Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis

T Miyazaki, M Wada, H Kawahara, M Sato, H Baba, S Shimada

Objective: To test the hypothesis that dynamic load at baseline can predict radiographic disease progression in patients with medial compartment knee osteoarthritis (OA).

Methods: During 1991–93 baseline data were collected by assessment of pain, radiography, and gait analysis in 106 patients referred to hospital with medial compartment knee OA. At the six year follow up, 74 patients were again examined to assess radiographic changes. Radiographic disease progression was defined as more than one grade narrowing of minimum joint space of the medial compartment.

Results: In the 32 patients showing disease progression, pain was more severe and adduction moment was higher at baseline than in those without disease progression (n=42). Joint space narrowing of the medial compartment during the six year period correlated significantly with the adduction moment at entry. Adduction moment correlated significantly with mechanical axis (varus alignment) and negatively with joint space width and pain score. Logistic regression analysis showed that the risk of progression of knee OA increased 6.46 times with a 1% increase in adduction moment.

Conclusions: The results suggest that the baseline adduction moment of the knee, which reflects the dynamic load on the medial compartment, can predict radiographic OA progression at the six year follow up in patients with medial compartment knee OA.

Osteoarthritis (OA) of the knee is one of the major causes of pain and physical disability in the elderly and occurs in almost 10% of those over 65 years. Thus, prevention of knee OA should be one of the major aims of health care, and requires clear knowledge of the risk factors of this disease.

Many investigators have previously reported a variety of risk factors for knee OA. However, relatively few have studied disease progression longitudinally. It is now recognised that risk factors for the development of OA are different from those for progression. Cooper et al suggested that prevention of the progression of OA to severe damage is a more effective public health strategy than attempting to prevent the initial development of the disease. OA is defined based on symptoms such as pain, together with radiographic changes. Dieppe et al reported a discrepancy between radiographic and clinical changes after three years' follow up in peripheral joint OA. Thus, it is important to differentiate between radiographic and clinical changes after three years' follow up in peripheral joint OA. It is considered that the baseline adduction moment is an important biomechanical factor but it is also associated with systemic and hormonal factors responsible for bone and cartilage metabolism, especially in women, thus making it difficult to interpret its biomechanical effects on the progression of OA.

In evaluating the effects of biomechanical factors on the progression of knee OA, one of the best methods may be to measure directly load on the specific site. Measurements performed under dynamic loading, such as during walking, should be considered to assess the biomechanical function of the knee. To achieve this, the magnitude of the load on the affected knee joint must be estimated quantitatively by measuring the kinematic knee joint moment. In particular, the adduction moment of the knee is considered to be the most influential factor, producing medial joint force in joints with varus deformity. Pain is also associated with dynamic load. In an individual patient with knee OA, the adduction moment decreases after administration of anti-inflammatory drugs and, without analgesics, the adduction moment tends to decrease to reduce load on the affected joint. In addition, previous studies have shown that the adduction moment negatively correlates with joint space width and positively with mechanical axis (varus alignment) in knee OA. Dynamic load during gait may significantly influence prognosis, but its long term effect has not yet been established.

Here we tested the hypothesis that adduction moment and related variables at baseline can predict radiographic disease progression in medial compartment knee OA.

Abbreviations: AP, anteroposterior; K/L, Kellgren and Lawrence; OA, osteoarthritis
from all patients. Written informed consent was obtained.

washout period of anti-inflammatory drugs and physio-
radiographic evaluations, and gait analysis after a four week
in each patient. Each subject underwent assessment for pain,
were performed on the more symptomatic side (index knee)
changes in the patellofemoral joint. To eliminate the con-
pain at the medial side of the knee, with or without minor
than the lateral compartment on knee radiographs and had
had narrower interbone distance in the medial compartment
those affecting the knee joints, history of major trauma or a
they had symptomatic musculoskeletal disorders other than
one or two knees. Patients were excluded from the study if
medial compartment knee OA to be present in those patients
50 and had knee pain in some daily activities. We considered
enrolled in this prospective study. All patients were aged over
ment knee joint OA managed at our orthopaedic unit were
During 1991–93, 106 patients with primary medial compart-

