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Original Article

Hylonome

Bone and cartilage characteristics in postmenopausal women with mild knee radiographic osteoarthritis and those without radiographic osteoarthritis

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Abstract

Objectives: To evaluate the association between radiographically-assessed knee osteoarthritis and femoral neck bone characteristics in women with mild knee radiographic osteoarthritis and those without radiographic osteoarthritis. **Methods:** Ninety postmenopausal women (mean age [SD], 58 [4] years; height, 163 [6] cm; weight, 71 [11] kg) participated in this cross-sectional study. The severity of radiographic knee osteoarthritis was defined using Kellgren-Lawrence grades 0=normal (n=12), 1=doubtful (n=25) or 2=minimal (n=53). Femoral neck bone mineral content (BMC), section modulus (Z), and cross-sectional area (CSA) were measured with DXA. The biochemical composition of ipsilateral knee cartilage was estimated using quantitative MRI measures, T2 mapping and dGEMRIC. The associations between radiographic knee osteoarthritis grades and bone and cartilage characteristics were analyzed using generalized linear models. **Results:** Age-, height-, and weight-adjusted femoral neck BMC (p for linearity=0.019), Z (p for linearity=0.033), and CSA (p for linearity=0.019) increased significantly with higher knee osteoarthritis grades. There was no linear relationship between osteoarthritis grades and knee cartilage indices. **Conclusions:** Increased DXA assessed hip bone strength is related to knee osteoarthritis severity. These results are hypothesis driven that there is an inverse relationship between osteoarthritis and osteoporosis. However, MRI assessed measures of cartilage do not discriminate mild radiographic osteoarthritis severity.

Keywords: Osteoarthritis, Bone Strength, Kellgren and Lawrence Grade, Quantitative MRI, Postmenopausal Women

Introduction

Osteoarthritis (OA) and osteoporosis (OP) may cause serious morbidity and impose a substantial burden on the health care system, especially among elderly women. Although OA affects all of tissues within a joint, a characteristic aspect of an osteoarthritic joint is a progressive degeneration of articular cartilage. In OP, the related bone loss leads to an increased risk of fracture. The relationship between these two diseases is not well understood and is a topic of controversy[1].

Even though clinical experience and some studies indicate that OA and OP are not mutually exclusive[2], previous reports, including large epidemiological studies and subsequent cross-sectional studies, suggested that OA is associated with higher bone mineral mass or density[3-6]. Moreover, subjects with OA seem to not only have higher bone mineral mass, but also bigger bone size compared with healthy controls[7]. Also, women with OA are observed to have larger muscle mass and force compared with age- and body size-matched osteoporotic women[8]. From the perspective of bone and cartilage interac-

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tion, there is some evidence showing that bone mineral mass is associated with knee cartilage volume in healthy adults[9,10]. In a longitudinal analysis, bone loss was associated with loss of cartilage volume in subjects with knee OA[11].

In addition to cartilage volumetric assessment, recent advances in quantitative magnetic resonance imaging (qMRI) techniques have enabled the use of biomarkers for structure and biochemical composition of cartilage. T2 relaxation time mapping is a qMRI technique sensitive to the integrity of the collagen network, collagen orientation, and hydration[12], whereas the delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) is sensitive to cartilage glycosaminoglycan (GAG) content[13-15]. Analogously, in order to be able to analyze bone structure and strength, software for dual energy x-ray absorption meter (DXA) and advanced hip structure analysis (AHA) were developed to derive hip geometry from bone mineral data for an estimate of hip strength[16]. Thus, concurrent use of qMRI and AHA provides potential tools for determining the biochemical composition of cartilage, and assessing bone structure and strength prior to gross morphologic changes of cartilage or bone fracture have occurred. However, to our knowledge there are no studies in subjects with mild OA and who may be at risk of OP focused on bone mass and strength and cartilage biochemical composition. Therefore, the aim of the present study was to investigate the association between radiographic knee OA with femoral neck bone characteristics using AHA in a sample of postmenopausal women with mild knee radiographic OA and those without radiographic OA.

