Longitudinal changes in bone mineral density, bone mineral content and bone area at the lumbar spine and hip in postmenopausal women, and the influence of abdominal aortic calcification

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ABSTRACT

Longitudinal studies often report that spine bone mineral density (BMD), measured by DXA, is stable in older adults, which has been attributed to osteophyte development and the presence of aortic calcification. A decline in projected spine area as a result of loss of intervertebral disc height might also contribute to higher BMD. We utilised data from 297 postmenopausal women (mean 73 years) who had DXA measurements of the lumbar spine, total hip and femoral neck 5 years apart, and abdominal aortic calcification scoring from vertebral morphometry. BMD declined by -4.4% at the total hip and -3.9% at the femoral neck ($p < 0.001$), but did not change at the spine (-0.5%, $p = 0.12$). In contrast, bone mineral content (BMC) declined by -4.0% at the total hip, -2.5% at the femoral neck and -1.7% at the spine (all $p < 0.001$). Bone area increased by 0.5% at the hip and 1.6% at the femoral neck but declined by -1.2% at the spine (all $p < 0.001$). 43% of the cohort had abdominal aortic calcification (AAC) present at baseline. The presence of AAC at baseline was not related to changes in BMD or BMC at the total hip or femoral neck, nor to BMD at the spine. However, women with AAC present had a smaller loss of BMC at the spine than those without (-0.8% versus -2.4%, $p = 0.03$). AAC score increased more over 5 years among those with AAC at baseline than those without (0.28 versus 0.16, $p = 0.036$). Thus, the stability of spine BMD is the result of both a loss of projected bone area (as a result of intervertebral disc changes and/or a decrease in projected area of the vertebral bodies) and the effects of aortic calcification. Future clinical trials should consider assessing changes in spine BMC as a more informative index of spine mineral status.

1. Introduction

Loss of volumetric BMD at the spine, assessed by quantitative computed tomography, starts during the third decade of life and accelerates during the perimenopausal period and in older age (Riggs et al., 2008). Conversely, longitudinal studies using dual energy X-ray absorptiometry (DXA) often report no change in areal BMD at the spine in older adults (Reid et al., 2008; Steiger et al., 1992; Melton et al., 2000; Warming et al., 2002; Jones et al., 1994). This has been attributed to age-related degenerative changes at the spine increasing the amount of mineral in this area, falsely inflating BMD values. These changes include osteophyte formation (Reid et al., 1991; Orwoll et al., 1990; Jones et al., 1995), and end-plate (Muraki et al., 2004) and facet-joint sclerosis (Drinka et al., 1992), and possibly calcification of the

aorta overlying the spine (Banks et al., 1994; Frye et al., 1992). Another characteristic of aging is the loss of body height (Forsmo et al., 2007); due in part to a reduction in the height of the spine through degeneration of the intervertebral discs (Pfirrmann et al., 2006) and the presence of vertebral deformities (Tobias et al., 2007). Areal BMD measured by DXA, is the ratio of bone mineral content (BMC) to the two-dimensional projection of the bone area. Reduction in the projected area of the lumbar spine might also be a major contributor to higher BMD values in older adults, since a decline in mineral could be masked by a concurrent decline in area.

We have utilised data from the placebo group of a randomised controlled trial of normal postmenopausal women, to examine changes in BMD, BMC and bone area at the lumbar spine over 5 years and compare them with changes at the total hip and femoral neck, with a

view to determining the comparative contributions of changes in bone area and abdominal aortic calcification (AAC) to the apparent stability of spine BMD in older women.

2. Methods

This cohort of normal postmenopausal women is from the placebo group of a randomised trial of postmenopausal women. The Methods have been described (Reid et al., 2005). Briefly, participants were recruited by mail-outs using the electoral roll. At recruitment, participants were aged > 55 years, were not using calcium supplements or receiving therapy for osteoporosis, and were free of major ongoing systemic disease. Their serum 25-hydroxyvitamin D was > 25 nmol/L. Their lumbar spine bone density was not below the age-appropriate normal range. Informed consent was obtained from all individual participants included in the study.