### PATIENTS AND METHODS

**Patients**

During 1991–93, 106 patients with primary medial compart-
ment knee joint OA managed at our orthopaedic unit were
enrolled in this prospective study. All patients were aged over
50 and had knee pain in some daily activities. We considered
medial compartment knee OA to be present in those patients
who had varus alignment; all subjects had varus alignment in
one or two knees. Patients were excluded from the study if
they had symptomatic musculoskeletal disorders other than
those affecting the knee joints, history of major trauma or a
sports injury of the knee, rheumatoid arthritis, gout, pseudo-
gout, autoimmune diseases, neuropathic arthropathy, infec-
tious disease, or other major systemic diseases. All patients
had narrower interbone distance in the medial compartment
than the lateral compartment on knee radiographs and had
pain at the medial side of the knee, with or without minor
changes in the patellofemoral joint. To eliminate the con-
founding variable of bilateral involvement, all measurements
were performed on the more symptomatic side (index knee) in
each patient. Each subject underwent assessment for pain,
radiographic evaluations, and gait analysis after a four week
washout period of anti-inflammatory drugs and physio-
therapy. The study was approved by the ethics committee of
our institution, and written informed consent was obtained
from all patients.

Table 1 shows the characteristics of patients entered into the
study. Of the original 106 patients recruited for the study,
eight patients died, 15 patients underwent total knee arthro-
plasties, and nine were lost to follow up at six years. The
remaining 74 patients completed the six year follow up. Twenty two knees of 74 patients were normal.

**Recorded variables**

Demographic data obtained at entry included age, sex, height,
weight, and assessment of knee pain. Radiographs of both
knees and legs and gait analysis were evaluated within a two
week interval. At the six year follow up, the main outcome
measure was changes in radiographic features of each index
knee. The radiographs were taken in exactly the same way as
at entry.

**Radiographic evaluation**

Standing radiographs of the knee in anteroposterior (AP), lat-
eral, and skyline views were obtained in all patients. All
patients had standing AP radiographs of the knee and full
length AP radiographs of the whole leg in a semiflexed
position. The projection angle of the radiograph was
determined using the lateral radiograph, by measuring the
posterior tilting of the medial tibial plateau. The AP
radiograph of the knee was then obtained with the
radiographic beam pointing parallel to the medial tibial
plateau. The full length weightbearing AP radiographs of the
leg were used to express the varus-valgus alignment of the leg
using the mechanical axis, which represented the angle
between the line connecting the centre of the femoral head
and the centre of the tibia plateau and the line connecting the
centre of the tibia plateau and the centre of the ankle joint (fig
1). All radiographs were evaluated by an experienced reader
(HK) who was unaware of all other data.

In this study the severity of tibiofemoral OA was assessed by
two systems. The degree of osteophyte formation of the whole
medial compartment knee OA was classified by the atlas of Kellgren
and Lawrence (K/L). K/L grade 2 indicates definite osteophyte
formation, which is a specific radiographic feature of OA. How-
ever, at the start of the study, patients with K/L grade 1
were included because all had knee pain sometimes during
activities of daily living. The other method used was based on
measurement of joint space narrowing of the medial
compartment by the atlas of Altman et al., which classifies the
severity of OA into four grades. Repeated radiographs were
taken using exactly the same technique as at entry.

Using the AP radiograph of the knee, we measured the nar-
rowest width of the joint space in millimetres in the medial
compartment. Minimum joint space width was measured in
the medial tibiofemoral compartment as the interbone
distance, where the length between the distal part of the
femur and the proximal part of the tibia was minimum. The
femoral point (f) was the lowest point of the convex line of the
distal femoral condyle. Then, a perpendicular line to the

