EXTENDED REPORT

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

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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.[1] 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.[2 3] 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.[3] 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.[4] Thus, it is important to differentiate between radiographic and clinical disease progression. To date, certain baseline variables such as obesity,[5–7] knee pain,[8] knee effusion or warmth,[9] and indometacin[10] have been found to be associated with disease progression. Bone scintigraphy predicts subsequent loss of joint space in patients with established knee OA.[11] Certain serum markers, such as cartilage oligomeric matrix protein[12] and hyaluronic acid,[13] and a small increase in serum C reactive protein[14] are other possible predictors of disease progression. In addition, a high level of pyrophosphate in the synovial fluid is associated with less radiographic progression.[15]

The role of biomechanical factors in the pathogenesis of knee OA has been well described. Radin *et al* suggested that one of the mechanisms of initiation and progression of articular cartilage damage is increased density or stiffness of the underlying subchondral bone.[16] Although chondrocytes of the articular cartilage can adapt to the changing demands placed upon them, they may still fail when subjected to supraphysiological mechanical stress for long periods of time.[17] In epidemiological studies, people whose occupations require repetitive knee bending and high physical demand show higher rates of subsequent radiographic knee OA than those with less physically demanding occupations.[18 19] Obesity is a potentially important biomechanical factor but it is also associated with systemic and hormonal factors responsible for bone and cartilage metabolism,[20 21] 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.[22 23] Pain is also associated with dynamic load. In an individual patient with knee OA, the adduction moment increases after administration of anti-inflammatory drugs and, without analgesics, the adduction moment tends to decrease to reduce load on the affected joint.[24] In addition, previous studies have shown that the adduction moment negatively correlates with joint space width[25] and positively with mechanical axis (varus alignment)[26] in knee OA. Dynamic load during gait may significantly influence prognosis, but its long term effect has not yet been established.[25 26] Here we tested the hypothesis that adduction moment and related variables at baseline can predict radiographic disease

Abbreviations: AP, anteroposterior; K/L, Kellgren and Lawrence; OA, osteoarthritis

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

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

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[34]; ‡see fig 1.

progression of medial compartment knee OA at the six year follow up.

PATIENTS AND METHODS

Patients

During 1991–93, 106 patients with primary medial compartment 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, pseudogout, autoimmune diseases, neuropathic arthropathy, infectious 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 confounding 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 physiotherapy. 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 arthroplasties, 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), lateral, 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.[27] 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 centre of the ankle joint (fig 1).[28] 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 tibiofemoral joint was classified by the atlas of Kellgren and Lawrence (K/L).[29] K/L grade 2 indicates definite osteophyte formation, which is a specific radiographic feature of OA. However, 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*,[30] 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 narrowest width of the joint space in millimetres in the medial compartment.[31] 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

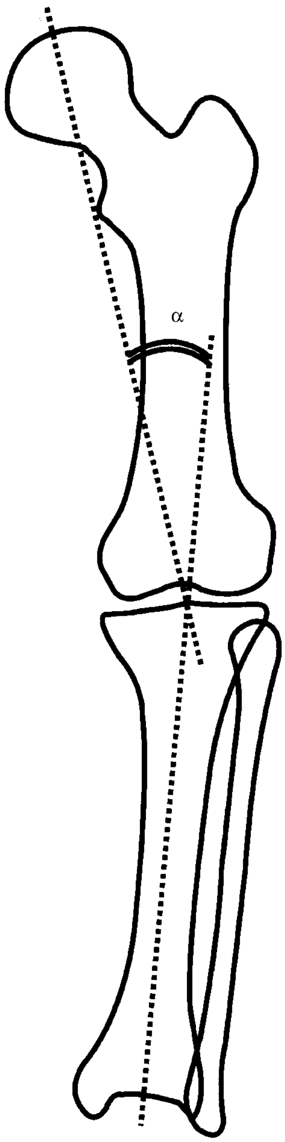

Figure 1 The mechanical axis (α) from the full length weightbearing AP radiograph of the leg.

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 width of the medial compartment according to the atlas of Altman *et al*.[30]

Gait analysis

The computed gait analysis system (Anima, Tokyo, Japan) used in this study included two force plates (each 250×40 cm) and a light source spot measuring device (consisting of light emitting diodes attached to the body and four optoelectronic cameras that capture the emitted light). The two force plates were placed on the floor on either side of the centre line of an 8 m walkway.[32]

