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Effect of degenerative spinal and aortic calcification on bone density measurements in post-menopausal women: links between osteoporosis and cardiovascular disease?

L. M. BANKS, B. LEES,* J. E. MACSWEENEY & J. C. STEVENSON* Department of Diagnostic Radiology, Royal Postgraduate Medical School and *Wynn Institute for Metabolic Research, London, UK

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Abstract. The effect of spinal degenerative changes and aortic calcification on bone mineral density measurements was studied in 115 healthy early post-menopausal women. Lateral lumbar spine radiographs and quantitative computer tomography images were used to determine the presence and severity of aortic calcification and degenerative changes in the lumbar spine. Women with spinal degenerative calcification had higher spine bone density when measured by dual photon absorptiometry compared to those without calcification ($P < 0{\cdot}01$), but this was not reflected by the quantitative computer tomography or the proximal femur bone densities, suggesting that spinal calcification artefactually increases spinal bone density when measured by dual photon techniques. Women with aortic calcification had significantly lower quantitative computer tomography and proximal femur bone density compared to those without calcification (both $P < 0{\cdot}05$). These women may be at increased risk for both osteoporosis and cardiovascular disease, suggesting a common aetiological factor such as oestrogen deficiency.

Keywords. Aortic calcification, bone density, cardiovascular disease, osteophytes, osteoporosis.

Introduction

Dual photon techniques are now widely used in the measurement of bone density (BMD) in the lumbar spine and the proximal femur [1–3]. A number of centres [4–8] have assessed the apparent increase in anteroposterior (AP) spinal BMD measurements caused by degenerative osteoarthritic changes and aortic calcification when using dual photon absorptiometry (DPA) and dual energy X-ray absorptiometry (DXA) techniques. This apparent increase is due to the fact that these techniques measure an integral of cortical and trabecular bone and thus may include any extra-osseous calcification. None of these studies have compared BMD measurements by QCT with those by DPA or DXA. With QCT, a cross-sectional image is taken at the mid-vertebral level and localization of a region of interest (ROI) within the vertebral body permits a measurement of solely trabecular BMD [9]. Since this method of measuring BMD is not subject to the influence of extraneous calcification and degenerative changes, QCT could theoretically be regarded as the 'gold standard'. The development of lateral DXA scanning of the lumbar vertebral bodies has been suggested as a technique for circumventing some of these problems by avoiding any extraneous calcification that might influence the BMD values [10]. The aim of this study was to assess the influence of degenerative change and extra osseous calcification, as demonstrated on radiographs and QCT, on DPA BMD measurements in a group of healthy early post-menopausal women.

Correspondence: Linda M. Banks, Department of Diagnostic Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 ONN, UK.

Patients and methods

The study group comprised of 115 normal, healthy, Caucasian, post-menopausal women recruited for participation in a placebo-controlled, double-blind therapeutic study of the prevention of post-menopausal bone loss. The age range of the group was 49–64 years with a mean age (±SD) of $56 \pm 4{\cdot}1$ years. The women were all within 12 years of their menopause with a mean time since menopause (±SD) of $5 \pm 2{\cdot}8$ years.

Menopausal status was supported in each case by elevated gonadotrophin levels. None of the women were taking, or had taken in the previous 6 months, any form of medication that might affect bone mineral metabolism.

DPA measurements of the lumbar spine (AP) and proximal femur (femoral neck and Ward's triangle) were made using a Lunar DP3 (Lunar Corporation, Madison, WI, USA). QCT measurements of the lumbar spine were made using a Siemens Somatom 2 CT scanner (Siemens, Erlangen, Germany). L2-L4 was scanned by both techniques. All of the volunteers had lateral lumbar spine radiographs on the same day

as the BMD measurements. The precision of the DPA measurements was 1·3% for the lumbar spine, 1·9% for the femoral neck and 2·3% for the Ward's triangle region [11]. The DPA measurements were acquired and analysed by the same operator (BL). The QCT precision was 2·2% [9] and scans were performed and analysed by the same operator (LB). The QCT images were assessed for the presence of aortic calcification by a single observer (LB). A region of interest (ROI) was drawn around the aorta and those with an average Hounsfield Unit (HU) at one or more QCT levels (12 mm per vertebrae) of 40–75 HU were classified mild, 76–120 HU moderate and > 120 HU severe. From the lateral lumbar spine radiographs, the presence of osteophytes, aortic calcification, apophyseal joint changes and other extraneous calcifications was assessed by an experienced radiologist (JMcS). The severity of these changes were classified subjectively as mild, moderate or severe. These assessments were made without the knowledge of the BMD values.