Materials and methods

Study participants

Baseline data from the previously reported randomized controlled trial (RCT)[17] with two trial arms: 1) a high-impact exercise and 2) a nonintervention were used in the current cross-sectional study. Seventy-eight postmenopausal women with mild knee OA were recruited via newspaper advertisement from the Central-Finland area. During the screening process of study participants, knee OA was radiographically confirmed at the symptomatic or most symptomatic knee. Subjects with Kellgren-Lawrence (K/L) grade 1 or 2 radiographic OA changes[18] in the tibiofemoral joint were included, while subjects with moderate or severe knee OA (K/L grades 3 or 4) were excluded after screening process. In addition of having knee K/L grade 1 or 2, other eligibility criteria for the RCT and the current cross-sectional study were postmenopausal status, age 50-65 years, knee pain on most days within the preceding year, no more than twice weekly regular intensive exercise, and no illness that contraindicated or limited participation in the exercise intervention. A subject was excluded if her T-score for femoral neck bone mineral density (BMD, g/cm^2) was lower than -2.5; body mass index (BMI, kg/m^2) was higher than 35 kg/m^2; and if she had any previous knee instability or severe trauma, inflammatory joint disease, or knee intra-articular steroid injections in the preceding 12 months. Moreover, a subject was excluded if she had any known contraindications to MRI, any known allergies to contrast agents, or renal insufficiency. Additionally, an age-, weight-, and height-matched sample of 12 women with no considerable knee symptoms were recruited to the study as a reference group from the same source population as those who were recruited into the parent RCT. The inclusion and exclusion criteria were same as for the women with mild knee OA, except that the women without clinically significant symptoms should not have had any frequent pain, aching or stiffness in or around the knee joint in either knee in the preceding year. The suitability of the women without significant symptoms was confirmed by the radiographs, and only subjects who had no radiographic OA changes (i.e., K/L grade 0) in both tibiofemoral joints were entered into the study. The exercise study protocol with the amendment of the study protocol of women without significant symptoms and radiographic OA (hereafter called K/L 0 group) were in agreement with Helsinki declaration with the approval of the Ethics Committee of the Central Finland Health Care District. Written informed consent was obtained from all participants prior to enrollment.

Knee radiography

The radiographs were acquired during screening examinations from both knees with a postero-anterior view of the tibiofemoral joint in a semi-flexed weight-bearing position. An experienced musculoskeletal radiologist blinded to subjects graded the X-rays according the radiological grading scale of Kellgren and Lawrence (K/L). This system uses the following global grades (for tibiofemoral OA): 0 = normal, 1=doubtful (possible osteophytes), or 2=minimal (definite osteophytes, possible joint space narrowing)[18]. In subjects with OA, the final grade was the highest one for the most severely-affected knee.

Bone assessment

Proximal femurs were scanned with dual-energy X-ray absorptiometry (DXA, GE Medical System, Lunar Prodigy, Madison WI, USA) at the narrowest femoral neck section from the side of the higher K/L grade knee in subjects with knee OA. Femoral neck bone mineral content (BMC, g) was used in the analysis, whereas femoral neck areal bone mineral density (BMD, g/cm^2) was used during screening of the study participants. Femoral neck cross-sectional area (CSA, [mm^2], the surface area of bone in the cross-section after excluding all trabecular and soft tissue space), and the section modulus (Z, [mm^3], an index of bending strength) were calculated with advanced hip structure analysis (AHA). In K/L 0 group, the average bone trait value of both femoral neck sites was calculated for the analysis.

The root mean square coefficient of variation (CV_{RMS}) for femoral neck BMC measurements with this population was 0.6%. Reproducibility of the DXA measurements was tested from the duplicate measurements of 8 participants within an average 6 (SD 2) days between imaging sessions. The scanner was calibrated daily with bone phantoms (GE Medical System, Lunar Prodigy, Madison WI, USA) for quality assurance.