### Table 1 Characteristics of patients. Results for continuous variables are expressed as mean (standard deviation)

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=106)</th>
<th>Patients who completed the study (n=74)</th>
<th>Patients who underwent TKA (n=15)</th>
<th>Patients who died or were lost (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>69.9 (7.8)</td>
<td>69.5 (7.5)</td>
<td>72.5 (6.0)</td>
<td>69.2 (10.0)</td>
</tr>
<tr>
<td>Sex</td>
<td>Men</td>
<td>20</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>86</td>
<td>58</td>
<td>14</td>
</tr>
<tr>
<td>Body mass index*</td>
<td>24.5 (3.2)</td>
<td>24.5 (3.3)</td>
<td>25.4 (3.0)</td>
<td>23.8 (2.8)</td>
</tr>
<tr>
<td>Pain†</td>
<td>23.5 (4.8)</td>
<td>24.3 (4.7)</td>
<td>20.3 (4.8)</td>
<td>23.2 (3.9)</td>
</tr>
<tr>
<td>Mechanical axis (°)‡</td>
<td>6.5 (4.7)</td>
<td>5.3 (4.0)</td>
<td>12.5 (4.8)</td>
<td>6.1 (3.2)</td>
</tr>
<tr>
<td>Joint space width (mm)</td>
<td>3.0 (1.3)</td>
<td>3.3 (1.1)</td>
<td>1.5 (1.3)</td>
<td>3.0 (0.9)</td>
</tr>
<tr>
<td>Adduction moment (% wt × ht)</td>
<td>5.3 (1.8)</td>
<td>4.9 (1.6)</td>
<td>6.8 (1.7)</td>
<td>5.4 (1.7)</td>
</tr>
<tr>
<td>K/L grade</td>
<td>1</td>
<td>21</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>27</td>
<td>22</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>36</td>
<td>23</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>22</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>JSN grade</td>
<td>0</td>
<td>7</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>58</td>
<td>46</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>25</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>16</td>
<td>4</td>
<td>11</td>
</tr>
</tbody>
</table>

Wt, weight; ht, height; TKA, total knee arthroplasty; K/L grade, Kellgren and Lawrence grade; JSN, joint space narrowing.

*Weight (kg)/[height (m)]²; †evaluated using a knee rating system of the Hospital for Special Surgery; ‡see fig 1.
ground was drawn from point f. The intersection between this line and the dense line of the tibia plateau was marked as point (t). Measurements were corrected for magnification, and the distance between them, f−t (minimum joint space width), was measured with a caliper. Minimum joint space measurements of 10 patients with OA on two different days were compared by analysis of variance with repeated measures and by intraclass coefficient. The reliability of measurement of the medial compartment was high (intraclass coefficient 0.92). In 3/74 patients, joint space width at follow up was greater than at entry (radiographic change is negative). The negative change seen in each of these patients was <1 mm. Because this change was considered to be a variation in the reading process, we regarded it as “no change” in this study. Radiographic disease progression was defined as a one grade or more increase in the narrowing of joint space.

Evaluation of knee pain
Knee pain was evaluated using the Hospital for Special Surgery pain subscale (0–30 points, 30, no pain both at rest and on walking). Even when the subject marked 30 on this scale, the patient had pain when going up and down stairs and squatting.

Statistical analysis
To compare knees with and without disease progression, the \( \chi^2 \) test was used for discrete variables and the unpaired t test was used to test for equality of the continuous variables. Simple and multiple regression analyses were used to test the relationships between adduction moment and other variables at entry, or joint space loss and baseline variables. In addition, a logistic regression model was used to examine radiographic disease progression as the dependent variable. A two tailed p value <0.05 was considered significant.

RESULTS
The patients of the group who underwent total knee arthroplasty at a later stage tended to be older, had more varus alignment, less joint space width, more pain, and higher adduction moment at entry than the other groups; the results could not be analysed statistically because of the small sample sizes of these subgroups (table 1). Patients were divided into two groups based on radiographic outcome after six years’ follow up; 32 patients showed radiographic disease progression while no progression was
seen in 42 patients. Table 2 shows the clinical and demographic data of these patients at study entry. The proportion of men and women and the number of patients with each radiographic scale (K/L grade and joint space narrowing grade) were similar in the two groups. However, there were some significant differences at entry between the two groups. In the group with radiographic progression, knee pain was more severe (p<0.05) and adduction moment was significantly higher (p<0.0001) than in the group without progression. Age, body mass index, mechanical axis, and joint space width at entry were not statistically different between the two groups (table 2).

The average loss of the joint space width during six years was 1.4 (1.2) mm (range 0–6). There were significant correlations between the amount of this change and baseline pain score (r=−0.37, p<0.001), mechanical axis (r=0.41, p<0.001), adduction moment (r=0.62, p<0.0001), and joint space width (r=−0.25, p=0.03). There were no significant correlations between loss of the joint space width and age, sex, and body mass index at entry.

