Relationships among bone mineral densities, static alignment and dynamic load in patients with medial compartment knee osteoarthritis

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Abstract

Objective. To investigate the relationships among bone mineral density (BMD), static alignment and the adduction moment of the knee in patients with tibiofemoral osteoarthritis (OA).

Methods. Sixty-nine patients with medial compartment knee OA underwent radiographic evaluation, gait analysis and BMD measurements at the proximal tibia and lumbar spine.

Results. The bone mineral distribution of the medial to lateral part of the proximal tibia correlated significantly with the peak knee adduction moment and the mechanical axis. Furthermore, the adduction moment correlated significantly with the mechanical axis. However, the BMD of the lumbar spine and the bone mineral distribution of the posterior to anterior part of the proximal tibia did not correlate with any other measurement.

Conclusions. Our results suggest that the bone mineral distribution of the proximal tibia is directly affected but lumbar BMD is not influenced by the local mechanical stress around the knee with medial compartment OA.

Key words: Bone mineral density, Alignment, Knee osteoarthritis, Mechanical load.

The negative relationship between general osteoporosis and osteoarthritis (OA) is well described. Patients with knee or hip OA show higher bone mineral density (BMD) compared with normal subjects [1–9]. In particular, women with osteophytes have significantly higher femoral BMD than women without osteophytes [2]. Belmonte-Serrano et al. [9] demonstrated that BMD of the total body and lumbar spine measured by dual-photon absorptiometry correlated positively with radiographic knee OA scores; these results did not seem to be due to the local effects of OA on specific areas but probably represented the general relationship between the disease and bone metabolism. Few investigators have attributed the high BMD in patients with knee OA mainly to increased bone turnover [2, 8], while other studies have indicated less bone turnover in premenopausal patients with knee OA [7]. Tibiofemoral knee OA usually shows varus or valgus alignment as well as eccentric high stress distribution in the affected compartment. However, very little is known about the influence of the static alignment or dynamic load of the OA knee joint on the BMD of the lumbar spine [10]. One of the mechanisms of initiation and progression of articular cartilage damage is increased density or stiffness of the underlying subchondral bone [11–14]. Previous in vitro studies have shown that the mechanical properties of the trabecular bone correlate with the load distribution at the proximal tibia [15–19]. Site-specific bone mineral contents of the proximal tibia have been measured by dual-photon absorptiometry and quantitative computed tomography [20–24]. Recently, BMD measurements in this area have been reported using dual-energy X-ray absorptiometry (DXA) in patients with knee OA [25–27]. Previous studies showed that the BMD of the medial tibial plateau was higher than that of the lateral tibial plateau and the bone mineral distribution was associated with the alignment of the lower extremity, suggesting that the load-bearing trabecular bone site has a higher bone mineral density than the unloaded site [20, 23, 24, 27]. Recently, Hurwitz et al. [28] demonstrated a significant relationship between proximal tibial BMD and the magnitude of the dynamic load in normal subjects. However, to our knowledge, the relationships among dynamic load, bone mineral distribution and static alignment of the lower extremity and whether such relationships hold in patients with tibiofemoral OA have not been determined. Among the

Submitted 7 February 2000; revised version accepted 27 November 2000

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components of the dynamic load on the knee during walking, the adduction moment of the knee is considered to be the most influential factor contributing to the medial joint force in joints with varus deformity [29, 30]. The purpose of this study was to determine the relationships among BMD of the lumbar spine and proximal tibia, static alignment and OA disease severity, and the adduction moment of the knee in patients with OA of the medial compartment of the knee.

Subjects and methods

Patients
Sixty-nine patients with bilateral medial compartment knee joint OA with radiographically similar disease severity, managed at Fukui Medical University Hospital, were enrolled in this study. All patients had a definitive diagnosis of OA according to the American College of Rheumatology criteria [31]. Patients were excluded from the study if they had symptomatic musculoskeletal disorders other than those affecting the knee joints, a history of major trauma or sports injury of the knee, rheumatoid arthritis, gout, pseudo-gout, autoimmune diseases, neuropathic arthropathy, infectious disease or another major systemic disease. The characteristics of the patients are shown in Table 1. Although all subjects had bilateral knee disease, measurements were performed on the more symptomatic knee in each patient. Each subject underwent measurements of BMD, radiographic evaluation and gait analysis after a 4-week washout period of anti-inflammatory medications and physiotherapy. The study was approved by the ethics committee of our institution and written informed consent was obtained from all patients.

Measurement of BMD
Proximal tibiae were scanned by DXA (QDR-1000; Hologic, Walham, MA, USA). Anteroposterior (AP) measurement was performed while the subject was in the supine position on the DXA table with the patella fixed in the upright position. The lower leg was fixed on the mattress with the knee flexed 20° so that the tibia was aligned parallel to the table. For the lateral scan, the lateral side of the knee was in contact with the table.