Knee cartilage assessment

Transverse relaxation time (T2) and dGEMRIC index, i.e., T1 relaxation time in the presence of Gd-DTPA^{2-} were determined using a Siemens Magnetom Symphony Quantum 1.5 T scanner (Siemens AG, Medical Solutions, Erlangen, Germany) with a standard transmit/receive knee array coil. Prior to the measurements, experienced radiologists and technicians were specifically trained to run the MRI research protocol. The participants were imaged lying supine. In the subjects with radiographically-confirmed OA, scans were performed on the side with the higher K/L grade knee, and in the right knee of K/L 0 group. The flexion angle and rotation of the knee was controlled by stabilizing the leg in a fixed position with a leg holder and a custom-made inflatable cushion. T2 mapping, which was performed prior to the dGEMRIC experiment, was carried out using a sagittal multislice, multiecho, fast-spin echo sequence (field of view [FOV] 140 mm, acquisition matrix 256×256, repetition time [TR] 2090 ms, eight echo times [TE] between 13 and 104 ms, echo train length [ETL] 8, 3-mm slice thickness, imaging time=8 min 55 s). The slices were positioned perpendicular to a line tangential to the posterior femoral condyles in the axial scout view. One slice covering the central region of the medial and lateral condyles, were chosen for the analyses. Monoexponential fitting was used to compute relaxation time maps.

For the dGEMRIC imaging, a double dose i.e., 0.4 ml/kg (0.2 mM/kg) intravenous administration of Gd-DTPA^{2-} (Magnevist, Schering, Berlin) was followed by a 90-minute delay with active flexion-extension exercises of the knee for 5 min while sitting, then while walking for 5 min and stair climbing for 5 min in order to enhance the penetration of contrast agent into the knee cartilage. T1 mapping was performed in the sagittal plane using a single slice inversion recovery fast-spin echo sequence (FOV=14 cm, matrix 256×256, TR=1800 ms, TE=13 ms, inversion time TI=50, 100, 200, 400, 800, 1600 ms, echo train length [ETL] 5, 3-mm slice thickness, imaging time per image=6 min 50 s). The slices were positioned perpendicular to a line tangential to the posterior femoral condyles in the axial scout view. The remaining slice was then positioned at the center of the medial and lateral condyles as viewed on the axial scout image.

Full-thickness cartilage regions-of-interest (ROIs) were manually segmented from the most load-bearing areas from single sagittal slices at the center of the medial and lateral femoral and tibial condyles using an in-house MATLAB application (Mathworks, Inc. Natick, MA, USA). The femoral ROI was defined anteriorly at a point opposite the middle of the tibial plateau regarding antero-posterior position, and posteriorly at a point of posterior end of meniscus towards the femoral bone. The tibial ROI was defined anteriorly at a point of meniscus' anterior tip of horn towards the tibial bone, and posteriorly at a point of meniscus' posterior tip of horn towards the tibial bone. Figure 1 shows ROIs from the center of the lateral tibiofemoral compartment. dGEMRIC index is an average T1 spin lattice relaxation time in the presence of Gd-DTPA^{2-} in a given ROI. The dGEMRIC indices were corrected by body mass indices (BMIs) as suggested by Tiderius et al.[19]. On average, the precision (CV_{RMS}) of dGEMRIC in asymptomatic subjects has been shown to be 7% for full-thickness ROIs and 5% for bulk cartilage[20]. The inter-observer error in our laboratory between two independent cartilage investigators (J.M. and E.L., with 6 and 12 years of experience in cartilage analyzing, respectively) was on average 2% for T2 full-thickness ROIs and 3% for dGEMRIC.