We also investigated the relationship between adduction moment and other variables at baseline. The adduction moment correlated with pain score (r=−0.33, p<0.001). It also correlated with mechanical axis (r=0.23, p<0.001), and negatively with joint space width (r=−0.28, p=0.04) after adjusting for age and pain.

To compare the predictive power for radiographic progression, the cut off point of each baseline variable was determined using a receiver operating characteristic curve analysis (fig 2). According to this analysis, the cut off values of the baseline adduction moment, mechanical axis, joint space width, and pain score for radiographic disease progression were 5%, 5°, 3 mm, and 25 points, respectively. Table 3 shows the relationships between radiographic progression and baseline variables using these cut off values. The sensitivity, specificity, and positive predictive value of baseline adduction moment for radiographic progression were 88% (28/32), 83% (35/42), and 80% (28/35), respectively. Likewise, the sensitivity, specificity and positive predictive value of baseline mechanical axis, joint space width, and pain score for radiographic progression were 66% (21/32), 62% (26/42), and

### Table 2 Baseline demographic data of 74 patients followed up for six years. Results for continuous variables are expressed as mean (standard deviation)

<table>
<thead>
<tr>
<th>Data at entry</th>
<th>Patients without disease progression (n=42)</th>
<th>Patients with disease progression (n=32)</th>
<th>p Value§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>68.7 (8.7)</td>
<td>70.5 (6.2)</td>
<td>0.30</td>
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<tr>
<td>Sex, male/female (n)</td>
<td>12/30</td>
<td>4/28</td>
<td>0.17¶</td>
</tr>
<tr>
<td>Body mass index*</td>
<td>24.1 (3.2)</td>
<td>24.5 (4.3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Pain†</td>
<td>25.5 (4.1)</td>
<td>22.7 (5.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mechanical axis [°]‡</td>
<td>4.6 (3.8)</td>
<td>6.3 (4.0)</td>
<td>0.06</td>
</tr>
<tr>
<td>Joint space width (mm)</td>
<td>3.4 (1.2)</td>
<td>3.2 (1.1)</td>
<td>0.31</td>
</tr>
<tr>
<td>Adduction moment [% wt × ht]</td>
<td>4.0 (1.4)</td>
<td>6.1 (1.0)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Kellgren-Lawrence grade

<table>
<thead>
<tr>
<th></th>
<th>Patients without disease progression (n=42)</th>
<th>Patients with disease progression (n=32)</th>
<th>p Value§</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>8</td>
<td>0.16¶</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
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<tr>
<td>4</td>
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Joint space narrowing grade

<table>
<thead>
<tr>
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<th>Patients without disease progression (n=42)</th>
<th>Patients with disease progression (n=32)</th>
<th>p Value§</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>1</td>
<td>0.16¶</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

*S=Weight (kg)/(height (m))^2; †evaluated using the knee rating system of the Hospital for Special Surgery34; ‡see fig 1; §continuous variables were examined by unpaired t test; ¶discrete variables were examined by χ² test.

### Table 3 Relationship between radiographic progression and baseline variables

<table>
<thead>
<tr>
<th></th>
<th>Patients with disease progression</th>
<th>Patients without disease progression</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adduction moment [% wt × ht]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5</td>
<td>28</td>
<td>7</td>
<td>35</td>
</tr>
<tr>
<td>&lt;5</td>
<td>4</td>
<td>35</td>
<td>39</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>42</td>
<td>74</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Patients with disease progression</th>
<th>Patients without disease progression</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint space width (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3</td>
<td>24</td>
<td>32</td>
<td>56</td>
</tr>
<tr>
<td>&lt;3</td>
<td>8</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>42</td>
<td>74</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Patients with disease progression</th>
<th>Patients without disease progression</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical axis (°)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5</td>
<td>21</td>
<td>16</td>
<td>37</td>
</tr>
<tr>
<td>&lt;5</td>
<td>11</td>
<td>26</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>42</td>
<td>74</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Patients with disease progression</th>
<th>Patients without disease progression</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;25</td>
<td>20</td>
<td>32</td>
<td>52</td>
</tr>
<tr>
<td>&lt;25</td>
<td>12</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>42</td>
<td>74</td>
</tr>
</tbody>
</table>
57% (21/37); 75% (24/32), 24% (10/42), and 43% (24/56); and 63% (20/32), 24% (10/42), and 38% (20/52), respectively.