Exclusions from the present analysis were: use of bone-active medications (bisphosphonates, prednisone or hormone replacement therapy) during the study period; use of calcium supplements during the study period; incident vertebral fracture during the study; follow-up BMD on a different densitometer from baseline; major deformity or degenerative artefact in spine DXA scans. A total of 297 participants were included in the present analysis. For this additional analysis formal consent was not required.

2.1. Measurements

At baseline, height was measured using a Harpenden stadiometer (Holtain, Crymych, United Kingdom) and weight using electronic scales. Fracture history and smoking status were assessed by questionnaire. Serum 25-hydroxyvitamin D concentrations were measured by radioimmunoassay (Diasorin, Stillwater, MN). At baseline and 5 years, scans of the lumbar spine (L1–L4) and total hip were carried out, and vertebral morphometry performed, using a Lunar Expert dual-energy X-ray absorptiometer (GE-Lunar, Madison WI, software version 1.7). The coefficients of variation for measurement of total hip and lumbar spine BMD in our laboratory are 1.1 and 1.4%, respectively.

The AAC-8 score was calculated from vertebral morphometric images as described elsewhere (Wang et al., 2010). The AAC-8 score is the sum of the total length of calcification of the anterior and posterior aortic walls in front of the L1–4 vertebral segments. For each wall, the aggregate length of calcification is scored between 0 and 4 relative to vertebral body height. Absent calcification is scored as 0, and if the aggregate length of calcification is 1 or less vertebral body height, the score is 1, and so on. The maximum score is 8 when the two walls are combined. The present analysis only considered AAC as present (AAC-8 score ≥ 1) or absent (AAC-8 score = 0).

2.2. Statistical analyses

Data are presented as mean (SD) or mean (95% CI) as indicated. Change from baseline was tested using Student's related group t-test overall. Student's independent group t-test was used to compare variables between those with and without aortic calcification. Aortic calcification and the change in aortic calcification are ordinal variables so correlations were sought using Spearman's test and difference between groups and change over time using non-parametric methods (Wilcoxon and sign test respectively). Since all comparisons were pre-planned no adjustment for multiplicity was performed to the critical p value (0.05). SAS (v9.4 SAS Institute Inc., Cary, NC, USA).

3. Results

The baseline characteristics of participants are presented in Table 1. Changes in spine, femoral neck and total hip BMC, BMD and bone area are presented in Fig. 1. BMD declined from baseline by −4.4%

Table 1
Baseline characteristics.

Characteristic	Mean (SD)
N	297
Age (year)	73 (4)
Height (cm)	159 (6)
Weight (kg)	67 (11)
BMI (kg/m^2)	26.6 (4.0)
Serum 25-hydroxyvitamin D (nmol/L)	54 (17)
Current smokers n (%)	6 (2.0%)
Prevalent fracture n (%)	110 (37.0%)
Lumbar spine	
BMD (g/cm^2)	1.03 (0.17)
BMC (g)	58.80 (11.8)
Bone area (cm^2)	56.65 (5.30)
Total hip	
BMD (g/cm^2)	0.88 (0.14)
BMC (g)	28.97 (4.92)
Bone area (cm^2)	32.99 (2.36)
Femoral neck	
BMD (g/cm^2)	0.83 (0.12)
BMC (g)	4.02 (0.61)
Bone area (cm^2)	4.84 (0.32)
Abdominal aortic calcification score n (%)	
0	166 (57%)
1–2	102 (35%)
3–6	24 (8%)
7–8	0 (0%)

Data are mean (SD) unless stated otherwise. BMD = bone mineral density; BMC = bone mineral content.

