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Associations Between Pain, Function, and Radiographic Features in Osteoarthritis of the Knee

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Objective. **To assess the associations between pain, loss of function, and radiographic changes in knee osteoarthritis (OA), taking into account both the patellofemoral and tibiofemoral compartments.**

Methods. **Both knees of 167 community-based patients with OA in at least 1 of their knees were assessed. Pain was measured by visual analog scale, and function was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index. Anteroposterior standing radiographs with the knee in extension and lateral 30° flexion were obtained and assessed for the Kellgren/Lawrence score and for individual features (osteophytes, joint space narrowing, and subchondral bone sclerosis) in each compartment.**

Results. **Knees with structural changes in both compartments were more likely to be painful and to be associated with loss of function than were knees in which only 1 compartment was affected. The individual feature most strongly associated with pain was subchondral bone sclerosis.**

Conclusion. **Studies exploring the associations between structural and symptomatic knee OA need to include an assessment of the patellofemoral compartment, and individual radiographic features rather than a global severity score should be considered in these studies.**

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Osteoarthritis (OA) is the most frequent form of arthritis and is a growing cause of social and economic burden to our aging society. Knee OA is particularly important in view of its high prevalence and association with severe pain and disability (1).

Despite much clinical research on knee OA, a clear definition of the disorder and diagnostic criteria remain elusive (2–5). One of the main reasons for this difficulty is the apparent discordance between radiographic knee OA and symptomatic knee OA (6–9). In 1992, Hadler noted, in an article entitled "Knee pain is the malady—not osteoarthritis" (10), that "The epidemiology of osteoarthritis and the epidemiology of pain have little in common, not nothing in common, but surprisingly little."

There are many possible explanations for this discordance. It may be that radiographs do not image those aspects of the pathology of OA that are related to pain (e.g., synovitis or bone marrow edema), or that joint damage predisposes patients to pain but is not the root cause (4,11,12). Alternatively, it is possible that the ways in which radiographic images have been obtained and read in the previous studies have been inappropriate. Several previous studies have been based on an assessment of the tibiofemoral compartment only (6–8,13–15) and have used only a crude composite score of joint damage, such as Kellgren/Lawrence (K/L) grading scores (13), rather than individual radiographic features.

In this report, we describe a cross-sectional analysis designed specifically to assess the relationships between pain, function, and radiographic features of knee OA, which include the patellofemoral joint as well as the tibiofemoral joint, and individual radiographic features as well as a composite score.

PATIENTS AND METHODS

The United Bristol Healthcare Trust Research Ethics Committee approved the study. Patients were identified from

the Somerset and Avon Survey of Health study (16). All fulfilled the American College of Rheumatology clinical and radiographic classification criteria for knee OA (17). Our selection method has been described in detail elsewhere (18,19). Briefly, patients with self-reported knee pain on most days in recent months and any evidence of radiographic OA in 1 or both knees were invited to participate in the study. Patients with actual synovial knee effusion were excluded from the study.

Patients were asked to identify their painful knee(s) as the right knee, the left knee, or both knees. The degree of self-reported global knee pain was recorded using a visual analog scale (VAS) (20). Function was assessed with the function subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Likert 3.0 version) (21). At the time of their interviews, patients were not receiving any analgesic agents, nonsteroidal antiinflammatory drugs, any specific treatment for OA, and were not on a waiting list for knee surgery.

Anteroposterior (AP) knee radiographs were obtained with the patient in the fully extended standing position, and lateral images were obtained with the patient in the supine position with the knee in 30° of flexion, as previously suggested (22–24). Each radiograph was read independently by 2 experienced observers (JRK and BS) who were blinded to patient identity or details. The K/L score was determined for each knee compartment. Individual radiographic features, including osteophyte formation, joint space width, and subchondral bone sclerosis, were recorded for each compartment, guided by the Osteoarthritis Research Society (OARS) atlas (25). Osteophytes and subchondral sclerosis were recorded as absent or present. Joint space width was measured to the nearest half millimeter in the tibiofemoral compartments at the narrowest intraarticular point, using a transparent plastic ruler; joint space narrowing (JSN) was then recorded as absent for widths of $\geq$4 mm and present for widths $<$4 mm. In the patellofemoral compartment, JSN was estimated as either absent or present using the OARS atlas. In instances where osteophyte scores from the 2 readers differed by more than 1 category, the subchondral sclerosis score differed, or the joint space width measurement differed by more than 2 mm, a third independent reader (SC) made the final decision on the score, as previously recommended (25,26).

