Original Article | Clinics in Orthopedic Surgery 2014;6:420-425 • http://dx.doi.org/10.4055/cios.2014.6.4.420

The Relationship between Osteoarthritis of the Knee and Bone Mineral Density of Proximal Femur: A Cross-Sectional Study from a Korean Population in Women

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Background: The relationship between osteoarthritis (OA) and osteoporosis (OP) is complicated and it may differ according to the site or stage of disease. The purpose of this cross-sectional study is to examine the relationship between the severity of radiological knee OA and the degree of OP in the ipsilateral proximal femur as denoted by bone mineral density (BMD) in a Korean population, especially among women.

Methods: One hundred ninety-five female patients who had knee pain and radiological knee OA were investigated with respect to the relationship of knee OA severity with BMD. The BMD of the proximal femur and spine was measured by dual energy X-ray absorptiometry, and the severity of knee OA was evaluated based on Kellgren-Lawrence (K-L) radiographic criteria, joint space narrowing (JSN) and mechanical axis of knee alignment. Partial correlation analysis and ANCOVA adjusted for confounding factors (age and body mass index) were performed to assess the relationship.

Results: There was a statistically significant relationship between the BMD of the proximal femur and JSN, and the BMD of the proximal femur was positively associated with increased joint space width. There was a lack of association between the spine BMD and JSN. The BMD of the proximal femur was also significantly lower in patients who had a higher K-L grade.

Conclusions: The radiographic finding of severe OA in the knee is associated with decreased BMD of the ipsilateral proximal femur including the femoral neck, trochanter, intertrochanter, and region of the entire hip (neck, trochanter, and Ward's triangle).

Keywords: *Knee osteoarthritis, Osteoporosis, Proximal femur, Bone density, Relationship*

The relationship between osteoarthritis (OA) and osteoporosis (OP), the two most common aging-related skeletal disorders, is puzzling and controversial. Cross-sectional studies have indicated that OA is associated with increased bone mineral density (BMD).[1-6] In addition, several longitudinal studies have found that higher axial BMD is associated with an increased risk of incident OA of the knee when defined by osteophytes and Kellgren-Lawrence (K-L) grade.[7-9] However, no definite relationship has been established when OA is defined by joint space narrowing (JSN) and mechanical axis.[3,4] Some studies have even shown that higher BMD is rather protective for OA progression.[10,11] These varied reports suggest that the relationship between OP and OA is complicated, and it may differ according to the site or stage of disease.[12,13]

Knee is the most common joint of the lower extremity that is affected by OA,[14] and fractures of the proximal femur in the elderly are associated with significant morbidity and mortality.[15] From a systemic point of view, high BMD in general can lead to increased incidence of knee OA with increased stiffness of the subchondral bone.[16,17]

Received September 2, 2013; Accepted February 3, 2014
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On the other hand, continuous pain and inactivity due to OA will lead to a local decrease in BMD with progression of OA.[18] However, there is a relative paucity of reports on the relationship between severity of knee OA and BMD of the proximal femur, particularly in Asian population. Therefore, the purpose of this cross-sectional study is to examine the relationship between the severity of radiological and symptomatic knee OA and the degree of OP in the ipsilateral proximal femur as denoted by BMD in a Korean population, especially among women.