(95%CI −4.9 to −3.9%) and −3.9% (95%CI −4.5 to −3.3%) at the total hip and femoral neck (p < 0.0001 for each), respectively, but did not change at the lumbar spine (−0.5%, 95%CI −1.2 to 0.2%, p = 0.15). In contrast, BMC declined from baseline at all three sites (p < 0.0001). Percentage changes in BMC were similar at the femoral neck (−2.5%, 95%CI −3.1 to −1.8%) and lumbar spine (−1.7%, 95%CI −2.5 to −1.0%), which were smaller than that at the total hip (−4.0%, 95%CI −4.5 to −3.4%). The projected bone area at all three sites changed from baseline over 5 years (p < 0.0001, for each). The areas of the total hip and femoral neck increased from baseline by 0.5% (95%CI 0.2 to 0.7%) and 1.6% (95%CI 1.1 to 2.1%) respectively, while the area of the lumbar spine declined by −1.2% (95%CI −1.7 to −0.6%).

Forty-three percent of participants had AAC present at baseline. Participants with AAC were not different from those without AAC with respect to any of the variables in Table 1 except for total hip area which was a significantly greater in those without AAC (33.3 cm^2 versus 32.6 cm^2 in those with AAC, p = 0.007). Changes in total hip and femoral neck BMD and BMC were similar among those with versus without AAC at baseline. At the lumbar spine, loss of BMC was significantly less among those with AAC at baseline (−0.8%, 95%CI −1.7 to 0.2%) compared with those without (−2.4%, 95%CI −3.5 to −1.3%). Changes in BMD at the spine by AAC status were not significantly different among those with AAC at baseline (0.2%, 95%CI −0.7–1.1%) versus those without (−0.9%, 95%CI −1.9 to 0.1%) (Fig. 2).

Forty-nine percent of participants had AAC present at 5 years. AAC score increased by 0.21 units from baseline to 5 years (p < 0.0001). Change in AAC score was greater among those with AAC present at baseline than among those without (0.28 versus 0.16 units, p = 0.036). Change in AAC score was not correlated with change in BMD or BMC at the femoral neck, total hip or lumbar spine at 5 years; however our ability to correlate change in AAC score with these endpoints was limited as AAC score did not change in the majority of participants (75%), or increased by only one unit (18%).
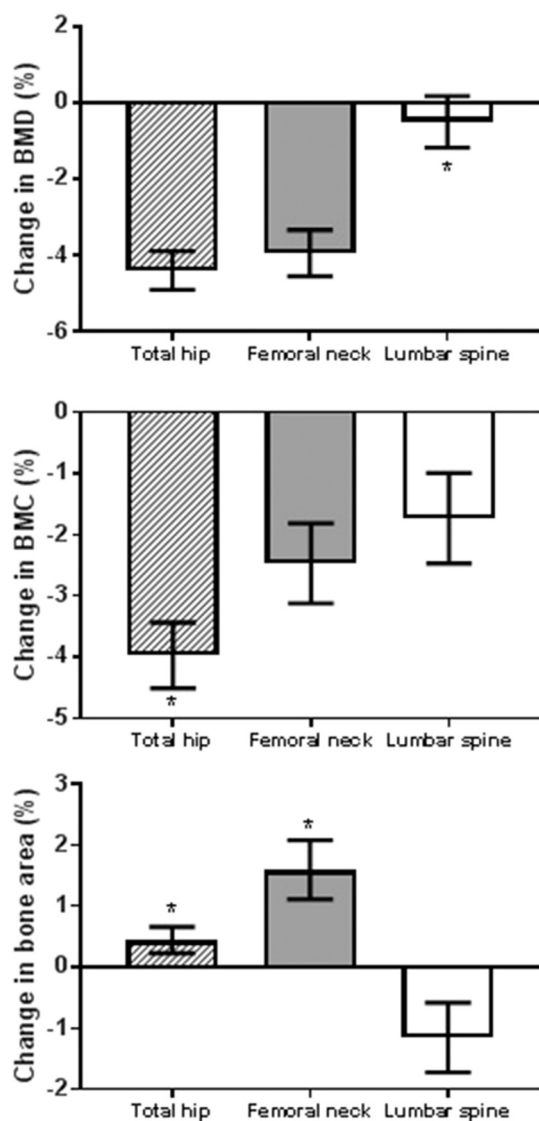
Fig. 1. Percentage changes in a) bone mineral density (BMD) b) bone mineral content (BMC) and c) bone area at the total hip, femoral neck and lumbar spine over 5 years in 297 normal postmenopausal women, data are mean ± 95%CI, *significantly different from all other sites, p < 0.0001.
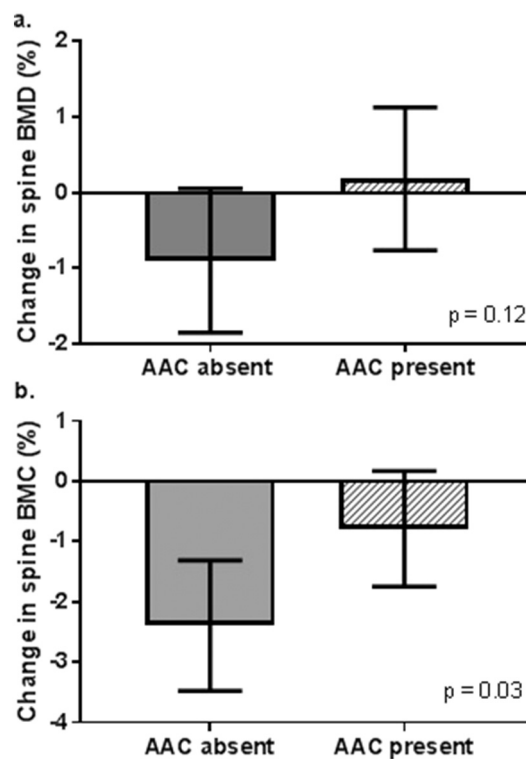