From the radiographic and QCT findings, the women were initially classified into two groups, those with or without (group 1) any form of degenerative calcification. Those women with calcification present were further subdivided into one of three groups: group 2—only spinal degenerative calcification present (e.g. osteophytes, apophyseal joint changes, end-plate sclerosis) (Fig. 1A); group 3—only aortic calcification present (Fig. 1B); group 4—both spinal degenerative and aortic calcification present (Fig. 1C). This further subdivision allowed the effect of different types of calcification on BMD measurements to be examined.

Statistical analyses

Analysis of variance with linear contrasts was used to examine differences between group means in patient characteristics. Analysis of covariance was used to examine differences in mean bone density measurements using age, time since menopause, height and weight as covariates.

Results

From the radiographic and QCT images, 68 women were found to have some type of calcification present and 47 women had no visible calcification (group 1). The demographic data of these two groups are shown in Table 1. DPA spine BMD measurements were significantly greater in the group with calcification compared to the women with no calcification (group 1) even after adjusting for age, time since menopause, height and weight (Table 1).

Of the 68 women with calcification present either on the radiographs or the QCT images, 23 were found to have spinal degenerative calcification only (group 2), 23 had aortic calcification only (group 3) and 21 had both spinal degenerative and aortic calcification (group 4). One woman with calcification observed on her QCT image could not be assigned to a group as radiographs were not available. The demographic data for these three groups are also shown in Table 1.

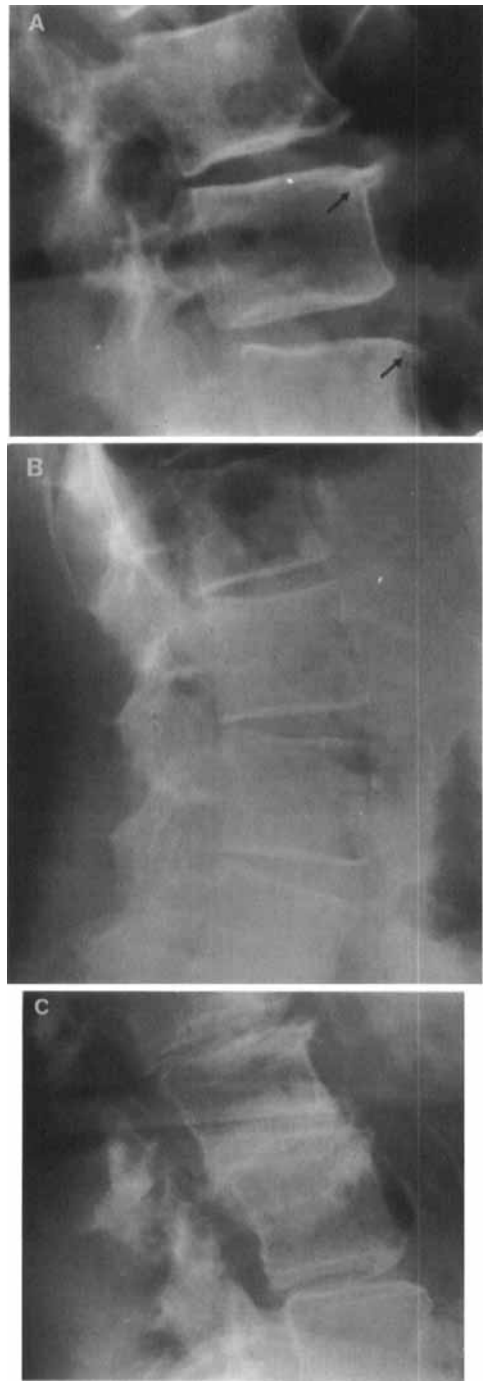

Figure 1. (A) Example of group 2. Lateral lumbar spine radiograph showing a moderate osteophyte on L3 and mild osteophyte on L4 (arrowed). (B) Example of group 3. Lateral lumbar spine radiograph showing aortic calcification at level of L1-L4 of moderate severity (moderate = 80–120 HU). (C) Example of group 4. Lateral lumbar spine radiograph showing both severe spinal degenerative changes and moderate aortic calcification.