Table 1. Characteristics of patients with OA of the knee

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>74 (58–82)²</td>
</tr>
<tr>
<td>Gender</td>
<td>Males: 10, females: 59</td>
</tr>
<tr>
<td>Measurement side</td>
<td>Right knee: 37, Left knee: 32</td>
</tr>
<tr>
<td>Body mass index</td>
<td>26.8 (19.4–37.7)³</td>
</tr>
<tr>
<td>Kellgren-Lawrence grade</td>
<td>1: 11, 2: 12, 3: 29, 4: 17</td>
</tr>
</tbody>
</table>

²Median and range.
³Weight (kg)/height (m²).
of the medial and lateral plateaux at the level of the joint line. The centre of the ankle joint was estimated at the mid-point between lateral and medial malleoli [28, 32, 33]. Data on distances from the skin marker to the centre were entered into the computer. Moments of the knee joint were computed by the use of the three-dimensional rigid body link model of Bresler and Frankel [34], incorporating the data on the three-dimensional location of each segment, the inertial properties of the limb segment and the data on the floor reaction forces [35].

**Radiographic evaluation**

All patients had standing AP radiographs of the knee and full-length AP radiographs of the whole lower extremity in full extension of the knee. The projection angle of the radiograph was determined from the lateral radiograph by measuring the posterior tilt of the medial tibial plateau. The AP radiograph of the knee was then obtained with the radiographic beam directed parallel to the medial tibial plateau. From the AP radiograph of the knee, the severity of medial compartment knee OA was classified according to the Kellgren–Lawrence grading system [36]. The narrowest width of the joint space was measured in millimetres in the medial compartment. From the full-length weight-bearing AP radiographs of the lower extremity, the static alignment of the lower extremity was expressed using the mechanical axis, which represented the angle between the line connecting the centre of the femoral head and the centre of the tibial plateau and the line connecting the centre of the tibial plateau and the centre of the ankle joint. In addition, the degree of varus deformity of the proximal tibia was expressed as the tibial condylar angle, representing the angle between the line parallel to the tibial plateau and the line connecting the centre of the tibial plateau and the centre of the ankle joint (Fig. 2).

**Statistical analysis**

Quantitative group data were expressed as median and range. The Mann–Whitney U-test was used to compare differences in disease severity and gender. The Wilcoxon signed rank test was used to compare BMD between the medial and lateral or anterior and posterior parts of the proximal tibia. Correlations among variables were assessed with Spearman’s rank correlation test. Multiple regression analysis was used to test for associations among variables after adjusting for age, sex and/or body
height and weight. A two-tailed $P$ value less than 0.05 was considered statistically significant.

Results

The results of BMD measurements are shown in Table 2. The tibial BMD of the medial compartment was significantly higher than that of the lateral compartment in both mild and severe OA ($P < 0.05$ and $P < 0.001$ respectively). Likewise, the BMD of the posterior tibial region was significantly higher than that of the anterior tibial region in both mild and severe OA ($P < 0.05$ for mild OA and $P < 0.001$ for severe OA). The BMDs of the tibial regions correlated significantly with each other ($r = 0.43–0.77$, $P < 0.01$). The ratio of the BMD of the medial tibial plateau relative to the lateral tibial plateau (M/L ratio) was higher in severe OA than in mild OA ($P < 0.01$), while the ratio of the BMD of the posterior tibial plateau relative to the anterior tibial plateau (P/A ratio) was not different between mild and severe OA. The BMD of the lumbar spine was also not different between groups. The peak adduction moment for severe OA was 30% higher than that for mild OA ($P = 0.06$). In severe OA, the mechanical axis was significantly larger ($P < 0.001$), the minimum joint space width was smaller ($P < 0.001$) and the tibial condylar angle was smaller ($P < 0.05$) than in mild OA (Table 1).

The BMD of each measured site in the proximal tibia was not significantly different between men and women except for the M/L ratio. In women, the M/L ratio was significantly higher ($P < 0.05$), the BMD of the lumbar spine was significantly lower ($P < 0.01$) and the mechanical axis was significantly larger ($P < 0.05$) than in men. The peak adduction moment, the minimum joint space width and the tibial condylar angle were not significantly different between men and women (Table 3).

There were significant correlations between the M/L ratio and the mechanical axis ($r = 0.53$, $P < 0.001$; $r = 0.77$, $P < 0.001$).