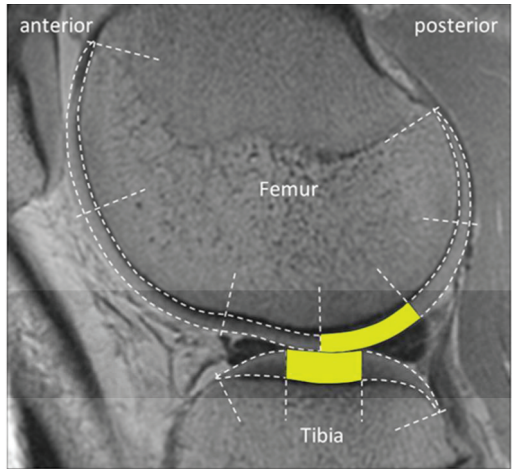

Figure 1. Sagittal T2 image of the segmented and analyzed cartilage regions-of-interest (ROIs) in lateral tibiofemoral compartment. The analyzed ROIs are shown as yellow-colored areas. In the study, the corresponding ROIs were also analyzed from a single sagittal slice in medial tibiofemoral compartment.

Physical function

Agility or dynamic balance was assessed with a standardized figure-of-eight running test of two laps around two poles placed 10 m apart[21]. Maximal isometric knee extension and flexion force was measured in a sitting position with a knee angle of 60° using a dynamometer chair (Good Strength, Metitur Oy, Jyväskylä, Finland)[22]. Leg power was determined by a maximal vertical counter movement jump on a force platform (University of Jyväskylä, Finland)[23]. Cardiorespiratory fitness (estimated oxygen consumption at maximum exertion i.e., VO_{2max}, mL/kg/min) was assessed with a standardized 2-km Walk Test (UKK Institute, Finland)[24].

Questionnaires

Knee pain, stiffness, and self-rated physical functioning were assessed with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[25]. General health and leisure time physical activity were assessed by a questionnaire. A health questionnaire addressed medical conditions, current medications and leisure time physical activity, which was converted into metabolic equivalent (MET) hours per week[26].

Variable	K/L 0 (n=12)	K/L 1 (n=25)	K/L 2 (n=53)	P for linearity
Mean age (SD), years	58 (3)	58 (4)	59 (4)	0.52
Mean height (SD), cm	161 (6)	163 (5)	163 (6)	0.64
Mean body mass (SD), kg	67.5 (10.8)	69.9 (9.6)	72.1 (11.3)	0.15
Mean body mass index (SD), kg/m^2	25.8 (3.7)	26.3 (3.1)	27.2 (3.9)	0.16
Mean time from menopause (SD), years	8.3 (5.5)	9.1 (5.9)	9.0 (5.4)	0.81
Current HRT[a] users, n (%)	3 (25)	13 (52)	18 (34)	0.88
Pain killers, n (%)	7 (58)	13 (52)	28 (53)	0.80
Occasional glucosamine use, n (%)	0 (0)	7 (28)	14 (26)	0.15
WOMAC, range 0–100				
Pain	2 (5)	6 (5)	8 (8)	0.008
Stiffness	5 (10)	8 (9)	11 (12)	0.036
Physical function[b]	2 (4)	4 (4)	5 (5)	0.033
Leisure time physical activity, METh/week	18.1 (12.6)	15.6 (7.0)	19.9 (17.8)	0.41
Muscle force, N				
knee extension	381 (49)	384 (79)	417 (82)	0.11[e]
knee flexion	172 (44)	174 (53)	184 (54)	0.55[e]
Power, W	1794 (286)	1888 (375)	1871 (363)	0.97[e]
Dynamic balance[c], s	16.5 (1.7)	17.2 (1.3)	17.2 (2.4)	0.87[e]
VO_{2max}[d], mL/kg/min	29.4 (2.9)	29.4 (2.9)	28.8 (4.5)	0.61[e]

[a]*Hormone replacement therapy.*
[b]*Negative number indicates better physical functioning.*
[c]*Negative number indicates better balance.*
[d]*VO_{2max}, estimated maximal oxygen uptake.*
[e]*Adjusted for age and body mass.*

Table 1. Demographic and clinical characteristics of the study population according to radiographic Kellgren-Lawrence (K/L) grades.

