EXTENDED REPORT

Increased bone mineral content and bone size in the femoral neck of men with hip osteoarthritis

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Objectives: Even though clinical findings support the idea that hip osteoarthritis (OA) is associated with increased bone mineral density (BMD), the subject remains controversial. This study was therefore initiated to investigate the relation between the severity of hip OA and femoral and calcaneal BMD.
Methods: On the basis of the American College of Rheumatology criteria on classification of OA of the hip, 27 men (aged 47–64 years) with unilateral or bilateral hip OA and 30 age matched randomly selected healthy men were studied. Plain radiographs were graded using Li's scale from 0 (no OA) to 4 (severe OA). According to the side of the highest radiographic score from the patients with clinical hip OA, 29.6% had grade 1, 29.6% grade 2, and 40.8% grade 3 OA. Bone mineral content (BMC), areal BMD (BMD_{areal}), and bone dimensions (area and width) were measured by dual *x* ray absorptiometry at the proximal femur. BMD_{areal} of the calcaneus was measured from the central area of the bone. Volumetric measurements from magnetic resonance images of the femoral neck were used to create a BMD measure that was corrected for the femoral neck volume (BMD_{mri}).
Results: There were no differences in weight, or body mass index between the study groups. There were no significant BMD_{areal} differences in any of the subregions of the proximal femur (femoral neck and trochanter) or calcaneus between the OA and control groups. Neither did the BMD_{mri} of the femoral neck differ between the groups. However, the BMC of the femoral neck was 18% higher ($p<0.01$) in patients with OA than in controls. Similarly femoral neck bone width and volume were 9% and 18% respectively higher ($p<0.001$) in patients with OA.
Conclusions: The results suggest that men with hip OA have larger femoral neck size and consequently higher BMC than healthy controls matched for age and sex. There is no significant difference in femoral neck BMD (BMD_{areal} or BMD_{mri}) between the groups. Furthermore, increased BMD_{areal} was not found in the peripheral skeleton. These findings suggest that hip OA is not associated with an increase in BMD_{areal} in the femoral neck. However, the increase in BMC and bone size in patients with hip OA may play a part in the pathogenesis of the disease.

Bone changes are thought to be an important element in the pathogenesis of osteoarthritis (OA).[1–4] According to Radin *et al*,[1] in OA, the thickening and stiffening of bone results from the repair of subchondral bone microfractures, caused by repetitive impact loading of the joint. This in turn leads to degeneration and loss of articular cartilage from stiffened bone ends. On the other hand, in osteoporosis it has been postulated that the less dense bone absorbs load more efficiently than normal bone so that less stress is transmitted to the overlying articular cartilage.[5] Whether changes in the cartilage or bone come first in OA remains an open question.[3 4 6]

Cross sectional studies have shown that patients with hip[7–11] or spine[12–14] OA have greater local bone mineral density (BMD) than healthy controls matched for sex and age. The evidence suggests that patients with hip OA have 3–10% greater femoral neck BMD than controls.[8–10] Femoral neck BMD has been observed to increase in early,[11] moderate, or severe hip OA.[8 10] This association is also supported by the inverse relation between osteoporosis and OA and with a possible negative association between OA and hip fracture.[5 15] Even though these clinical findings support the idea that OA is associated with increased local BMD, the subject remains controversial.[3 5] In some studies on hip OA, differences in the BMD did not reach statistical significance after correction for body weight or were not observed at all.[13 16] Bruno *et al*[11] also noticed that hips with Kellgren-Lawrence scores of 1 or 2 had increased BMD throughout the proximal femur, but as the disease progressed, the BMD declined.

A correlation between peripheral radiographic OA findings (knee, hip, and spine) and BMD measurements from different skeletal regions, or from the whole body, has been examined.[12 13 17–22] For example, it has been reported that the BMD of the second metacarpal bone, forearm, or total body was increased in patients with hip, knee, or spine OA compared with control subjects.[12 13 18 19 22] However, Solomon *et al*[21] observed that the BMD of the second metacarpal was not increased in all patients with OA. Then Carlsson *et al*[20] noticed that the BMD of the trabecular but not the cortical bone was increased in patients with OA. In addition, Alhava *et al*[17] observed that the BMD of forearm bones, or the second metacarpals, was not increased in patients with hip OA compared with controls. In patients with primary generalised OA, no significant correlation has been noticed between BMD and OA.[22–24] Thus there is no clear evidence that hip OA is associated with an increase in BMD.