The BMD measurements for the women with no calcification were compared with each group with calcification (Table 1). After adjusting the data for

Table 1. Patient demographic and BMD data (mean±SD)

	Group 1	Calcification group	Group 2	Group 3	Group 4
n	47	68†	23	23	21
Age (years)	54·6 (3·6)	57·1 (4·1)**	57·4 (4·1)**	56·4 (4·1)	57·7 (4·0)**
Time since menopause (years)	4·3 (2·4)	5·9 (2·8)**	6·0 (3·1)*	5·4 (2·6)	6.4 (2·8)**
Height (cm)	161·3 (6·6)	161·7 (5·1)	161·5 (4·7)	161·6 (4·7)	161·7 (5·4)
Weight (kg)	62·3 (7·1)	62·6 (7·9)	63·8 (8·4)	61·7 (9·0)	62·1 (5·7)
QCT (mg/cm^3)	107 (24)	99 (22)	103 (19)	91 (21)*	101 (23)
DPA-spine (g/cm)	1·086 (0·129)	1·129 (0·140)*	1·152 (0·117)**	1·045 (0·094)	1·183 (0·158)**
DPA-femoral neck (g/cm)	0·842 (0·104)	0·825 (0·084)	0·843 (0·095)	0·784 (0·076)*	0·847 (0·067)
DPA-Ward's triangle (g/cm)	0·726 (0·124)	0·710 (0·105)	0·726 (0·113)	0·672 (0·099)	0·728 (0·092)

Group 1, women with no calcification; calcification group = all women with calcification (†total $n = 68$ but X-rays unavailable in one patient); Group 2, women with spinal calcification only; Group 3, women with aortic calcification only; Group 4, women with spinal and aortic calcification. Analysis of covariance between group 1 and groups with calcification with age, time since menopause, height and weight as covariates; $^*P < 0{\cdot}05$, $^{**}P < 0{\cdot}01$.

age, time since menopause, height and weight, the mean QCT BMD was significantly lower in group 3 compared to group 1 ($P < 0{\cdot}05$) and BMD was also significantly reduced in the femoral neck ($P < 0{\cdot}05$). The mean DPA spine BMD was significantly increased in group 2 and group 4 (both $P < 0{\cdot}01$), but this was not observed in the QCT BMD measurement or the DPA femoral neck and Ward's triangle measurement.

The radiographs showed the presence of apophyseal joint changes in 13 (11%) of the women and osteophytes were seen in 38 (33%). Other extraneous calcifications such as sclerosis of the end-plates were seen on the radiographs of four women (4%). On the radiographs, aortic calcification was observed in 19 (17%) of the women compared to 45 (39%) noted on the QCT images. The distribution of the severity of each type of calcification is summarized in Fig. 2. Mild and moderate calcification was more common than the severe type of calcification.

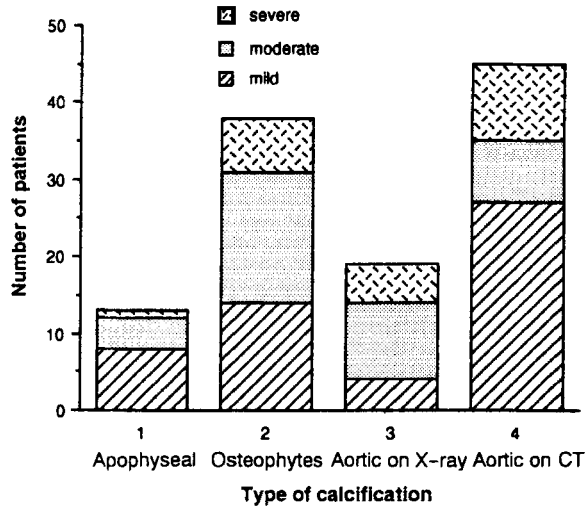

Figure 2. Distribution of the severity of calcification seen on QCT scans and radiographs.