The reflective skin markers for the light source measuring device were attached to both acromions, anterior superior iliac supine, iliac crest, greater trochanter, lateral joint line of the knee, lateral malleolus of the fibula, lateral side of the calcaneus, and the head of the fifth metatarsal bone. Signals of three dimensional reaction forces detected by the force plates were digitised through an analogue/digital converter and stored on a computer. Joint angles were calculated from the relative translations and rotations of the segments, which were detected directly as the three dimensional positions of the skin markers by the optoelectronic cameras. The captured marker coordinates were filtered using a low-pass digital filter at a cut off frequency of 6 Hz. The resolution of the cameras to detect three dimensional locations of the floor reaction forces was <0.5%, the errors of the floor reaction forces obtained from the force plate were estimated to be <0.5%. After several walking trials, the patient was asked to walk on the force plate at his/her natural walking speed three times, with both arms folded in front of the chest so as not to interfere with the light from the light source. The sampling frequency was set at 50 Hz (20 ms). As the average walking speed of the subjects was 0.7 m/s, the gait data of individual patients with walking speed nearest to 0.7 m/s were selected. The positions of the centre of the hip, knee, and ankle joints were identified relative to the positions of the skin markers. The centre of the hip joint was approximated at the point that was located some distance inward from the greater trochanter. The distance was measured on the AP radiographs of each hip joint. The centre of the knee on the frontal plane was located by identifying the mid-point of the line between the peripheral margins of the medial and lateral plateaus at the level of the joint line. The centre of the ankle joint was estimated at the lateral and medial malleoli. Data of distances from the skin marker to the centre were entered into the computer. Moments of the knee joint were computed using the three dimensional rigid body link model of Bresler and Frankel[33] and incorporated the results of three dimensional location of each segment, inertial properties of the limb segment, and the data of the floor reaction forces.[32]

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).[34] 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 χ^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

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

Data at entry	Patients without disease progression (n=42)	Patients with disease progression (n=32)	p Value§
Age	68.7 (8.7)	70.5 (6.2)	0.30
Sex, male/female (n)	12/30	4/28	0.17¶
Body mass index*	24.1 (3.2)	24.5 (4.3)	0.14
Pain†	25.5 (4.1)	22.7 (5.1)	0.01
Mechanical axis (°)‡	4.6 (3.8)	6.3 (4.0)	0.06
Joint space width (mm)	3.4 (1.2)	3.2 (1.1)	0.31
Adduction moment (% wt × ht)	4.0 (1.4)	6.1 (1.0)	<0.0001
Kellgren-Lawrence grade			
1	12	8	0.16¶
2	13	9	
3	15	8	
4	2	7	
Joint space narrowing grade			
0	9	1	0.16¶
1	22	20	
2	9	9	
3	2	2	

*Weight (kg)/(height (m))^2; †evaluated using the knee rating system of the Hospital for Special Surgery[34]; ‡see fig 1; §continuous variables were examined by unpaired *t* test; ¶discrete variables were examined by χ^2 test.

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

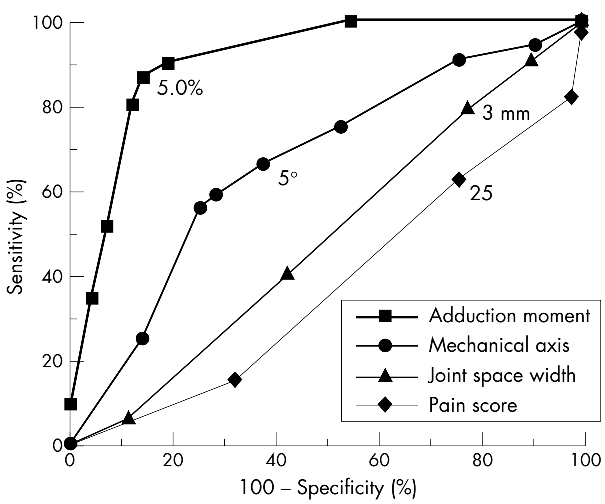

Figure 2 Receiver operating characteristic curves of the baseline adduction moment, mechanical axis, joint space width, and pain score for discriminating radiographic disease progression in medial compartment knee OA.

Table 3 Relationship between radiographic progression and baseline variables

	Patients with disease progression	Patients without disease progression	Total
Adduction moment (% wt × ht)			
≥5	28	7	35
<5	4	35	39
Total	32	42	74
Joint space width (mm)			
≥3	24	32	56
<3	8	10	18
Total	32	42	74
Mechanical axis (°)			
≥5	21	16	37
<5	11	26	37
Total	32	42	74
Pain			
≥25	20	32	52
<25	12	10	22
Total	32	42	74

Table 4 Multivariate odds ratios (OR) and 95% confidence interval (CI) for baseline factors associated with radiographic progression of medial compartment knee osteoarthritis. Analysis by logistic regression model

	p Value	OR	95% CI
Age	0.01	1.22	1.05 to 1.41
Sex	0.42	2.14	0.34 to 13.50
Body mass index*	0.19	1.21	0.91 to 1.61
Pain†	0.43	0.93	0.78 to 1.11
Mechanical axis (°)‡	0.50	0.90	0.66 to 1.23
Joint space width (mm)	0.59	0.74	0.25 to 2.19
Adduction moment (% wt × ht)	0.0002	6.46	2.40 to 17.45

*Weight (kg)/(height (m))^2; †evaluated using the knee rating system of the Hospital for Special Surgery[34]; ‡see fig 1.

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.[35] 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,[11] but this figure was arbitrary. Sharma *et al* used an atlas[30] that classifies joint space width into four grades,[36] 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[11] 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.[25] 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[37]; thus it is responsible for the biomechanical abnormality of the medial compartment knee OA.[38] Sharma *et al* reported that dynamic load during gait correlated with disease severity in tibiofemoral knee OA.[25] 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,[36] 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[22]; 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.[32] Even after valgus 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.

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