The aim of this study was to test the hypothesis that the BMD of the proximal femur in hip OA differs from that in healthy subjects. Using dual *x* ray absorptiometry (DXA), we examined the pattern of bone mass and bone size in the proximal femur. To examine whether hip OA is associated with a generalised change in BMD, peripheral DXA measurements were also carried out on the calcaneus. One aim of this study

Abbreviations: OA, osteoarthritis; BMD, bone mineral density; BMC, bone mineral content; DXA, dual *x* ray absorptiometry; MRI, magnetic resonance imaging; ROI, region of interest.

Table 1 Clinical characteristics of the control and osteoarthritic (OA) subjects

	Control group (n=30)			OA group (n=27)		
	Mean	SD	Range	Mean	SD	Range
Age (years)	56.3	4.5	(47–64)	56.2	4.9	(47–64)
Weight (kg)	81.4	9.6	(63–105)	83.9	11.3	(60–116)
Height (cm)	173.8	4.8	(165–185)	176.7	4.8	(168–186)*
BMI (kg/m^2)	26.9	2.9	(20.6–33.9)	26.9	3.5	(21.3–37.4)
Duration of OA symptoms (years)				6.4	5.2	(1–25)

There were no differences in age, body weight, or body mass index (BMI) between the groups (Student's *t* test). *p <0.05, Student's *t* test.

was to improve the practical implementation of DXA by converting areal BMD (BMD_{areal} (g/cm^2)) into a volumetric measurement (BMD_{mri} (g/cm^3)) by using magnetic resonance imaging (MRI) analysis of bone size. This was important because the DXA method does not correct for the anteroposterior depth, and when values are expressed as BMD_{areal} rather than a volumetric measurement, the data obtained from DXA are greatly influenced by the size of the bones.[25] It is thought that failure to control for femoral neck size can lead to erroneous interpretation of BMD values obtained by DXA.[25]

METHODS

Subjects and selection

A total of 27 male patients (age 47–64 years) were selected by the clinical criteria of unilateral or bilateral hip OA. Subjects either had pain in the hip in the preceding month or functional impairment—for example, limitation of hip motion or stiffness of the joint—according to the clinical criteria of the American College of Rheumatology (table 1).[26] They were recruited by advertising in the press or were selected from those waiting for a total hip replacement in Kuopio University Hospital (three subjects). The recruitment period was April 1999 to May 2000 and the region of recruitment was the city of Kuopio and nearby areas. The patients with OA responded positively. Exclusion criteria included a history of trauma of the hip joint or the pelvis region, a previous hip fracture or hip surgery, a hip joint infection, and a congenital or developmental disease. Furthermore, subjects were excluded if they had the following diagnoses, symptoms, or medication: cancer, rheumatoid arthritis, endocrine disease, epilepsy, Parkinson's disease, cerebrovascular disease, polyneuropathia, neuromuscular disorder, debilitating cardiovascular disease in spite of medication, atherosclerosis of the lower extremities, painful knee OA, previous back surgery, painful back problem (spinal stenosis or sciatica due to lumbar disc herniation), or were taking corticosteroids. These conditions might have interfered with the evaluation of pain and function of the hip joints. Possible polyneuropathia and acute severe sciatica were also excluded by electromyography.

Thirty healthy age matched 47–64 year old men living in the city of Kuopio and nearby areas were randomly selected from the population register to be used as controls. They were contacted by mail and interviewed (by JA and MA). They had neither unilateral nor bilateral hip OA according to the radiographic criteria used in this study (see below), nor hip pain or functional impairment. Exclusion criteria for the control subjects were the same as for the patients with OA. Initially 217 men randomly selected from men aged 47–64 years (n=10 175) living in Kuopio and nearby areas were contacted. Some (12.4%) could not be reached either by letter or telephone, 67.7% did not meet the health criteria, and 3.2% refused. Of those who fulfilled the inclusion criteria, two were excluded after electromyography which showed polyneuropathia, and four were excluded because of a non-symptomatic radiographic OA score of 1 in one of the hip joints.