Discussion

In agreement with the findings of others [4–7] we found that degenerative changes in the spine have a more significant effect than aortic calcification on AP DPA spine measurements. However, a number of new observations arise from our study. We have shown that even in a healthy population of early post-menopausal women entering a clinical trial, over half the women (59%) had some type of spinal degenerative change. We found that the women with calcification were older in terms of both chronological and menopausal age compared to the women with no calcification confirming other studies [5,12]. However, as far as we are aware, no other study has examined the effects of time since menopause on degenerative change in relation to BMD.

The women with aortic calcification alone had a significantly lower QCT BMD compared with women with no calcification and this was also reflected in the DPA proximal femur BMD measurements. Reid *et al.* [5] found no effect of aortic calcification on spine BMD in normal women. Others [4,6,7,12] have found significant increases in spine BMD but these were most pronounced when severe calcification was present. One explanation for our finding of reduced BMD in women with aortic calcification is that the other studies measured spine BMD by dual photon techniques only, whereas we measured BMD by QCT which does not include extraneous calcification in its measurement. In the other studies, a reduction in BMD in the proximal femur was not observed, but this may be due to differences in the age and gender of the populations studied. Knight *et al.* [13] have suggested that where osteoarthritis of the hip is present proximal femur BMD may be increased compared with projected control values. A higher incidence of early aortic calcification was found on QCT images (39%) compared with that found on radiographs (17%). The incidence of aortic

calcification found on the radiographs was similar to that reported by Elkeles [14] who found an incidence of 13% on radiographs of women aged between 50 and 60 years. The improvement in detection of aortic calcification using QCT images instead of radiographs was due to the superior spatial resolution of computed tomography images.

We found that women with aortic calcification also have a high incidence of osteopenia, as reported previously [15–17]. In these early studies, low bone mass was determined using radiographs of the spine and hand, and the presence of aortic calcification was noted on radiographs of the spine. Using more accurate techniques our study confirms these early observations. Frye *et al.* [12] demonstrated a significant negative correlation between the number of calcified aortic plaques and spine BMD by DPA in an age-adjusted random sample of 200 women. Some workers have suggested that the high incidence of aortic calcification with low bone mass occurs purely by chance as both conditions worsen with age [16]. However, Browner *et al.* showed that women with lower BMD have a higher mortality from cardiovascular disease (CVD), especially strokes [18]. Witteman *et al.* [19] found that, after adjustment for age and other indicators of CVD risk, women with a natural menopause had a 3·4 times higher risk of atherosclerosis (determined by radiographic detection of calcified deposits in the aorta) than premenopausal women. Similarly, after adjustment for age, the risk of osteoporotic fracture (determined by BMD measurements) is also increased after the menopause [20]. It is possible that these women are more at risk for both osteoporosis and CVD, suggesting a common aetiological factor such as oestrogen deficiency. We were surprised that we did not find a reduced bone density in the group with both aortic and spinal calcification as we did in the group with aortic calcification only. One explanation for this might be that where degenerative changes in the spine are present there are reactive sclerotic changes of the bone causing an increase in bone density in cortical and trabecular bone [21].

As a group, the women with degenerative calcification had higher DPA spine BMD measurements although this was not reflected by the QCT or DPA proximal femur BMD measurements, suggesting that this was not a true increase in BMD but that spinal degenerative calcification was artefactually affecting the measurement. This confirms other studies [4–8], although the extent to which BMD is affected varies according to the age and gender of the population studied. The degenerative changes found in this population were mostly of the mild to moderate category. Accordingly, when studying an older population these changes may become more severe [12,19,22]. These influences on BMD are important to consider when measuring BMD using DPA or by the more recent DXA technology, especially in longitudinal studies where such degenerative changes may progress and mask 'true' changes in BMD. The use of QCT for measuring BMD will certainly circumvent these problems but this technique is not as widely available as DPA and DXA. It has been suggested that lateral DXA scanning may also avoid problems caused by degenerative change. However, the precision of lateral measurements is generally poorer than that of AP [23] but Slosman *et al.* [24] showed that precision may be increased by altering the technique from decubitus to supine lateral scanning.

In conclusion, we found that the majority of healthy post-menospausal women entering a clinical trial had some type of spinal degeneration or aortic calcification. Spinal degenerative calcification artefactually increased DPA spinal BMD measurements. The presence of aortic calcification was associated with reduced BMD, suggesting increased atheromatous disease risk in patients at risk from osteoporosis.

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