this equation, we obtained the evaluated (theoretical) aortic calcification values to compare with its empirical values.

Figure 3 shows a scatter plot of aortic calcification and ΔBMD. There was a positive association between these variables. The data from each of the 56 patients was displayed as a collection of colored points (red square, blue circle, and white circle) determining the bone strength presented by T-score. Each point had the value of one variable determining the position on the horizontal axis and the value of the other variable determining the position on the vertical axis. Linear regression lines computed by data acquired from different BMD patient's status (normal, osteopenia, and osteoporosis) were plotted and shown by different color and line styles (orange solid line, brown

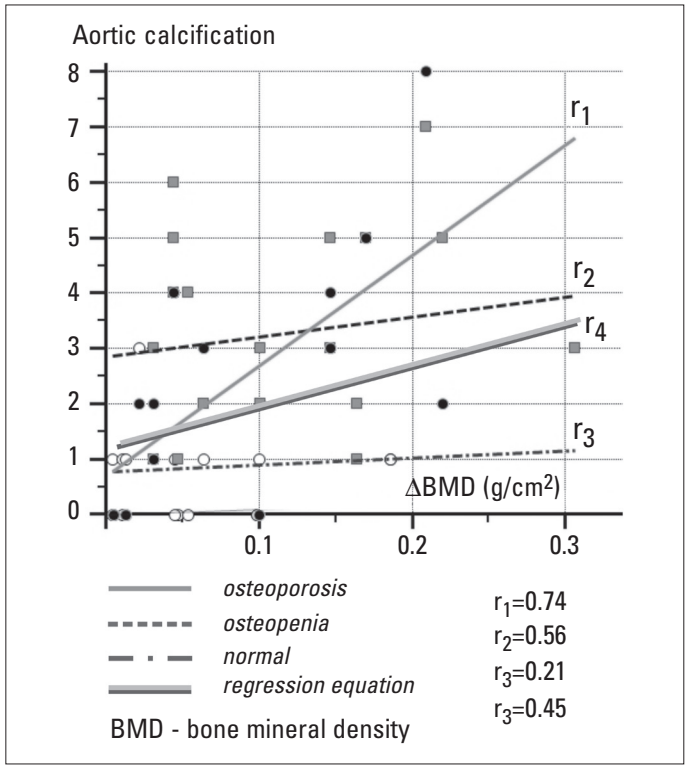


Figure 3. Scatter plot of ΔBMD and aortic calcification

dashed line, and blue dash-dot line). The linear regression line plotted with the double-colored line (red-purple) shows a positive correlation between aortic calcification and ΔBMD in the entire examined female group independent of their bone strength status (BMD). The strongest ΔBMD and AAC correlation is presented with the orange line of regression during osteoporosis and Pearson coefficient r_1=0.74 (p<0.00001). BMD and AAC correlation in normal bone density cases (blue dot-dashed regression line) had no statistical significance (r=0.21, p=0.121).

Assessments [standardized coefficient β (βst)], standard error of βst, t, and p-value) of the independent predictor (ΔBMD) or determinants (femoral neck BMD, diabetes, and hypertension) for increasing of AAC in postmenopausal women after backward multiple regression analysis are shown in Table 3. The p-values followed the order of statistical significance: ΔBMD (<0.0001), diabetes (0.0091), and femoral neck BMD (0.0241). There was no statistical significance of βst coefficients expressed by p-value for hypertension (0.0560) and spine BMD, smoking, BMI, and age with p>0.1. The coefficient of determination R^2 (0.4758) showed that 47.58% of the total variability was explained with the linear relation between aortic calcification and ΔBMD accompanied by other determinants, or that 47.58% from aortic calcification was dependent on ΔBMD as the predictor and other determinants (femoral neck BMD, diabetes, and hypertension). There was an inverse correlation (negative βst coefficient, βst=-3.1871) between the femoral neck BMD and AAC only. This means that any reduction in the femoral neck BMD results in an increased AAC.