Intrarater reliability was assessed by each reader recording data from the same, randomly selected 60 films on 2 separate occasions, 6 weeks apart. Interrater reliability was determined by comparison of each feature recorded by the 2 main observers on the same 60 films.

The VAS pain scores were related to radiographic changes in the different compartments of the knee joint by one-way analysis of variance with Bonferroni correction (27); WOMAC function scale measurements were analyzed in the same way, using the Kruskal-Wallis test with Dunn's correction (27). *P* values less than 0.05 were considered significant. In reproducibility data analyses, the kappa statistic was used for K/L scores, osteophytes, and subchondral sclerosis, while the intraclass correlation coefficient was used for joint space width values (28).

RESULTS

The demographic features of the study population are shown in Table 1. Data were obtained for both knees of 167 patients (334 knees). One hundred twelve of the patients (67%) were female and 55 (33%) were male; the mean age was 66 years, and the mean self-reported disease duration was 9 years. A large proportion of the study population was obese (mean body mass index 30.2 kg/m^2). Knee pain was unilateral in 46 patients, while in the remaining 121, VAS scores differed for each knee. The radiograph reading reliability data are summarized in Table 2. It shows that intraobserver agreement was good for all features, and interobserver agreement was good for all features except the K/L score.

Table 1. Demographic features of the 167 study subjects

Female/male, no. (%)	112 (67)/55 (33)
Age, mean ± SD years	65.5 ± 9.8
Disease duration, mean ± SD years	9.4 ± 7.0
Body mass index, mean ± SD kg/m^2	30.2 ± 6.5
Knee involvement, bilateral/unilateral, no. (%)	121 (72)/46 (28)

The frequency of the different radiographic features is shown in Table 3. Because the frequency of isolated lateral tibiofemoral radiographic features was $<$2%, the medial and lateral tibiofemoral compartment changes were analyzed together for clarity. Table 3 shows that osteophyte formation could be detected in 55% of the tibiofemoral and 65% of the patellofemoral compartments. Joint space narrowing was present in 61% of the tibiofemoral and 48% of the patellofemoral compartments. Subchondral bone sclerosis was found in 44% of the tibiofemoral and 31% of the patellofemoral compartments.

Pain and function were correlated with the severity of knee OA based on K/L scoring, as shown in Figure 1. There was no significant difference in the mean pain score for knees with no K/L change (29.0 mm on the VAS) compared with knees with OA in the tibiofemoral and the patellofemoral compartments only (37.7 and

Table 2. Reproducibility of radiography scores*

	K/L score	Osteophytes	JSW	Sclerosis
Observer 1 intraobserver error	0.987	0.692	0.895	0.828
Observer 2 intraobserver error	0.993	0.750	0.954	0.774
Interobserver error	0.588	0.629	0.868	0.773

* Radiographs were read 4–6 weeks apart by the same observer. Values for Kellgren/Lawrence (K/L) score, osteophytes, and subchondral bone sclerosis (sclerosis) are the Kohen's kappa statistic. Values for joint space width (JSW) are the interclass correlation coefficient. 0.81–1.00 = almost perfect agreement; 0.61–0.80 = substantial agreement; 0.41–0.60 = moderate agreement; 0.21–0.40 = fair agreement; 0.00–0.20 = poor agreement.

Table 3. Frequency of radiographic features in all knees (n = 334)*

Feature	Tibiofemoral compartment	Patellofemoral compartment
Osteophytes	184 (55)	218 (65)
Joint space narrowing	205 (61)	159 (48)
Subchondral bone sclerosis	148 (44)	103 (31)

* Values are the number (%).

32.2 mm, respectively). In contrast, knees with OA in both compartments had significantly more pain than knees without OA (41.0 mm; $P < 0.05$). WOMAC function scores were compared for knees with and those without radiographic changes of OA. As with pain, there was no significant difference in function scores between knees with no OA (median 20.0 mm) and those with either tibiofemoral or patellofemoral OA (median 20.5 and 18.0 mm, respectively). However, patients with OA in both compartments had significantly reduced function (median 26.5 mm; $P < 0.01$).