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**Table 2.** BMD (g/cm$^2$), static alignment and adduction moment of the knee in patients with mild (Kellgren-Lawrence grades 1 and 2) and severe (grades 3 and 4) knee OA

<table>
<thead>
<tr>
<th></th>
<th>K/L grade 1–2 ($n = 23$)</th>
<th>K/L grade 3–4 ($n = 46$)</th>
<th>$P^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>70 (54–83)</td>
<td>74 (60–84)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24.5 (20.3–32.9)</td>
<td>27.3 (19.4–37.7)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>BMD$^b$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MT</td>
<td>0.67 (0.23–1.13)$^d$</td>
<td>0.77 (0.10–1.51)$^e$</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>LT</td>
<td>0.52 (0.15–0.94)$^d$</td>
<td>0.54 (0.12–1.11)$^e$</td>
<td>0.83</td>
</tr>
<tr>
<td>M/L ratio, tibia</td>
<td>1.33 (0.86–1.55)</td>
<td>1.54 (0.21–2.69)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>AT</td>
<td>0.60 (0.38–0.92)$^d$</td>
<td>0.62 (0.32–1.39)$^g$</td>
<td>0.58</td>
</tr>
<tr>
<td>PT</td>
<td>0.79 (0.41–1.33)$^f$</td>
<td>0.90 (0.45–1.95)$^g$</td>
<td>0.24</td>
</tr>
<tr>
<td>P/A ratio, tibia</td>
<td>1.13 (0.82–1.85)</td>
<td>1.20 (0.53–2.97)</td>
<td>0.82</td>
</tr>
<tr>
<td>Lumbar</td>
<td>0.86 (0.52–1.01)</td>
<td>0.84 (0.40–1.24)</td>
<td>0.73</td>
</tr>
<tr>
<td>Mechanical axis ($^\circ$)</td>
<td>10 (0–15)</td>
<td>14 (5–33)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Tibial condylar angle ($^\circ$)</td>
<td>85 (81–90)</td>
<td>82 (74–93)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>JSW$^c$ (mm)</td>
<td>2 (1–7)</td>
<td>0 (0–1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Peak adduction moment of the knee (% body weight × height)</td>
<td>3.5 (1.1–7.4)</td>
<td>5.3 (0.4–8.4)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Data are median (range).

$^a$Mann-Whitney U-test.

$^b$MT, LT, AT and PT are the medial, lateral, anterior and posterior parts of the proximal tibia.

$^c$Minimum joint space width of the medial compartment of the knee.

$^d$Statistically significant (d, f, $P < 0.05$; e, $P < 0.001$; g, $P < 0.01$) by Wilcoxon signed rank test.
Table 3. BMD (g/cm²), static alignment and adduction moment of the knee in male and female patients with knee OA

<table>
<thead>
<tr>
<th></th>
<th>Men (n = 10)</th>
<th>Women (n = 59)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>70 (54–84)</td>
<td>74 (54–83)</td>
<td>0.55</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24.0 (20.3–33.5)</td>
<td>27.0 (19.4–37.7)</td>
<td>0.18</td>
</tr>
<tr>
<td>BMDb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MT</td>
<td>0.76 (0.45–0.85)</td>
<td>0.68 (0.10–1.51)</td>
<td>0.74</td>
</tr>
<tr>
<td>LT</td>
<td>0.62 (0.31–0.80)</td>
<td>0.50 (0.12–1.11)</td>
<td>0.06</td>
</tr>
<tr>
<td>M/L ratio, tibia</td>
<td>1.16 (0.94–1.72)</td>
<td>1.42 (0.21–2.69)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>AT</td>
<td>0.73 (0.42–1.13)</td>
<td>0.61 (0.32–1.39)</td>
<td>0.46</td>
</tr>
<tr>
<td>PT</td>
<td>0.94 (0.51–1.39)</td>
<td>0.81 (0.41–1.95)</td>
<td>0.41</td>
</tr>
<tr>
<td>P/A ratio, tibia</td>
<td>1.11 (0.82–2.08)</td>
<td>1.18 (0.53–2.97)</td>
<td>0.95</td>
</tr>
<tr>
<td>Lumbar</td>
<td>1.03 (0.82–1.24)</td>
<td>0.84 (0.40–1.01)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Mechanical axis (°)</td>
<td>8 (0–17)</td>
<td>13 (5–35)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Tibial condylar angle (°)</td>
<td>84 (77–85)</td>
<td>83 (74–93)</td>
<td>0.68</td>
</tr>
<tr>
<td>JSW* (mm)</td>
<td>0 (0–1)</td>
<td>1 (0–7)</td>
<td>0.20</td>
</tr>
<tr>
<td>Peak adduction moment of the knee (%/body weight × height)</td>
<td>4.3 (2.6–5.3)</td>
<td>5.0 (0.4–8.4)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Data are median (range). *Mann–Whitney U-test. **MT, LT, AT and PT are the medial, lateral, anterior and posterior parts of the proximal tibia. *Minimum joint space width of the medial compartment of the knee. dStatistically significant (d, P < 0.01; e, P < 0.001; f, P < 0.001) by Wilcoxon signed rank test.