Variable	K/L 0 (n=12)	K/L 1 (n=25)	K/L 2 (n=53)	P for linearity
Bone trait				
Bone mineral content (BMC), g	4.183 (0.836)	4.463 (0.874)	4.726 (0.575)	0.019[a]
Section modulus (Z), mm^3	543 (98)	611 (170)	628 (101)	0.033[a]
Cross sectional area (CSA), mm^2	135 (22)	142 (28)	150 (19)	0.019[a]
T2, ms				
MEDIAL CONDYLE				
Posterior part of central femur	50.4 (2.8)	49.6 (6.3)	50.2 (5.4)	0.85[a]
Central tibia	44.2 (5.2)	44.9 (4.8)	45.1 (4.2)	0.60[a]
LATERAL CONDYLE				
Posterior part of central femur	50.8 (5.4)	50.5 (6.0)	50.4 (5.6)	0.83[a]
Central tibia	38.4 (2.4)	43.5 (6.5)	42.0 (7.3)	0.20[a]
dGEMRIC index, ms				
MEDIAL CONDYLE				
Posterior part of central femur	446 (60)	461 (55)	456 (78)	0.79[b]
Central tibia	362 (67)	412 (72)	402 (58)	0.17[b]
LATERAL CONDYLE				
Posterior part of central femur	474 (67)	512 (75)	469 (59)	0.28[b]
Central tibia	426 (107)	433 (82)	437 (77)	0.63[b]

[a]*Adjusted for age, body mass, and height.*
[b]*Adjusted for age.*

Table 2. Bone and cartilage trait values (mean, SD) from different anatomical regions according to radiographic Kellgren-Lawrence (K/L) grades.

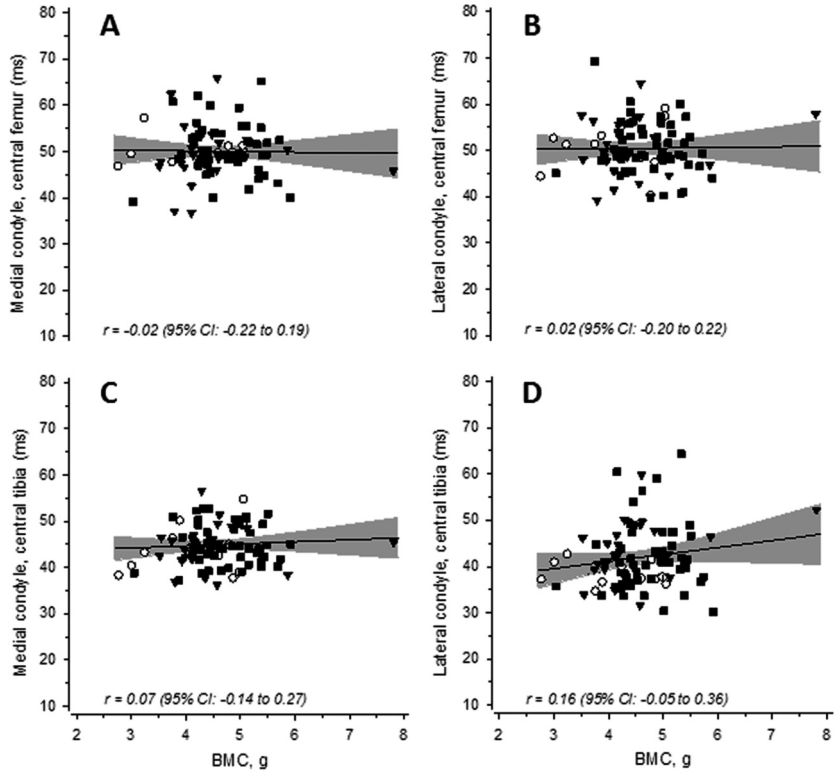

Figure 2. Scatter plots showing the association between the femoral neck bone mineral content (BMC) and knee cartilage T2 relaxation times. Panels in the upper row show the association between BMC and T2 in the posterior part of the central femoral cartilage in both the medial (A) and lateral (B) condyles. Panels in the lower row show the corresponding associations in the central part of the medial (C) and lateral (D) tibial condyles. ○= K/L 0; ▼= K/L 1; ■= K/L 2. The gray band shows the 95% confidence intervals.