All subjects completed the questionnaires, including medical history and symptoms of the hip joints. Duration of OA symptoms (years) was asked for. The subjective severity of hip pain was rated on a visual analogue scale, the results of which were reported in centimetres (range 1–10 cm; end points: no pain and unbearable pain). Lequesne's algofunctional index (points 0 (minimum)–21 (maximum)) was used to describe the subjective severity of hip disability.[27] Anthropometric measurements were taken including height (cm) and weight (kg). Body mass index was calculated as the weight in kilograms divided by height squared (kg/m^2). Written consent was obtained from each participant. The study was approved by the ethics committee of the Kuopio University Hospital.

Radiographic measurements and grading

Supine anteroposterior and Lauenstein radiographs were taken for both hips as well as radiographs of the pelvis during weightbearing. The radiographs were evaluated blind by a trained radiologist (LN) using the Kellgren-Lawrence grading radiographs of the Atlas of Standard Radiographs[28] and Li's OA scale for the hip,[29] which is modified from the Council for International Organisations of Medical Sciences scale (Kellgren-Lawrence grading system)[30] as follows: grade 0=normal; grade 1=possible narrowing of joint space and possible osteophytes around the femoral head; grade 2=definite narrowing of the joint space, definite osteophytes, and slight sclerosis; grade 3=appreciable narrowing of the joint space, osteophytes, cyst formation, and deformity of the femoral head and acetabulum; grade 4=gross loss of joint space with sclerosis and cysts, appreciable deformity of the femoral head and acetabulum, and large osteophytes. Two hip OA gradings were recorded for each patient in repeated sessions on separate days with a one week interval. Grade $\geqslant 1$ was considered positive for radiological hip OA. The hip with the highest radiographic score was used for the analysis. There were no cases where the scores differed by more than one score between the two analytical sessions. The κ value for the intraobserver (test-retest) reliability for hip radiographic grading was 0.84 ($p<0.0001$).

Bone densitometry

BMD_{areal} (g/cm^2) and bone mineral content (BMC (g)) of the subregions of the proximal femur (femoral neck and greater trochanter) and calcaneus of the legs were measured using DXA; Lunar Expert; Lunar Radiation Corp, Madison, Wisconsin, USA). Regions of interest (ROIs) in the proximal femur were determined in an automated fashion using the Lunar software version 1.72 (Lunar Expert) (fig 1A). The bone width (cm) of the femoral neck was determined. All measurements were carried out by trained personnel. It was checked from the DXA images that no osteophytes were localised within the ROIs during DXA analysis. The scanner was calibrated according to the standard guidelines of the manufacturer. Reproducibility of the BMD_{areal} measurement (coefficient of variation) of the femur was 1.80% (femoral neck) and 2.05% (greater trochanter) as assessed in 10 volunteers, with repositioning between two measurements.[31] The BMD_{areal} measurement of the calcaneus was made manually with the ROI (circle, diameter 2.54 cm) located in the centre of the calcaneus (fig 1B).

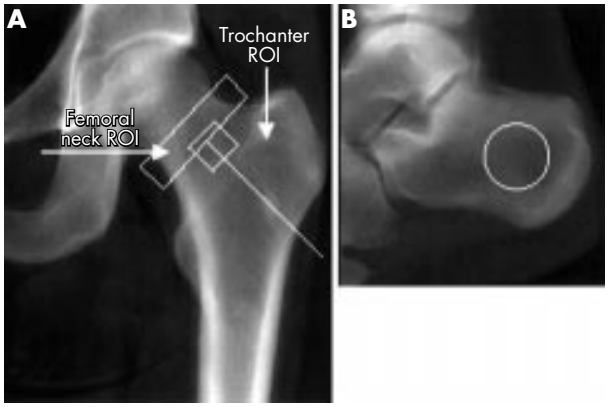

Figure 1 Location of the regions of interest (ROIs) in the proximal femur (A) and calcaneus (B).

The coefficient of variation of the BMD_{areal} measurement of the calcaneus was 2.95%, as assessed in 10 healthy volunteers with repositioning between two measurements.