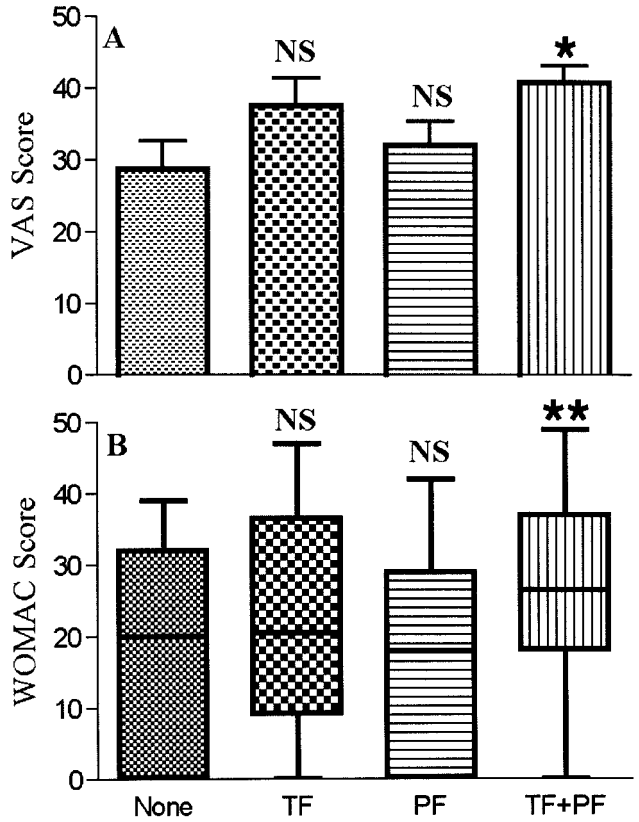

Figure 1. Visual analog scale (VAS) pain scores (**A**) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) function subscale scores (**B**) for knees with no change in Kellgren/Lawrence (K/L) score (none), and knees with K/L scores of 1–4 in the tibiofemoral compartment (TF) only, the patellofemoral compartment (PF) only, or both the tibiofemoral and patellofemoral compartments. Values for VAS pain are the mean and SD. Values for WOMAC function score are presented as box plots, where the boxes represent the 25th and 75th percentiles, the lines within the boxes represent the median, and the lines outside the boxes represent the 10th and 90th percentiles. * = $P < 0.05$; ** = $P < 0.01$ versus knees with no K/L change, by one-way analysis of variance with Bonferroni correction for VAS pain scores and by Kruskal-Wallis test with Dunn's correction for WOMAC function scores. NS = not significant.

Figure 2 illustrates the associations found between knee pain and the 3 separate radiographic features of osteophytes, JSN, and subchondral sclerosis for each compartment. No difference could be detected in the mean pain score for knees with no osteophytes (31.14 mm), compared with knees with osteophytes in either the tibiofemoral or patellofemoral compartments only (35.6 and 30.4 mm, respectively). In contrast, knees with osteophytes in both compartments had significantly more pain (43.5 mm; $P < 0.05$ versus knees with no osteophytes) (Figure 2A). Similarly, JSN (Figure 2B) and subchondral sclerosis (Figure 2C) were related to the presence of pain only if they were in both compartments. The most significant association found between pain and radiographic features was the association with the presence of subchondral bone sclerosis in both compartments (46.4 versus 29.9 mm; $P < 0.001$).

Figure 3 shows the same analysis as described for knee pain, done for the WOMAC function score. Figure 3A shows that no significant difference could be detected in the function score for knees without osteophytes and knees with osteophytes in either compartment alone or in both compartments. We found a weak but significant association between JSN in both compartments and reduced function (Figure 3B). However, no association with function was found in patients with evidence of subchondral sclerosis (Figure 3C).

DISCUSSION

These data illustrate that in this cohort, knee pain and reduced function were more likely to be found if radiographic OA changes were present in both the tibiofemoral and patellofemoral compartments, rather than either separately, and that the presence of pain correlated better with the presence of osteophytes and subchondral sclerosis than with JSN. In addition, we observed a weak association between loss of function and JSN in both compartments.

Our first conclusion from these findings is that inclusion of the patellofemoral joint in any assessment of the relationships between structural changes at the knee and symptoms should now be mandatory. Several