Fig. 2. Percentage changes in a) spine bone mineral density (BMD) and b) spine bone mineral content (BMC) over 5 years in 297 normal postmenopausal women by absence or presence of abdominal aortic calcification (AAC) at baseline, data are mean ± 95%CI, p values are for comparisons between women with or without AAC.

4. Discussion

Consistent with what has been reported in previous longitudinal studies of older men and women (Melton et al., 2000; Warming et al., 2002; Jones et al., 1994), we found that BMD at the lumbar spine did not change over 5 years, while BMD at the femoral neck and total hip declined by 2–4%. The stability of spine BMD in older adults has been attributed to age-related accumulation of mineralised artefacts in the spine. However, in the present analysis, we found that BMC at the lumbar spine significantly declined over 5 years, and that the rate of loss was similar to that at the femoral neck. Thus, differences in the rate of BMD loss were due to differences in the change in bone area: that is, the area of the femoral neck increased over this time, while the area of the lumbar spine declined. These findings suggest that differences in the rates of loss of BMD at the spine and hip may not be entirely explained by growth of spinal osteophytes, and that alterations in bone area also play a role.

The area of the lumbar spine measured by DXA includes the vertebral bodies and the intervertebral spaces, and a reduction in the area of the spine might reflect a reduction in the area of either component.

Intervertebral disc degeneration is common among older adults, although the estimated prevalence varies widely, probably due to inconsistencies in its definition (Battie et al., 2004). One study estimated the prevalence of disc degeneration among adults aged > 50 years to be ~90%, with the lumbar spine the area most likely to be affected (Teraguchi et al., 2014). Disc degeneration is associated with a loss of disc height (Pfirrmann et al., 2006). Vertebral fractures are also associated with a loss of height (Tobias et al., 2007); however, women who suffered a vertebral fracture (defined as reduction in vertebral height of > 20%), were excluded from our analysis. In cross-sectional studies, decreases in vertebral body height are reported across increasing age groups (Rea et al., 1998; Diacinti et al., 1995; Evans et al., 1993). Conversely, a prospective study over 15–20 years found no change in vertebral dimensions with age (Davies et al., 1989), suggesting that increasing body height across generations may explain some or all of the cross-sectional difference in vertebral height. Thus, while decreasing height of the intervertebral discs seems most likely to explain the reduction in lumbar spine area, it is also possible that a reduction in vertebral body height explained or contributed to the reduction in spine area.