We used discrimination, the ability of a model (estimation of cut-off point) to distinguish between patients with or without

Table 3. Multiple backward regression analysis of determinants of aortic calcification

Multiple regression				
Sample size	56			
Coefficient of determination R^2				0.4758
Residual standard deviation				1.5067
Regression equation				
Independent variables	Coefficient βst	Std. Error	t	P
ΔBMD, g/cm^2	13.5244	2.7833	4.859	<0.0001
BMD FN, g/cm^2	-3.1871	1.369	-2.328	0.0241
Diabetes	1.7008	0.6266	2.715	0.0091
Hypertension	0.8546	0.4366	1.957	0.0560

Variables not included in the model: Spine BMD-Smoking, Age and BMI.
BMD - bone mineral density; BMI - body mass index; FN - femoral neck; Std. Error - standard error.

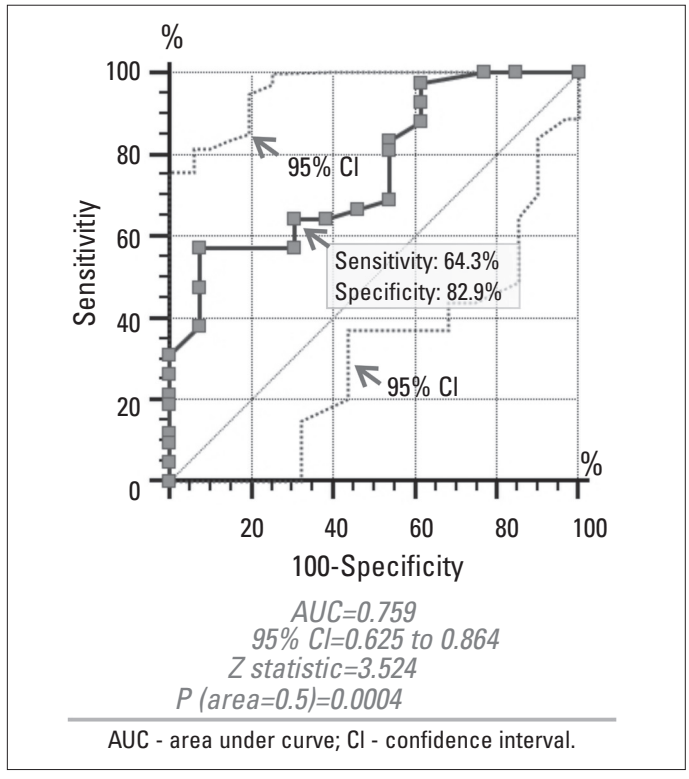


Figure 4. Receiver operating characteristics curves for ΔBMD as a prognostic diagnostic marker for AAC and area under curve (AUC)

calcification. We assessed them by receiver operating characteristic (ROC) curve analysis, a fundamental tool for diagnostic test evaluation. The area under the ROC curve (AUC) is a measure of how well a parameter can distinguish between the two diagnostic groups (with AAC/without AAC). ROC curves for ΔBMD as a prognostic diagnostic marker associated with AP DXA predicting the presence of AAC as detected by LLR, sensitivity, specificity, AUC, 95% CI for sensitivity and specificity, Z statistic, criterion value of ΔBMD variable, and p-value are shown in Figure 4.

Each point on the ROC curve represented a sensitivity/specificity pair corresponding to a particular threshold (ΔBMD in the detection of AC). The results we got by the ROC curve analysis were as follows: AUC (0.759), Z statistic (3.524), significance level (p=0.0004), sensitivity (64.3%), and specificity (82.9%). The ΔBMD cut-off point where the parts of sensitivity/specificity points were the highest was 0.094 g/cm^2. Because of the small number of participants, CI of sensitivity and specificity was too wide. The accuracy of this diagnostic test is fair (AUC=0.759).

Discussion

To our knowledge, this is the first cross-sectional study that investigates the relationship between ΔBMD and AAC in postmenopausal women. Several studies detect AAC by computed tomography (CT). We know that CT is currently the gold standard of AAC measurement, but it is limited by high radiation dose exposure. The study by Cecelja et al. (22) determines the accuracy of lateral-DXA scan in detecting AAC compared with CT in healthy women. In our study, we determined the accuracy of AP DXA in detecting AAC compared with LLR (at a subtracted BMD_{FN} from BMD_{LS}).