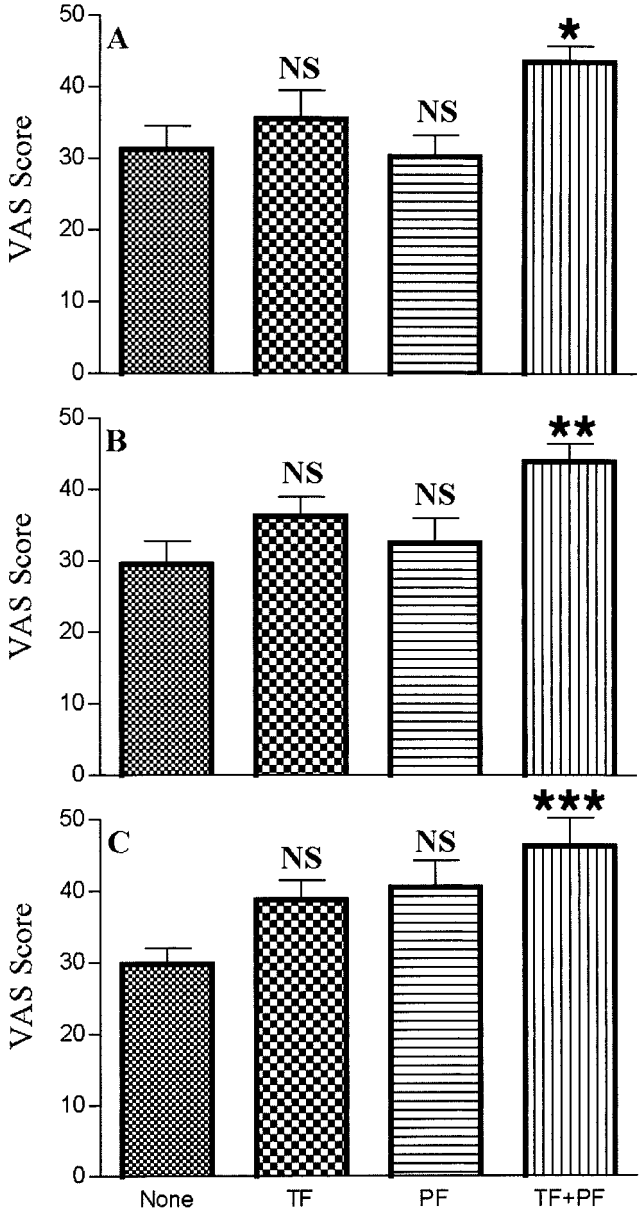

Figure 2. **A**, VAS pain scores for knees with no osteophytes (none), TF osteophytes only, PF osteophytes only, or both TF and PF osteophytes. **B**, Pain scores for knees without joint space narrowing (JSN), TF JSN only, PF JSN only, or both TF and PF JSN. **C**, Pain scores for knees with no subchondral sclerosis, TF sclerosis only, PF sclerosis only, or both TF and PF sclerosis. Values are the mean and SD. * = $P < 0.05$; ** = $P < 0.01$; *** = $P < 0.001$ versus knees with no change, by one-way analysis of variance with Bonferroni correction. See Figure 1 for other definitions.