Statistical analysis

The results are presented using means, standard deviations (SD) and frequency distributions. Statistical significance for the hypothesis of linearity between radiographic knee OA grades (0 normal, 1 doubtful and 2 minimal) and bone and cartilage characteristics were evaluated by using generalized linear models with appropriate distribution and link function. In addition, the associations of bone and cartilage traits with K/L grading were tested with an effect size, which was calculated using partial Eta-squared (η^2). By convention, values of 0.01, 0.06, and 0.14 are called small, medium, and large effect sizes, respectively[27].The bone traits and cartilage T2 relaxation times were adjusted by age, body mass, and height. The cartilage dGEMRIC indices were adjusted for age. The normality of the variables was tested by using the Shapiro-Wilk W test. All reported p values are two sided, and statistical significance was set at <0.05. Statistical analyses were conducted using Stata v.12.1 (StataCorp, College Station, TX, USA).

Results

Table 1 shows the demographic and clinical characteristics of the subjects according to radiographic K/L grades. There was a linear relationship between perceived knee pain, stiffness, physical functioning, and OA grade, showing that the higher the OA grade was, the more the subjects experienced knee pain (p=0.008 for linearity), stiffness (p=0.036), and physical disability (p=0.033). There were no linear relationships between the OA grade and use of medication, leisure time physical activity, or physical function measures (Table 1).

In the femoral neck, there was a statistically significant linear trend showing that BMC, Z, and CSA increased with higher OA grades (Table 2). The effect sizes indicated that in the bone traits the linear association was at moderate level, i.e. in BMC the η^2 was 0.08, in Z 0.04 and in CSA it was 0.05. The age, body mass, and height-adjusted mean ratio of BMC was 1.10 (95% CI: 1.01 to 1.19), Z was 1.12 (95% CI: 1.02 to 1.21), and CSA was 1.08 (95% CI: 1.01 to 1.16) in the K/L 2 group compared with the K/L 0. The ratios did not differ between the K/L 1 and K/L 0 grades.

In knee cartilage regions, none of the T2 or dGEMRIC indices in the center of the medial or lateral femoral or tibial condyles were linearly related with radiographic grades (Table 2). The effect sizes indicated that in the cartilage traits, the linear associations were considered as not meaningful. There were no relationships between BMC and T2 or dGEMRIC index at any anatomical site (Figures 2 and 3, respectively).