The lumbar spine BMD (0.833±0.157 g/cm^2) was greater than the femoral neck BMD (0.744±0.184 g/cm^2). This difference was statistically significant (p<0.0001). The reason for the greater BMD in the spine than the femoral neck may lie in the fact that DXA relied on measurement of the relative absorption of dual energy X-ray beams blindly projected through the body. The dense aortic calcification rather than the spine absorbs the X-ray causing a falsely elevated BMD reading (23, 24). The patients with a higher score of aortic calcification results with more X-ray absorption expressed with an elevated spine BMD value. Vertebral BMD is usually measured in the AP plane, though this method may falsely give high values in the presence of lumbar spondylosis or osteoarthritis, especially when associated with osteophytes and aortic calcification in the same time.

Sclerosis and joint narrowing had little effect on BMD at the lumbar spine or hip. The indirect effects of osteoarthritis on BMD are small and inconsistent across genders (25). Multiple regression analysis, including weight, age, and vertebral calcification scores, demonstrate a small but significant effect of osteophyte score on lumbar BMD (partial r^2=0.04; p=0.012) (26).

An advantage of our study is the fact that the association between aortic calcification and BMD was estimated in postmenopausal women, the period from which the prevalence of atherosclerosis and osteoporosis increases. Human association studies suggest that older age, chronic kidney disease, and osteoporosis are the most important risk factors for AAC (27). Walsh et al. (28) revealed that more severe AAC was associated with cardiovascular events. Kauppila et al. (17) investigated the association between AAC and cardiovascular disorders in the 2515 Framingham study participants followed-up for more than 20 years. They concluded from this study that AAC is a subclinical marker of atherosclerosis and an independent predictor of subsequent cardiovascular morbidity and mortality (29) because stiffer arteries and increased pulse wave velocity (PWV) when measured over the aorta. PWV does not increase during the early stages of atherosclerosis, as measured by intima-media thickness and non-calcified atheroma, but it increases in the presence of aortic calcification that occurs within advanced atherosclerotic plaques (30). Lebrun et al. (31), in a cross-sectional study among postmenopausal women, provides evidence that most of the established cardiovascular risk factors are determinants of aortic PWV. Increased PWV marks an increased risk of stroke, coronary heart disease, and death within 10-12 years.

Bone loss during menopause may result from a common etiologic factor such as estrogen deficiency (1). Arteries and bones are the target organs for estrogen. Estrogen receptors have been demonstrated on vascular endothelial and smooth cells, osteoblasts, and osteoclasts, suggesting a direct effect of estrogen on vascular and bone cells (32). Estrogen deficiency may have indirect effects on arteries and bone by the production of inflammatory agents, such as interleukin-1 and -6 and tumor necrosis factor, which are involved in atherogenesis and contribute to accelerated bone resorption (33).

Many different biomarkers, such as calcium-regulating hormones, vitamin D deficiency, serum calcium, calcium-phosphorus product and plasma homocysteine, contribute to accelerated bone resorption and atherosclerosis. The aim of our study was not the investigation of their effect on bone resorption and atherosclerosis but only to find an association between them. We found (by bivariate Pearson correlation) a significant positive correlation between aortic calcification and ΔBMD (r=0.449, p=0.0006), aortic calcification and hypertension (r=0.268; p=0.47), aortic calcification and smoking status (r=0.352, p=0.008) but a negative correlation between femoral neck BMD and age (r=-0.325, p=0.015), femoral neck BMD and BMI (r=-0.291, p=0.031) (Table 2). We found a positive correlation between aortic calcification as a dependent variable and ΔBMD as an independent variable (by linear regression analysis, R^2=0.2019, p=0.0006). We expressed the predictable power of subtracted BMD_{FN} from BMD_{LS} for aortic calcification detection by linear regression equation and its β coefficients. Each increase of one ΔBMD unit results in an elevated percent of detected aortic calcification by LLR. In other words, the aortic calcification score increases for 5.2 to 17.8 times for each single increase of ΔBMD in the true population not only in the participants in our study.