METHODS

Study Design

A retrospective study design was used. Subsets of 270 participants who visited our hospital for knee pain and met the American College of Rheumatology criteria for symptomatic OA of the knee[19] from October 2005 to September 2013 were evaluated. We limited the subsets to women for avoiding the confounding variables and bias, because there were only a few male patients (n = 8). All of the patients had a K-L grade ≥ 1 in the affected knee and DXA scan was taken of the ipsilateral proximal femur (femoral neck, trochanter, intertrochanter, total hip-neck, trochanter, and Ward's triangle) and lumbar spine (L1–4) within 6 months of the first visit (mean interval, 2.7 months). To avoid confounding in the statistical analysis, patients with valgus alignment of knees (≥ 3° valgus about the mechanical axis), and other comorbidities (e.g., rheumatoid arthritis, septic arthritis) that could also be the causes of knee pain and change in bone structure were excluded. We also excluded smokers since smoking affects the BMD. Subjects who had unsatisfactory medial tibial plateau alignment in the radiographs were also excluded from the final analysis. A total of 195 knees were finally included in the study. Weight was measured to the nearest 0.1 kg using a single pair of electronic scales. Height was measured to the nearest 0.1 cm using a stadiometer. From these data, body mass index (BMI; weight/height^2, kg/m^2) was calculated. Mechanical axis in the scanogram, JSN in the anteroposterior (AP) view and the Rosenberg view, and K-L grade were measured to assess the severity of OA. Thus, the relationship between the measured values of BMD and radiographic severity of osteoarthritic changes was analyzed considering the confounding variables.

Radiological Measurements

Standing AP films of the knee in full extension were obtained with the horizontal X-ray beam centered at the level of the superior patellae. Views were standardized with the back of the knees in contact with the cassette, the patella centralized over the lower end of the femur, and the beam centered 2.5 cm below the apex of the patella, with a tube-to-film distance of 100 cm. Also, the Rosenberg view of the knee in 45° of flexion was obtained for accurate detection of JSN in the state of maximal load weight-bearing. The Rosenberg view is a 45° flexion, posteroanterior, weight-bearing view of the knee with the patellae touching the image receptor. The X-ray tube is 100 cm away from the image receptor, centered at the patellae, and pointing caudad 10°.

The mechanical axis of the knee was measured from the angle formed by a line drawn from the center of the femoral head to the medial tibial spine and a line drawn from the medial tibial spine to the center of the ankle joint. As mentioned above, patients who having valgus alignment of knees were excluded.[20]

The radiographic determinations of knee alignment were made by two examiners who had adequate knowledge about the measurement techniques and the K-L grading scale. All of the radiographs were digitized by the picture archiving and communication system software (PiViewStar, Infinit Technology, Seoul, Korea) in our hospital, and all of the distances and angles were measured by using the calipers and goniometer provided in the software. The software enables straight-line measurements with an accuracy of 0.01 mm and 0.01°. JSN was defined as the narrowest interbone distance between the medial femoral condyle and the tibial plateau. K-L grades were assessed using a standard atlas.[21]

Reproducibility

The inter-observer reproducibility between two examiners was assessed in a randomly chosen subset of 30 radiographs. Intra-observer variability was determined by reading these films 1 month apart. The level of agreement was quantified using the intraclass correlation coefficient (ICC). ICC for inter-observer variability was more than 0.94 and ICC for intra-observer variability was more than 0.97 in all of the measurements.

Statistical Analysis

SPSS ver. 12 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Partial correlation analysis was performed to analyze the relationship between the BMDs (femoral neck, femoral trochanter, femoral intertrochanter, total hip and spine) and joint space distance in the AP and the Rosenberg views, between the BMDs and mechanical axis of the knee adjusted for demographic variables (age, BMI). Analysis of covariance (ANCOVA) was used to analyze the difference in BMD in the K-L grade category groups, which was also adjusted for covariates (age, BMI).

We determined the sample size after conducting a pilot study with 50 cases. In the pilot study, the correlation coefficient was about 0.2. We set the level of significance (α) and power to 0.05 and 0.8, respectively; therefore, the result of sample size calculation was 193 and we ensured that a sufficient number of patients were included in the study.

RESULTS

The demographic features of participants are listed in Table 1. The study population included 195 females who had radiographic features of knee OA (K-L grade ≥ 1). The mean age of study participants was 68.5 years, with a range of 38 to 83 years. The mean height, weight, and BMI were 151.58 cm (range, 139.40 to 177.90 cm), 60.25 kg (range, 39.10 to 96.00 kg), and 26.17 kg/m^2 (range, 18.39 to 39.33 kg/m^2), respectively. Mean JSN in the AP view was 2.00 mm, and mean JSN in the Rosenberg view was 1.48 mm. Thirty participants were classified into K-L grade 1, 22 into K-L grade 2, 51 into K-L grade 3, and 92 into K-L grade 4.