Fig. 3A), the peak adduction moment of the knee (r = 0.52, P < 0.001, Fig. 3B), the minimal joint space width of the medial compartment (r = 0.46, P < 0.05), the tibial condylar angle (r = −0.41, P < 0.01) and the grade of OA severity (r = 0.48, P < 0.01). Significant correlations were still present after adjusting for age, sex, height and body weight.

The adduction moment of the knee correlated significantly with the mechanical axis (r = 0.62, P < 0.001; Fig. 3C) and tibial condylar angle (r = −0.50, P < 0.01) in addition to the M/L ratio. Significant correlations were still present after adjusting for age and sex.

The BMD of the lumbar spine correlated significantly with the BMD of the anterior (r = 0.41, P < 0.01), posterior (r = 0.52, P < 0.001) and lateral (r = 0.34, P < 0.05) parts of the proximal tibia, and significant correlations were still present after adjusting for age, sex, height and body weight. The P/A ratio did not correlate with any other measurement.

Discussion

In this study, the BMD of the proximal tibia was higher in the medial compartment than in the lateral compartment and higher in the posterior region than the anterior region in OA of the medial compartment of the knee. This finding is probably due to increased weight bearing on the medial condyle relative to the lateral condyle with varus deformity [20, 24, 27] and seems to be associated with the fact that the articular cartilage of medial compartment knee OA is predominantly affected in the posterior part of the articular cartilage or flexion contracture that is usually seen in advanced knee OA. In addition, we found that the M/L ratio of the proximal tibial BMD increased with increasing adduction moment, more varus alignment and more advanced medial compartment OA grade. However, the bone mineral distribution of the proximal tibia in the sagittal plane (the P/A ratio) did not correlate with any other measurement. Therefore, the bone mineral distribution of the proximal tibia in medial compartment knee OA was associated mainly with the articular load distribution in the frontal plane, and the load distribution in the sagittal plane varied widely with the severity of OA.

On the basis of our cross-sectional study, we do not think one can conclude that the higher BMD was a consequence of a higher load. However, other groups have shown changes in subchondral bone density of the proximal tibia in knee OA [12, 27]. Previous studies have shown the presence of thick trabecular bone in areas with high BMD that could have formed by higher mechanical load [13, 20]. Thus, it is likely that higher BMD was a consequence of higher load in this study. In addition, others have postulated that repetitive cumulative microdamage leads to the remodelling and stiffening of bone [11]. Therefore, both thicker trabecular bone and microfracture of the cancellous bone may be caused by the high BMD, and the presence of stiff subchondral bone may result in further damage to the articular cartilage in our patients with established OA. If these relationships are applied clinically, our results suggest that the evaluation of BMD at the proximal tibia, the adduction moment of the knee or the static alignment may help in predicting disease progression in patients with medial compartment knee OA. In addition, it has been reported that, in normal adults, bone mineral distribution in the proximal tibia is associated with the peak adduction moment of the knee [28]. Therefore, evaluation of the BMD at the proximal tibia and the adduction moment in healthy adults may help in predicting those at risk of knee OA.

In this study, we have shown a significant relationship between the adduction moment and the static alignment of the lower extremity or varus deformity of the upper
tibia. However, there is controversy regarding the relationship between the peak knee adduction moment and the static alignment of the lower extremity [37–43]. Even in studies that supported positive relationships [38, 39, 43], the associations were relatively weak. It is suggested, therefore, that the adduction moment of the knee and static alignment do not correlate when the individual patient adopts a compensatory mechanism to unload the knee [44].

It has been reported that the BMD of the lumbar spine correlates with disease severity [5] or varus deformity at the proximal tibia [10] in knee OA. However, we did not find such a relationship in the present study. This discrepancy may be due to the different characteristics of the participating subjects or to sample size. In addition, our results showed the lack of relationship between the BMD of the lumbar spine and the adduction moment of the knee. These results suggest that lumbar BMD may not be affected directly by changes in local biomechanical characteristics or biological events such as osteopenia as a result of inflammatory cytokines [26] around the knee joint, although it is also possible that general or total body osteoporosis causes local osteopenia independently of the magnitude of local stress distribution.

In conclusion, we have demonstrated that the bone mineral distribution of the proximal tibia is affected directly but that the lumbar BMD is not influenced by local mechanical stress in patients with OA of the medial compartment of the knee.

References