We presented the predictable power of the different stage of bone strength by three linear regression lines for normal bone, osteopenia, and osteoporosis, and the fourth, for a common predictable line for all postmenopausal women, independent of their bone mineralization stage (Fig. 3). The orange line of regression (presenter of osteoporosis) because of its bigger elevation angle compared with the brown and blue line angle (presenters

of osteopenia and normal bone state) has a stronger power in predicting AAC.

In the multiple regression analysis, we found an independent predictor (ΔBMD, p<0.0001) for aortic calcifications (Table 3). Routine LLR for the detection of aortic calcification of all women is not feasible for most populations; hence, the identification of a high-risk subset of women by DXA will be an important element of effective preventive strategies for bone resorption and atherosclerosis. By multiple regression analysis, we found diabetes as a determinant for increasing of AAC and femoral neck BMD as a determinant with inverse correlation with aortic calcification. Tanko et al. (34) found in a multiple regression model that AC significantly contributes to the variation in hip BMD (β=-0.10, p=0.004). Their study presents different results compared with those of our study (β=-3.19, p=0.02) because they did not estimate BMD diversity in two different sites, which is the aim in our study.

Arterial structure and function state changes as a result of the abnormal metabolic state accompanied with diabetes. The higher number of diabetes patients (with those suffering a vascular disease included) demonstrate abnormalities of vascular regulation and endothelial function (35). Normal nitric oxide loss together with local increase in these proinflammatory factors is associated with an increase in adhesion, leucocyte chemotaxis, transmigration, and transformation into foam cells, which in the latter process is augmented by a local oxidative stress increase. The earliest atheroma formation and calcification is foam cell transformation (36, 37). There was a positive correlation between ΔBMD and AAC; approximately 47.58% from the total variability was explained with the linear positive correlation between the above-mentioned covariates.

AP DXA imaging may therefore provide an important low-radiation tool for detecting patients at an increased risk of large artery stiffening, isolated systolic hypertension, and cardiovascular events. Cardiovascular disease remains the leading cause of death in women, with approximately 30% of cardiovascular events unexplained by conventional risk factors (17). During the last six months, we used Figure 3 as a nomogram [statistical predictive model that can provide the aortic calcification score (y-axis) based of the subtracted BMD_H from BMD_{LS} value], which we plotted from the DXA results. For example, in postmenopausal osteoporotic woman with ΔBMD of 0.2 g/cm^2 after reflexion on line for osteoporosis, we got 4.5 AAC score units on the y-axis. After LLR X-ray radiography in this woman, we found the AAC score to five, with a minimal error of 11.1%. In this way, we discovered patients who showed an increased risk for AAC, and we sent for the further verification of aortic calcification by X-ray LLR or CT.

AP DXA scans therefore provide a low-radiation method (only 0.001 mSv for DXA) compared with 8-10 mSv for abdominal CT and 1-1.5 mSv for LLR) (38) with high sensitivity (64.3%) and specificity (82.9%) to detect initial or extensive aortic calcification in postmenopausal women. This subtracting BMD DXA method provides a useful tool for detecting subclinical AAC compared with LLR using a simple, semiquantitative, and accurate scoring system with minimal radiation exposure dose and low cost.

Study limitations

The first limitation of this study was the small number of patients sampled. Recruiting male and female patients in sufficient numbers ultimately proved unfeasible. Due to the limitation of the current imaging techniques, we were unable to distinguish between intimal and medial aortic calcifications. CT is the gold standard of AAC detection and measurement despite the higher radiation dose exposure compared with radiography.

Using LLR instead of CT because of its higher accuracy is the second limitation of this study. The other limitation of this study includes the need for validation of the results in broader trial general populations. The last limitation of our study was because we did not evaluate the results of lumbar spine osteoarthritis on the available LLR to check its effects on the spine BMD results.

Conclusion

This AP subtracting BMD DXA method provides a useful proven tool for detecting and scoring subclinical and extensive AAC in postmenopausal women using a simple, semiquantitative, and accurate scoring system with minimal radiation exposure (0.7 mSv, 70 mrem-1) and low cost. Future prospective studies will be required to define the clinical implications of aortic calcification as detected by AP DXA.

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