Logistic regression analysis was performed with radiographic disease progression as the dependent variable. Seven independent variables were entered into the analysis (age, sex, body mass index, pain, mechanical axis, joint space width, and adduction moment). Of these, the variables found to be significant were adduction moment (p=0.0002) and age (p=0.01). The risk of progression of knee OA increased 6.46 times with a 1% increase in adduction moment and 1.22 times with a one year increase in age (table 4).

**DISCUSSION**

Measurement of joint space narrowing is one of the sensitive methods used to assess radiographic disease progression. However, the cut off value for disease progression has not yet been established. Dieppe *et al.* defined a change of more than 2 mm in joint space narrowing as radiographic progression, but this figure was arbitrary. Sharma *et al.* used an atlas that classifies joint space width into four grades, and defined progression as more than one grade advancement during the follow up interval. We used Sharma’s system in this study. In addition, the magnitude of radiographic change in joint space was used to investigate the correlations with baseline variables.

We divided patients at entry into three subgroups in order to identify those who later required total knee arthroplasty. Patients who subsequently underwent total knee arthroplasty tended to have more severe OA at entry. Dieppe *et al.* used the same analysis in their five year longitudinal study and reported that the only difference between patients who underwent surgery and those who did not was a higher body mass index; we did not find such a difference. The reason for these different findings is not clear, but the high female to male ratio in our group probably accounts for the relatively lower body mass index than in the subgroup of the study of Dieppe *et al.*

At entry, severity of pain was associated with adduction moment in this study. Patients with less pain had a lower adduction moment and those with more pain had a higher adduction moment. This is consistent with the study of Sharma *et al.*, who reported that the magnitude of the adduction moment correlated with OA disease severity. Although baseline mechanical axis and joint space width were also associated with adduction moment, the correlation between these two variables and adduction moment was relatively weak. This suggests that these variables do not reflect biomechanical stress on the diseased medial compartment as strongly as the adduction moment does.

The adduction moment of the knee is a major determinant of medial to lateral load distribution; thus it is responsible for the biomechanical abnormality of the medial compartment knee OA. Sharma *et al.* reported that dynamic load during gait correlated with disease severity in tibiofemoral knee OA. They suggested that the magnitude of the adduction moment possibly influences the structural outcome in medial compartment knee OA. Their recent longitudinal work also showed that varus alignment increased the risk of medial compartment OA progression in knee OA, which suggests that the degree of adduction moment correlates with radiographic joint space narrowing of the medial compartment because our baseline data also showed significant relationships between adduction moment and the mechanical axis (varus alignment).

High tibial valgus osteotomy is an effective treatment for medial compartment knee OA. High eccentric load concentration of the medial compartment can be reduced by lateral shift of the axial load. With this intervention, a high adduction moment can be also reduced to normal. Prodromos *et al.* reported that the preoperative adduction moment could predict surgical outcome for knee OA with varus deformity; when the adduction moment was higher preoperatively, it significantly changed to varus alignment again while lower adduction moment did not. In addition, we have reported previously that the adduction moment decreased significantly soon after high tibial osteotomy but tended to increase gradually after one year. Even after varus alignment was obtained, the adduction moment tended to increase with time. Furthermore, logistic regression analysis showed that the risk of progression of knee OA increased 6.46 times with a 1% increase in adduction moment. Finally, the positive predictive value of the adduction moment for radiographic disease progression was 80% using a cut off value of 5% weight/height. These results suggest that the value of the adduction moment at baseline can predict radiographic disease progression in medial compartment knee OA. Although measurement of adduction moment requires a precise gait analysis system, which is available in only a limited number of hospitals and laboratories, it is one of the most useful screening tests to detect radiographic disease progression. However, our results should be interpreted with caution because the patients in this study were patients with knee OA who were receiving drugs. Whether the results are also true for subjects in the general population or for the development of knee OA remains to be determined.

**REFERENCES**