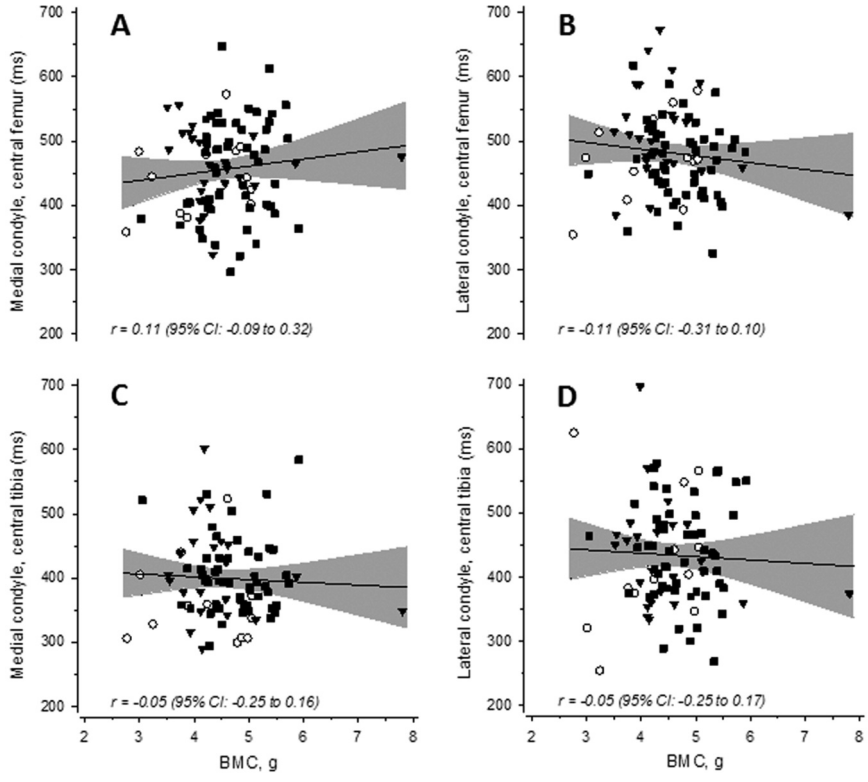

Figure 3. Scatter plots showing the associations between femoral neck bone mineral content (BMC) and knee cartilage dGEMRIC indices. Panels in the upper row show the association between the BMC and dGEMRIC index in the posterior part of the central femoral cartilage in both the medial (A) and lateral (B) condyles. Panels in the lower row show the corresponding associations in the central part of the medial (C) and lateral (D) tibial condyles. ○= K/L 0; ▼= K/L 1; ■= K/L 2. The gray band indicates the 95% confidence intervals.

Discussion

The primary finding of this study was that there was a linear association between femoral neck mineral mass and bending strength, and radiographic grades from K/L 0 to K/L 2. In other words, as the knee OA became radiographically worse the femoral neck bone mineral mass and strength increased. We also found that T2 or dGEMRIC index which reflect the biochemical composition of knee cartilage, was not related to radiographic OA grades. It is also noteworthy that knee pain, stiffness, and physical function disability increased significantly with OA grades, although the symptom values were relatively low even in the highest OA grade (K/L 2).

The bone results of this study are consistent with those of previous large epidemiological surveys showing that radiographic knee OA is associated with high femoral neck bone mineral mass[28-31]. However, so far there are no studies that have simultaneously investigated the relationship between hip bone structure and strength, and estimated biochemical composition of cartilage in mild knee OA. The mechanism whereby OA subjects have more advanced bone structure and strength than non-OA subjects remains unknown. However, Burr & Gallant[32] have suggested that because of the rapid turnover of bone in early OA, the subchondral bone plate and calcified cartilage thickens leading to a subchondral sclerosis while the subchondral trabecular bone may even remain osteopenic. Whether these subchondral bone changes occur at the same time as cartilage deteriorates, and whether these changes occur in more local or general level, is still debatable. Nevertheless, most of the studies in hip and knee OA subjects have demonstrated increased bone mineral mass or density values of different skeletal sites compared with age-matched healthy controls[6,31,33]. In contrast, there are also indications that knee OA is associated with significantly lower BMD values in the affected side compared with the contralateral hip[34], thus, it is important to investigate associations between cartilage and bone at the different sites in same limb.

Our result showing that T2 values were not linearly associated with radiographic OA grades is in accordance with the findings by Koff et al.[35] indicating no association between T2 values and patellar cartilage OA grades. However, our finding is contrary to that of Dunn et al.[36] and Li et al.[37], who showed that regional T2 relaxation times became elongated (high value correspond to compromised cartilage structure degeneration) with higher OA grades. The results of Dunn et al.[36] and Li et al.[37] should be considered with caution, however, due to small sample sizes, and a limited number of echo images used to de-

termine T2 values in the study by Dunn et al.[36]. Similarly, dGEMRIC index showed no association with OA grades. This is in line with the study by Williams et al.[38] who found no relationship between dGEMRIC index and knee OA (K/L grades 1-4) in erosive, narrowed, tibiofemoral joint space compartments. However, when they also analyzed compartments without joint space narrowing, there was a trend toward lower dGEMRIC indices with increasing K/L grades, yet there was significant overlap in dGEMRIC indices between different OA grades. The study was limited by the small sample sizes in different K/L grades.