There was a statistically significant relationship between mechanical axis of the knee and femoral neck, trochanter, intertrochanter, and total hip BMD ($p < 0.05$). Less severity of varus alignment was positively associated with the BMD of the proximal femur. There was also a statistically significant difference in spine BMD in terms of the mechanical axis. In terms of the joint space distance, there were statistically significant relationships between BMD of the proximal femur (femoral neck, trochanter, intertrochanter, and total hip) and joint space distance in the AP view ($p < 0.05$). There were also statistically significant differences between BMD of the proximal femur and joint space distance in the Rosenberg view ($p < 0.05$). The BMD values of the proximal femur were positively associated with increased joint space distance. Joint space distance increased with greater total hip BMD both in the AP view and the Rosenberg view (in the AP view: femoral neck, r = 0.147, p = 0.041; femoral trochanter, r = 0.251, p = 0.000; femoral intertrochanter, r = 0.224, p = 0.002; total hip, r = 0.233, p = 0.001 and in the Rosenberg view: femoral neck, r = 0.226, p = 0.002; femoral trochanter, r = 0.289, p = 0.000; femoral intertrochanter, r = 0.295, p = 0.000; total hip, r = 0.307, p = 0.000). Spine BMD, however, was not significantly associated with joint space distance (Table 2).

The mean values of BMD of the proximal femur had a tendency to decrease with increasing K-L grades,

Table 1. The Demographic Features of Participants

Variable	Study participant (n = 195)
Age (yr)	68.51 ± 9.13 (38–83)
Height (cm)	151.58 ± 6.29 (139.40–177.90)
Weight (kg)	60.25 ± 10.39 (39.10–96.00)
BMI (kg/m^2)	26.17 ± 3.74 (18.39–39.33)
K-L grade	
1	30
2	22
3	51
4	92
Joint space distance (AP view, mm)	2.00 ± 1.72 (0–7.50)
Joint space distance (Rosenberg view, mm)	1.48 ± 1.66 (0–7.90)

BMI: body mass index, K-L: Kellgren-Lawrence grade (exclusion of grade 0: cases without arthritic changes), AP: anteroposterior.

Table 2. Relationship between BMD and Mechanical Axis and Joint Space Distance

Variable	Femoral neck BMD		Femoral trochanter BMD		Femoral intertrochanter BMD		Total hip BMD		Spine BMD (L1–L4)	
	r	p-value*	r	p-value*	r	p-value*	r	p-value*	r	p-value*
Mechanical axis†	0.255	0.000‡	0.269	0.000‡	0.209	0.004‡	0.245	0.001‡	0.207	0.004‡
Joint space distance (AP view)	0.147	0.041‡	0.251	0.000‡	0.224	0.002‡	0.233	0.001‡	0.102	0.161
Joint space distance (Rosenberg view)	0.226	0.002‡	0.289	0.000‡	0.295	0.000‡	0.307	0.000‡	0.056	0.445

BMD: bone mineral density, AP: anteroposterior.
*Statistically significant differences according to the partial correlation analysis adjusted for age and body mass index. †The higher increase in the value means the less varus alignment of the knee. ‡$p < 0.05$.

Table 3. Mean BMD Values in different K-L Grade Groups

Variable	Femoral neck BMD		Femoral trochanter BMD		Femoral intertrochanter BMD		Total hip BMD		Spine BMD (L1–L4)	
	F	*p*-value*	*F*	*p*-value*	*F*	*p*-value*	*F*	*p*-value*	*F*	*p*-value*
K-L grade (grade 1–4)	3.088	0.028†	4.604	0.004†	5.194	0.002†	4.853	0.003†	2.371	0.072
K-L 1 vs. 2, 3, 4	-	0.003†	-	0.043†	-	0.006†	-	0.006†	-	0.009
K-L 1, 2, 3 vs. 4	-	0.046†	-	0.000†	-	0.001†	-	0.001†	-	0.295