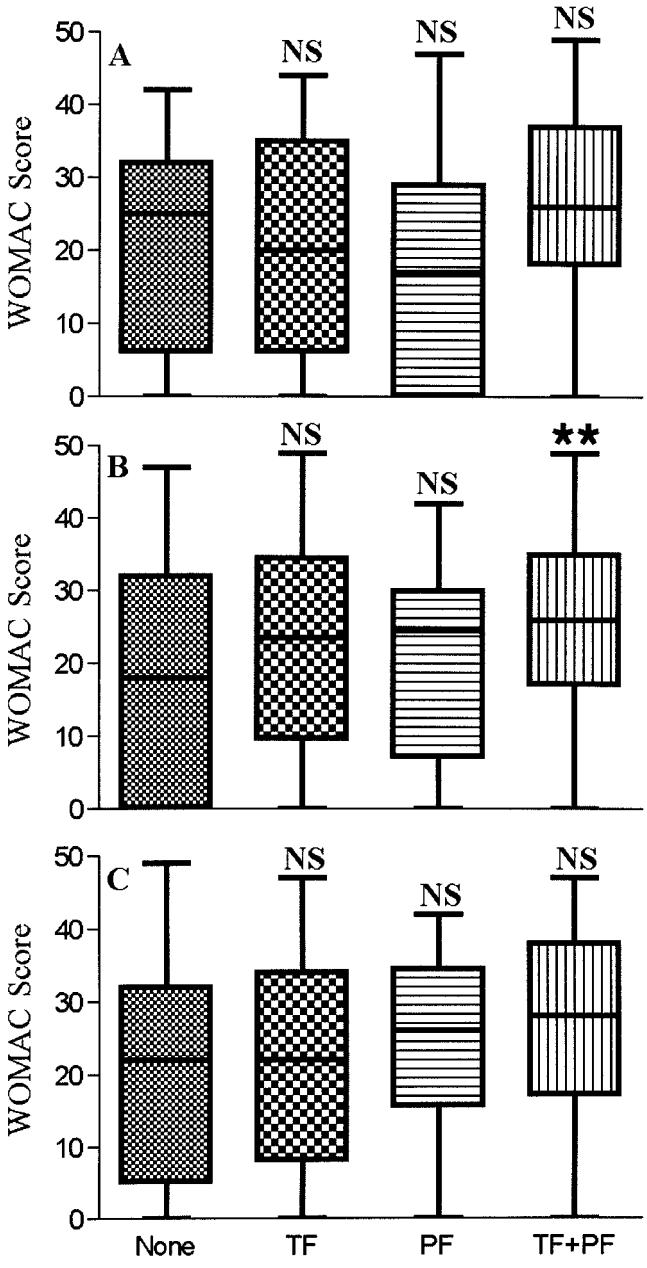

Figure 3. **A**, WOMAC function subscale scores for knees with no osteophytes (none), TF osteophytes only, PF osteophytes only, or both TF and PF osteophytes. **B**, WOMAC function subscale scores for knees without joint space narrowing (JSN), TF JSN only, PF JSN only, or both TF and PF JSN. **C**, WOMAC function subscale scores for knees with no subchondral sclerosis, TF sclerosis only, PF sclerosis only, or both TF and PF sclerosis. The data are presented as box plots, where the boxes represent the 25th and 75th percentiles, the lines within the boxes represent the median, and the lines outside the boxes represent the 10th and 90th percentiles. ** = $P < 0.01$ versus knees with no change, by Kruskal-Wallis test with Dunn's correction. See Figure 1 for other definitions.

community-based studies have shown that the patellofemoral joint is frequently affected by structural OA changes (9,29–32); however, assessment of this compart-

ment was not done in many of the most frequently cited studies on the association between radiographs and pain (6–8,14,15,33,34). Our observations of the highest frequency of radiographic change in the patellofemoral compartment (65%) and in the tibiofemoral compartment (61%) are similar to those of McAlindon et al (29) from a community-based study (51% and 55%, respectively), and also to the observations of Ledingham and et al (30) with regard to hospitalized patients (74% and 60%, respectively).

Our second conclusion is that subchondral bone changes may be as or more important to pain generation than loss of cartilage and osteophyte formation. There is a considerable body of evidence to support the hypothesis that bone changes generate pain, including associations between pain and intraosseous pressure (35), retention of radiolabeled bisphosphonates at the knee (36), increased bone mineral density in the subchondral bone region (37), an increase in the fine trabecular structure in the proximal tibial area detected by microfocal radiography (38), subchondral bone remodeling in early OA (39), and the presence of bone marrow edema on magnetic resonance imaging (40,41). Pain has been previously associated with osteophyte formation (30), but we believe this is the first time that it has been associated with subchondral bone sclerosis.

Taken together, these findings suggest that some of the lack of concordance between radiographic and symptomatic knee OA found by previous investigators can be explained by the use of composite scores that do not adequately reflect bone changes, and exclusion of the patellofemoral joint from analyses. However, our data do not indicate how much of the variance in pain can be attributed to structural changes discernable on radiographs, and only account for a global assessment of pain, rather than distinct patterns such as night pain, pain at rest, or pain on use.

There are considerable other limitations to this study. It is cross-sectional rather than longitudinal, and the patients had symptomatic OA of mild-to-moderate severity. The AP radiographs were obtained with the leg in full extension, rather than in the partially flexed view that is now preferred (42,43), and the x-ray beam angle and leg rotation were not controlled. This combination of radiographic views was chosen because the existing methods for the tangential (axial) image of the patellofemoral joint, although helpful in the evaluation of chondromalacia, patellar compression syndrome, and recurrent subluxation or dislocation (44), are highly affected by the degree of knee flexion, weight-bearing or not weight-bearing, the x-ray beam angulation, the magnification factor, and the radioanatomic landmarks used (45). In a recent comparative trial, it was also concluded that the lateral patellofemoral view is preferable to the axial view for use in clinical or epidemiologic studies (24).

In addition, the only patient-related data we collected were global pain and the WOMAC function subscale, so we were not able to assess the separate contribution of other factors that have been associated with pain in knee OA, such as anxiety and depression (12). Finally, we dichotomized the radiographic data for convenience of analysis.

In spite of these limitations, we believe the findings from this cohort have important implications. Hopefully, our research will provide insight into the dichotomy between the disease and symptoms of knee OA.

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