MRI

MRI was performed with a 1.5T scanner (Siemens Magnetom 63SP, Erlangen, Germany). The volume of the femoral neck (Vol_{mri} (cm^3)) was measured from reconstructions of fat saturated T1 FLASH 2D coronal sequences (flip angle 60°; TR 770; TE 11.0/1; slice thickness 3.0 mm; FOV 420 × 420; matrix 384 × 512; in plane resolution 1.09 × 0.82) at the location corresponding to the BMD measurement of the femoral neck (by MA). Multiplanar reconstruction was made in two planes parallel and perpendicular to the axis of the femoral neck with five 3 mm slices without a gap just beneath the femoral head. The area of the bone was drawn five times, and an average of the three areas in the middle was taken. Thus 0.3 cm × area (cm^2) indicated the volume (cm^3) of one slice, and the sum of five slices was the volume of a 1.5 cm long piece of the femoral neck. This corresponds to the height of the ROI of the femoral neck in the DXA measurement. The coefficient of variation between two reconstruction measurements for the Vol_{mri} of the femoral neck was 2.01%, as assessed in four volunteers with repositioning between two measurements. These measurements from MRI were used to create a BMD measure that was corrected for the volume of the femoral neck ($BMD_{mri} = BMC/Vol_{mri}$ (g/cm^3)).

Statistical analysis

All values are expressed as mean (SD). Normality of the distribution was assessed using the Kolmogorov-Smirnov test with the significance level set at 0.05. If parameters were normally distributed, Student's *t* test was used to test the significance of the difference between the controls and subjects with OA. The hip with the highest radiographic OA score and clinical symptoms of a patient were used for the analysis. The differences were compared with the hip on the same side of an age matched control subject. Comparisons between sides were made with a paired *t* test. Differences between the OA subgroups and controls were determined by the two tailed non-parametric Mann-Whitney U test because of the low number of the subjects and because all parameters were not normally distributed within each subgroup. Differences between the radiographic OA subgroups (grades 1–3) were determined by the non-parametric Kruskal-Wallis test. Results were regarded as significant if $p<0.05$.

RESULTS

Tables 1 and 2 show the clinical features and radiographic characteristics of the groups. There were no differences in body weight, or body mass index between the groups (table 1).

Table 2 Number of patients with radiographic hip osteoarthritis (OA) and clinical features (pain and Lequesne index) in the OA and control subjects

	Hip	
Radiographic criteria	Right hip	Left hip
OA patients		
Grade 0	6*	6
Symptomatic	3	0
Pain (VAS‡) (cm)	4.3 (3.1)†	0
Lequesne index (points)	4.7 (2.5)	0
Asymptomatic	3	6
Grade 1	7	6
Symptomatic	7	5
Pain (VAS) (cm)	4.4 (2.4)	5.6 (2.4)
Lequesne index (points)	3.0 (2.2)	7.6 (4.8)
Asymptomatic	0	1
Grade 2	7	8
Symptomatic	7	8
Pain (VAS) (cm)	4.4 (4.0)	6.0 (3.5)
Lequesne index (points)	6.0 (6.6)	6.5 (6.0)
Asymptomatic	0	0
Grade 3	7	7
Symptomatic	7	7
Pain (VAS) (cm)	7.4 (2.6)	5.4 (2.1)
Lequesne index (points)	10.0 (5.7)	10.9 (6.4)
Asymptomatic	0	0
Grade 4	0	0
Control subjects		
Grade 0	30	30
Symptomatic	0	0
Pain (VAS) (cm)	0	0
Lequesne index (points)	0	0
Asymptomatic	30	30

Radiographic grading was made as described by Li *et al*.[29]
*Number of OA patients or control subjects.
†Values are mean (SD).
‡VAS = visual analogue scale for subjective hip pain.

The height in the group with OA was slightly greater than that in the control group ($p<0.05$). Fifteen subjects with OA had unilateral clinical OA and 12 had bilateral disease. The mean (SD) duration of the hip symptoms was 6.4 (5.2) years (table 1). In the OA group, three patients with radiographic grade 0 OA had pain symptoms in their hip joints, and one (radiographic grade 1) was asymptomatic (table 2). These joints were not taken into account when the clinical patients with OA were compared with the controls matched for age and sex. The distribution of the radiographic OA scores was as follows: 29.6% had grade 1, 29.6% grade 2, and 40.8% grade 3 OA.

BMC and BMD

There were no significant differences in BMD_{areal} in any of the subregions of the proximal femur (femoral neck, trochanter) or calcaneus between the OA and control groups (table 3). The BMD_{mri} of the femoral neck did not differ between the groups either. However, the BMC of the femoral neck was 18% higher ($p<0.01$) in subjects with OA than in controls. This was seen especially in the patients with radiographic grade 3 OA.