BMD: bone mineral density, K-L: Kellgren-Lawrence grade.
*Statistically significant differences according to the ANCOVA test adjusted for age and body mass index. †$p < 0.05$.

and there were significant differences in the BMD of the proximal femur (femoral neck, trochanter, intertrochanter, total hip) according to the K-L grade groups (p = 0.028, p = 0.004, p = 0.002, and p = 0.003, respectively). The contrast test was also conducted, and the K-L grade 1 group showed a statistically significant difference in the BMD of the proximal femur compared to K-L grade 2, 3, and 4 groups, and K-L grade 1, 2, and 3 groups showed statistically significant differences in the BMD of the proximal femur compared to K-L grade 4 group. There was no significant difference in spine BMD among the K-L grade groups (p = 0.072) (Table 3).

DISCUSSION

In this study, we focused on the relationship between the BMD of the proximal femur and severity of radiological knee OA in the ipsilateral side based on the cross-sectional data in a Korean population especially among women, while studying the relationship between spine BMD and the severity of radiological knee OA at the same time. The overall results demonstrated that after adjusting for demographic variables (age, BMI), low BMD of the proximal femur (femoral neck, trochanter, intertrochanter and total hip) was positively correlated with joint space width. Also, higher K-L grade was associated with lower BMD of the proximal femur. On the other hand, the BMD of lumbar spine lacked such an association.

A number of studies about the relationship between BMD and OA have been reported and the inverse relationship between OP and OA has been shown in the cross-sectional data.[1-6] In the Framingham study, mean femoral BMD at the 3 proximal femur sites was 5%–9% higher in patients with either grade 1, grade 2, or grade 3 knee OA compared with those with no knee OA.[3] Another cohort study reported that higher bone density was associated with an increased prevalence of knee OA and an increased risk of incident knee OA, but higher BMD was associated with a decreased risk of progressive knee OA.[11] Other cross-sectional studies showed that OA subjects had a 6%–9% increase in lumbar spine BMD[4] and patients who had hip OA were found to have 8%–10% higher spine and hip BMD.[6] Our data are obtained from patients who had both symptomatic and radiological knee OA. Also, we made an effort to minimize the difference in the time between the assessment of knee OA and the BMD measurement (≤ 6 months) for collecting the cross-sectional data. Development of OA is associated with changes in the subchondral bone[22,23] and crosstalk between the subchondral bone and the cartilage contributes to progression towards different stages of OA.[24] As the initiation of OA precedes the appearance of radiographic features,[23] it may be more difficult to analyze the actual relationship between BMD and OA.

Severity of radiological OA, as demonstrated by a narrower joint space or a higher K-L grade, had a negative correlation with the BMD of the ipsilateral proximal femur. Also, contrary to the result of a previous study,[25] there was no correlation between the spine BMD and knee OA (in terms of joint space distance and the K-L grade). Pain and disuse of the affected limb may have caused a local decrease in BMD of the proximal femur on the ipsilateral side, while spine BMD was relatively unaffected by these effects. So in our setting, it can be suggested that local factors affected the interaction between OA and bone density in addition to systemic factors.

Our data, obtained from a Korean population, especially from women, may reflect a different lifestyle compared with that of Caucasian population[3,6,9-11] as the patients with pain due to OA mostly avoid physical activities and exercises. Therefore, we think that these factors led to the obtainment of results, which are the different from those in previous studies. As a corollary, while studying the relationship between OA and OP, various factors should be taken into consideration.

There were several limitations to this study. Only females were included in the study population; hence, it did not accurately reflect the Korean population. Although we made an effort to adjust for physical variables, we were not able to control for individual lifestyle and physical activity of knee OA patients. Also, we only included symptomatic patients with knee OA; therefore, we could not assess the relationship between the BMD and radiographic knee OA in healthy groups and could not analyze the association between BMD and the incidence of knee OA. However, we believe that this report provides useful information about the relationship between OA and OP in Asian patients.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

This study was supported by a grant from the National Research Foundation of Korea (2009-0092196).

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