Studies have reported conflicting findings with regards to whether lumbar spine BMD is artifactually increased by calcification of the aorta overlying the spine, with some reporting an effect of calcification on spine BMD (Banks et al., 1994), while others have reported a minimal (Frye et al., 1992) or null contribution (Reid et al., 1991; Drinka et al., 1992). We found that loss of BMC at the spine was significantly smaller, and the increase in AAC greater, among those with AAC present at baseline than among those without, suggesting that calcification of the aorta is contributing to the quantum of mineral measured at the spine. Indeed, the loss of BMC at the spine among those without AAC present at baseline (−2.4%) was very similar to that in the entire cohort at the femoral neck (−2.5%). Although the pattern of change in spine BMD

was suggestive of greater loss among those without AAC, the difference was not significant.

Strengths of this study were the measurement of BMD, BMC and bone area over a 5 year period in a cohort free from bone-active medications and major diseases. As this study was performed in healthy, predominantly white, postmenopausal women, these findings might not apply to men or other age or ethnic groups. The prevalence and severity of AAC in our study was less than that in studies in women of a similar age (Szulc et al., 2015; Lewis et al., 2018), as well as older women (Schousboe et al., 2008) and men (Szulc et al., 2008), and the present findings may underestimate any influence of AAC on spine BMD measurements in other populations. While the presence of AAC influenced spine BMC loss, we were not able to examine whether other degenerative changes at the spine (such as changes in osteophytes) also contributed to BMC or BMD. Changes in the projected area of the spine and the presence of aortic calcification may be just two of several age-related changes that could confound lumbar spine BMD measurements to some degree. We did not directly measure changes in intervertebral disc height, so we were unable to determine whether the decline in lumbar spine area was explained by decreasing height of intervertebral discs or a reduction in vertebral body area. Studies using higher resolution radiographic techniques, such as plain radiography or QCT, have the potential to examine this question with greater precision. It is possible that changes in soft tissue mass during follow-up might have changed the magnification of images (Pocock et al., 1997) impacting on assessment of bone area, but this effect is likely to be minimal since mean body weight during follow-up reduced by only 0.9%. A weight loss of this magnitude projected over the area of the trunk and thighs (almost 1 m^2) would reduce the height of the spine above the scanning table by approximately 0.7 mm, *increasing* magnification of the image by about 0.1%, whereas a 1% reduction in bone area is reported here. Any such magnification change would also apply to the hip where we see increases in bone area, demonstrating that there is a biological difference between these sites, not simply a measurement artefact. These arguments are supported by a further analysis of a sub-group of 277 women from this cohort selected to have a mean weight change of 0.009 kg, in which the changes in area at the three scanning sites were nearly identical to those shown in Fig. 1 (data not shown).

In summary, despite reductions in BMD over 5 years being greater in the proximal femur than in the spine, we found that reductions in BMC at the spine and femoral neck were similar, and that the differences in BMD changes were due, at least in part, to differences in changes in bone area. Future studies of longitudinal changes in spine BMD, including clinical trials, should consider also examining spine BMC (despite its poorer precision), as a decline in bone area, secondary to decreasing height of the intervertebral discs and/or a decrease in vertebral body area, appear to mask a decline in mineral. Calcification of the aorta also influences spine BMC measurements.

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Transparency document

The Transparency document associated with this article can be found, in online version.

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