When the difference in radiographic scoring was ⩾1 grade between the hips, the BMD_{areal} of the femoral neck was 4% higher ($p<0.05$) on the side of the higher score (table 4). On the same side, the BMC of the femoral neck was 10% higher ($p<0.01$). However, BMD_{mri} did not differ between the hips (table 4).

There were no significant differences in the BMC and the size (area) of the trochanter between the OA and control groups (table 3). In patients with OA, the BMC of the

Table 3 Bone variables in the hip with higher radiographic osteoarthritis (OA) grade compared with age matched control subjects

Bone variables	Grade 1 (n=8) (age 53–64) Mean (SD)	% of controls (n=7)	Grade 2 (n=6–8) (age 47–60) Mean (SD)	% of controls (n=6–7)	Grade 3 (n=11) (age 47–63) Mean (SD)	% of controls (n=15–16)	Grade 1–3 (n=25–27) (age 47–63) Mean (SD)	% of controls (n=28–30)
Proximal femur								
Femoral neck								
BMC (g)	6.28 (0.92)	114	6.37 (0.81)	114	7.11 (1.76)	124*	6.68 (1.36)	118**
Area (cm^2)	6.11 (0.46)	107	6.16 (0.17)	111*	6.33 (0.26)	110*	6.22 (0.47)	109***
Width (cm)	4.08 (0.30)	107	4.11 (0.25)	113*	4.22 (0.37)	110*	4.15 (0.32)	109***
BMD_{areal} (g/cm^2)	1.030 (0.165)	106	1.040 (0.173)	102	1.123 (0.261)	123	1.074 (0.212)	108
Vol_{mri} (cm^3)	16.08 (2.24)	120	16.29 (1.43)	122**	16.73 (3.26)	116	16.39 (2.49)	118***
BMD_{mri} (g/cm^3)	0.392 (0.089)	94	0.411 (0.070)	97	0.441 (0.119)	108	0.416 (0.097)	101
Trochanter								
BMC (g)	15.13 (1.69)	95	14.97 (2.22)	101	14.98 (4.72)	100	15.02 (3.38)	99
Area (cm^2)	15.73 (1.17)	95	15.99 (0.89)	104	15.45 (2.55)	97	15.69 (1.83)	98
BMD_{areal} (g/cm^2)	0.969 (0.152)	101	0.935 (0.117)	97	0.952 (0.198)	101	0.951 (0.160)	100
Calcaneus								
BMD_{areal} (g/cm^2)	0.806 (0.082)	107	0.740 (0.099)	106	0.858 (0.193)	107	0.809 (0.150)	105

Radiographic grading was made as described by Li *et al*.[29]
*p<0.05, **p<0.01, ***p<0.001, compared with age matched healthy controls (Student's *t* test and Mann-Whitney U test).
BMC = bone mineral content; Area = area of the measured region of interest; Width = width of the femoral neck; BMD_{areal} = areal bone mineral density; Vol_{mri} = volume of the femoral neck from magnetic resonance images (MRI); BMD_{mri} = BMD corrected with MRI derived volume.

Table 4 Differences in bone variables in the osteoarthritis (OA) group

Bone variables	Ratio between sides (RGD ⩾1)
Proximal femur	
Femoral neck	
BMC (g)	1.10**
Area (cm^2)	1.06***
Width (cm)	1.06***
BMD_{areal} (g/cm^2)	1.04*
Vol_{mri} (cm^3)	1.13***
BMD_{mri} (g/cm^3)	0.96
Trochanter	
BMC (g)	0.94**
Area (cm^2)	0.96*
BMD_{areal} (g/cm^2)	0.98
Calcaneus	
BMD_{areal} (g/cm^2)	0.98

The results are presented as ratios between the hip side with higher OA grade and the hip with lower OA grade when the radiographic scoring difference (RGD) is ⩾1 grade (n=20). Radiographic grading was made as described by Li *et al*.[29]
*p<0.05, **p<0.01, ***p<0.001 (Student's *t* test and Wilcoxons's matched pairs signed rank test).
BMC = Bone mineral content; Area = area of the measured region of interest; Width = width of the femoral neck; BMD_{areal} = areal bone mineral density; Vol_{mri} = volume of the femoral neck from magnetic resonance images (MRI); BMD_{mri} = BMD corrected with MRI derived bone volume.

trochanter area was 6% lower (p<0.01) in the hip with the higher OA grade than in the hip with the lower grade (table 4). There were no significant differences (Kruskal-Wallis test) in the BMD_{areal} and BMD_{mri} in the radiographic OA subgroups. BMD_{mri} correlated positively (r = 0.858, p<0.001, n=57) with BMD_{areal}.