All in all, the quantitative MRI methodology applied was unable to categorize subjects with mild knee OA according to K/L radiographic criteria. This result could be due to the techniques used (X-ray and qMRI) that focus on different tissue types. In OA, both osteophyte formation and increased bone mineral mass are features of bone, which were measured using the same methodology derived from increased attenuation of X-rays in bone mineral mass. Thus, these bone hypertrophy forms can be expected to be associated with each other. However, the qMRI methods are surrogates for cartilage matrix constituents, indicating cartilage biology beyond radiographic detection. Moreover, the cartilage compositional changes most likely precede changes in bone and cartilage quantity in early OA. Furthermore, there are conflicting results about the cartilage GAG content changes in early OA[39]. GAG content may increase[40,41] or diminish[42,43] in early OA. For instance, in a recent study Stubendorff et al.[44] suggested that dGEMRIC-derived sulphated glycosaminoglycan (sGAG) content may remain at rather constant levels in early hip OA due to compensative sGAG synthesis. This might explain our findings why there were no linear associations between dGEMRIC indices and radiographic knee OA grades, or between dGEMRIC indices and femoral neck BMC. An anomalous behavior of cartilage GAG content may reflect a more complex pattern of early OA progression than anticipated. Alternatively, dGEMRIC may not be a specific method for detecting early cartilage degeneration. On the other hand, previous cross-sectional studies reported differences in dGEMRIC indices between asymptomatic versus OA knees[45], and arthroscopically normal femoral compartments versus diseased compartments[46]. Nonetheless, our qMRI results challenge the role of radiographic evaluation of OA, since articular cartilage has an important role in OA development and is not adequately addressed using K/L scoring.

The strength of the present study is that, to our knowledge, it is the first to simultaneously investigate the relationship between bone mineral mass and OA by detecting bone structural characteristics and articular cartilage measures. In previous knee OA and OP relationship studies, which were published largely in the 1990s[28-31], the biochemical composition of knee cartilage was not taken into account mainly because appropriate *in vivo* cartilage imaging techniques were not available. Additionally, recent cross-sectional studies using standard MRI techniques have focused on delineating cartilage morphology[9,10] rather than the biochemical composition of cartilage. Standard MRI sequences, however, cannot detect the initial stages of OA, including glycosaminoglycan loss, increased water content, and disorganization of the collagen network[47].

The present study has some limitations. Only one radiologist graded knee OA according the K/L scoring system; however, it is unlikely that two radiologists would have improved the grading reliability as we had a musculoskeletal radiologist with 20 years of experience. The study was also limited because bone traits in the hips and cartilage traits in the knees according to radiographic knee OA were not obtained of the same body part. This cannot though be considered as a crucial failure due to systemic disease component of both OP and OA. The participants' history of development of knee OA was not available. In addition, we had a rather select group of study participants with K/L grades 1 and 2 because of the related exercise intervention study[17], and a relatively small sample size in the K/L grade 0 group. To investigate this aspect, further investigations including subjects across a radiographic spectrum of OA are required with prospective longitudinal follow-ups.

In conclusion, this study demonstrated that femoral neck structure, strength and mineral mass were inversely related to mild knee OA in postmenopausal women, i.e. the femoral neck rigidity improvement was associated with severity of radiographic knee OA. These results have implications for the hypothesis that there is an inverse relationship between OA and OP. However, with this population there was no association between radiographic OA grades and knee cartilage biochemical composition assessed using quantitative MRI measures; T2 relaxation time and dGEMRIC. The reason for this inconsistent periarticular cartilage-bone interaction remains unclear, but the radiographic K/L scoring system may not be sensitive to cartilage changes in early to mid-stage knee OA.

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