Bone size

The area of the femoral neck was 9% greater (p<0.001) in the OA group than in the controls matched for age and sex (table 3). Also the femoral neck bone width and Vol_{mri} was 9% and 18% higher (p<0.001) in the OA group than in the controls. The difference was greatest between the radiographic grade 2 and 3 OA hip joints (table 3). In subjects with OA, when the radiographic grading difference was ⩾1 between the hip joints, the area of the femoral neck was 6% greater (p<0.001) in the hip of higher OA grade (table 4). Also in the hip of higher OA grade, the Vol_{mri} was 13% higher (p<0.001) (table 4). There were no significant differences in the size (area) of the trochanter between the OA and control groups (table 3). The size of the trochanter area was 4% smaller (p<0.05) in the hip with the higher OA grade than the opposite side (table 4). Size of the subregions, width, and Vol_{mri} of the femoral neck were not significantly different (Kruskal-Wallis test) in the radiographic OA subgroups. Vol_{mri} correlated positively (r = 0.879, p<0.001, n=57) with area of the femoral neck.

DISCUSSION

Our results clearly show that men with hip OA have significantly higher femoral neck BMC and greater femoral neck volume than healthy controls matched for age and sex. There is no significant difference in femoral neck BMD (BMD_{areal} or BMD_{mri}) between the groups. These findings suggest that hip OA is not associated with an increase in BMD of the femoral neck.

According to Wolff's law, both bone density and organisation of bone trabeculae correlate with the magnitude and lines of compressive and tensile stresses of loading.[32] Thus an increase in the local mechanical forces—for example, on account of reduced resilience of the articular cartilage—may have contributed to the larger size of the femoral neck observed in this study. The increase in femoral neck size can also be speculated to be a compensatory and adaptive mechanism of the bone end to meet the biomechanical forces that act in the joint. The changes may also improve the congruence of the articulating surfaces. In this study, the differences in bone size were shown in the femoral neck, not in the trochanter area. On account of hip OA, the mechanical demands are probably more changed in the femoral neck bone than in the more distal trochanter region.

In hip OA, the most notable bone changes are the osteophytes and subchondral bone sclerosis. Based on animal models, subchondral bone plate thickness is increased both in the early and advanced stages of hip OA.[33–36] In clinical studies of hip OA, morphometric analyses have shown that the subchondral and trabecular bone thickness is increased,[37 38] but the subchondral bone has a lower mineralisation pattern compared with controls.[37 39] It can be argued that, distal to the subchondral bone plate, DXA is not the method of choice to evaluate the structural changes in subchondral bone in hip

OA. Thus this study does not allow us to conclude that the bone changes in the femoral neck area are similar to possible changes in the subchondral bone plate and subchondral trabecular bone just below the articular cartilage.

Most previous studies using DXA have reported increased BMD_{areal} in the femoral neck in patients with hip OA compared with healthy controls matched for age and sex.[8 10 11 40 41] It has also been reported that an increase in the severity of hip OA simultaneously yields an increased femoral neck BMD_{areal}.[8] Our results showing a 4–8% higher BMD_{areal} in the femoral neck, even though not statistically significant, are comparable to the results of previous population based, cross sectional studies on hip OA.[8–10] It was also observed that, in the subjects with OA, BMD_{areal} of the femoral neck was significantly higher (4%) in the hips with more severe OA than in those with lower grade OA. However, when the BMD_{areal} values were corrected for the size of the femoral neck (BMD_{mri}), no significant differences were observed. The severity of OA seemed to have no significant effect on BMD_{areal}, BMD_{mri}, or BMC in this study.

To our knowledge, this study is the first to show significant changes in femoral neck size in subjects with hip OA. The significance of bone mass and width in generalised OA was previously pointed out by Roh *et al*,[19 42] Hochberg *et al*,[43] and Dequeker *et al*.[44] Roh *et al*[19 42] showed that, in cases of primary OA of the hip, the width of the metacarpal and the radius are significantly greater than in controls and that the bone width has a major effect on the percentage cortical area or BMD. Hochberg *et al*[43] noticed that men with definite knee OA have significantly greater radial bone mass and width than controls. Thus, because of the generally larger bone dimensions in hip and knee OA, it is very unlikely that the local mechanical effects could alone explain the increase in size of the femoral neck in our study. In generalised OA, bone volume, measured from the cortical bone of the iliac crest, appears to be increased as a result of low bone turnover and a high content of growth factors such as insulin-like growth factors I and II, transforming growth factor β, and osteocalcin.[45] This may explain the greater size of the femoral neck observed in this study. The increase in size of the femoral neck can also be expected to increase its strength, because the structural strength of bone depends not only on its density but also on its size and gross geometry.[46] These results are consistent with previous findings that OA protects from hip fractures.[5 15]

In the calcaneus, there was no significant difference in BMD_{areal} between the groups. This suggests that the changes in this measure in hip OA are localised. Most previous studies have focused on either the BMD_{areal} of the proximal femur[10 11 40 41] or the BMD_{areal} measured at a distance from the OA hip joint.[12 17–22] One previous study measured both the local BMD_{areal} of the proximal femur and the BMD_{areal} at a specified distance from the OA hip joint.[8] These authors noticed that women with grade 3–4 hip OA had not only a significantly higher BMD_{areal} at the femoral neck (8%) but also in the calcaneus (5%) compared with those with grade 0–1 OA. The study design, however, differed from that of our study and therefore direct comparisons cannot be made.

DXA is widely used and provides an accurate method for the in vivo measurement of BMD_{areal} of the proximal femur. However, an increase in BMC, bone area, and width in OA joints may result from an error caused by the presence of osteophytes within the ROI, for example. However, the ROIs are distal to the sites of the femoral osteophytes. We also checked from the DXA images that no osteophytes were localised within the ROIs during DXA analysis. Subject positioning in the DXA method can also be critical because patients with OA may be less able to rotate the hip internally, which leads to a falsely increased BMD.[47] However, Nevitt *et al*[8] showed that adjustment for restricted internal rotation of the hip does not alter hip BMD.

Failure to adjust for bone size in DXA can also lead to an erroneous interpretation of BMD values. To our knowledge, this is the first time that volume of the femoral neck was determined to produce a BMD measure that was adjusted for femoral neck volume (BMD_{mri}). Normalisation of BMD values for the size of the femoral neck is necessary when subjects with different femoral neck sizes are compared with each other. We previously presented a method for calculating apparent volumetric BMD (BMD_{vol} (g/cm^3)).[25] In this method, the lumbar and femoral neck body was assumed to have a cylindrical shape. The DXA derived BMD_{vol} correlated moderately well with BMD_{mri} (r=0.665–0.822) in lumbar vertebrae.[48] Although the use of MRI to produce a true volumetric density has not previously been validated, the DXA derived BMD_{vol} of the femoral neck also correlates highly with BMD_{mri} (r=0.737) (unpublished data).

The selection criteria for patients with OA for this study were based on both radiographic changes and symptoms of hip OA. If the subjects had been selected only on the basis of radiographic changes in the hip joint, osteophytes and joint space narrowing might have indicated a physiological alteration or individual variation. The selection criteria used meant that patients with minimal radiographic changes (OA grade 1) and clinical symptoms were also examined. The control group consisted of a random sample from the general population. Excluding any hip pain at all in control subjects might have caused some bias, because there may be non-specific hip pain in subjects who do not have radiographic or clinical hip OA or other exclusion diagnoses or symptoms. However, the use of these criteria made the logistics of the study easier. There were no differences in weight, or body mass index between the OA and control groups. Therefore differences in the femoral neck bone could not be due to anthropometric differences between the patients with OA and healthy subjects.

The small number of subjects is a limitation of the study, because the statistical power to detect differences with 27–30 subjects in a group may be low. It is possible that, if we had used a larger group of control subjects, we would also have observed significantly higher BMD_{areal} levels in the OA group. Relatively few subjects were used for economic reasons; MRI and DXA measurements are expensive. However, the statistical findings between groups were comparable to differences noted in subjects with OA when the hips with more severe OA were compared with the hips with lower grade OA.

Owing to the cross sectional design of this study, we cannot determine the cause-effect relation between bone structure and hip OA. It is also premature to state that bone remodelling initiates the OA changes in hip articular cartilage. However, our results clearly show that men with hip OA have significantly higher BMC and greater bone size in the femoral neck. Whether these changes have a role in the pathogenesis of hip OA remains to be elucidated.

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