Patellofemoral osteoarthritis coexistent with tibiofemoral osteoarthritis in a meniscectomy population

Extended Report by:
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Running head:
Patellofemoral OA in a meniscectomy population

Key words:
Osteoarthritis/knee, Radiography, Meniscectomy, Symptoms, Risk factors
ABSTRACT

Objectives: To evaluate the frequency of patellofemoral (PF) osteoarthritis (OA) and the relevance of PF OA to symptoms and function in a meniscectomy population.

Methods: We evaluated 317 patients (mean ± SD age 54 ± 11 years) with no cruciate ligament injury. The subjects had undergone meniscal resection 15-22 years earlier (followup rate 70%). Standing tibiofemoral (TF) and skyline PF radiographs were graded according to the OARSI atlas. The Knee injury and Osteoarthritis Outcome Score (KOOS) was used to quantify symptoms and function. We used 68 unoperated subjects identified from national population records as controls.

Results: In patients, PF OA (isolated or coexisting with TF OA) was present in 66/317 index knees (21%) and 21/263 unoperated contralateral knees (8%, p<0.001). In 57/66 (86%) of these index knees TF OA was present (mixed OA). In a model adjusted for age, sex, and body mass index, the odds ratio for PF OA (alone or in combination with TF OA) was 2.6 (95% confidence interval [95% CI] 1.1–6.6) after medial meniscectomy and 5.3 (95% CI 1.9–15.0) after lateral meniscectomy, using controls as the reference. Individuals with mixed knee OA pattern had more symptoms, lower function in sports and recreation, and worse knee-related quality of life than subjects with isolated TF OA.

Conclusions: Mixed PF and TF OA is common in a meniscectomy population. Patellofemoral OA is a contributing cause of knee symptoms and reduced knee-related quality of life and relevant to the management of knee complaints of this group of patients.
Osteoarthritis (OA) is a joint disorder contributing to the top 10 list of the world disease burden according to the World Health Organization [1]. The knee is one of the joints most frequently affected. The prevalence of symptomatic knee OA is about 6% of citizens in the United States 30 years of age or older and increases with age [2]. In the majority of the epidemiological studies performed, as well as in ongoing trials of potential disease modifying OA drugs, the focus is on radiographic OA changes in the 2 tibiofemoral compartments and symptoms. Consequently, risk factors for patellofemoral OA are less well investigated compared with risk factors for tibiofemoral OA. However, previous reports have shown that OA of the patellofemoral joint is an important cause of knee pain and disability [3]. A few reports have indicated that risk factors are largely similar for the different patterns of radiographic disease [4-6], but the occurrence of patellofemoral OA has never been reported in a meniscectomy population.

Meniscectomy is recognized as a strong risk factor for tibiofemoral OA [7, 8]. We have previously shown a 6-fold increased relative risk of developing tibiofemoral OA after total meniscectomy compared with unoperated controls [9, 10], and evaluated risk factors for symptomatic OA in a meniscectomy population [11, 12]. The objective of the present study was to investigate the frequency of radiographic patellofemoral OA in a meniscectomy population, using unoperated control subjects as reference. As a secondary objective, we explored the relevance of patellofemoral OA to symptoms and function. The radiographic assessment of the well-defined cohort included skyline (i.e., axial) patella view, and the subjects completed the validated and self-administered questionnaire, the Knee injury and Osteoarthritis Outcome Score (KOOS).

PATIENTS AND METHODS

Patients

The ethics committee of the Faculty of Medicine, Lund University, approved the study and informed consent was obtained from all participating subjects. Patients undergoing isolated meniscectomy at Lund University Hospital in 1973, 1978, or between 1983 and 1985 were identified retrospectively through the surgical code system or by manual search through the surgical records. Data extraction procedures, exclusion criteria, and loss to followup analysis have been detailed [11].

A total of 456 patients fulfilled the criteria and were invited to radiographic and clinical assessment in 1994, 1995, or in 2000. Current addresses were obtained from the National Population records. Of the 329 responders, patellofemoral radiographs were not obtained in 12 cases, leaving 317 subjects included in this study, which represents 70% of the available cohort (table 1). The nonresponders were in general younger than responders (p < 0.001), but did not differ with regard to injury or surgical characteristics [11].

Controls

The control group comprised 68 individuals without knee surgery and no clinical meniscal or cruciate ligament injury. Controls were identified using national population records, matching sex, birth year, and zip code for the patients who underwent surgery in 1973 [9]. Age at examination, sex ratio, and general geographic living area were also similar to other patients in the study cohort (table 1).
Table 1  Characteristics of the patients and control subjects.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients N = 317</th>
<th>Controls N = 68</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic data at followup</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men, no. (%)</td>
<td>251 (79)</td>
<td>50 (74)</td>
</tr>
<tr>
<td>Age, mean ± SD years</td>
<td>54 ± 11</td>
<td>56 ± 12</td>
</tr>
<tr>
<td>Followup time, mean ± SD years</td>
<td>18 ± 2</td>
<td>-</td>
</tr>
<tr>
<td>Body mass index, mean ± SD kg/m²</td>
<td>26 ± 4</td>
<td>26 ± 4</td>
</tr>
<tr>
<td>Occupational workload, median</td>
<td>light labor</td>
<td>clerical work</td>
</tr>
<tr>
<td>Spare-time physical activity level, median</td>
<td>moderate</td>
<td>moderate</td>
</tr>
<tr>
<td>Demographic data at index surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD years</td>
<td>36 ± 12</td>
<td>-</td>
</tr>
<tr>
<td>Arthroscopic technique, no. (%)</td>
<td>48 (15)</td>
<td>-</td>
</tr>
<tr>
<td>Medial meniscectomy, no. (%)</td>
<td>250 (79)</td>
<td>-</td>
</tr>
<tr>
<td>Total meniscectomy, no. (%)</td>
<td>155 (49)</td>
<td>-</td>
</tr>
<tr>
<td>Degenerative meniscal tear, no. (%)</td>
<td>121 (38)</td>
<td>-</td>
</tr>
</tbody>
</table>

SD = standard deviation

The Knee injury and Osteoarthritis Outcome Score
To evaluate knee-specific patient-relevant outcome we used the Swedish version of KOOS, www.koos.nu [13]. KOOS was developed for short- and long-term followup studies of knee injury and knee OA [14], and comprises 5 subscales: Pain, other Symptoms, Activities of Daily Living (ADL), function in Sports and Recreation (Sport/Rec), and knee-related Quality of Life (QOL). A score from 0 to 100 is calculated for each subscale, with 100 representing the best result. The patients examined in 1994 completed the KOOS questionnaires in 1996 by mail. Their radiographic knee status was still considered to be relevant to their self-report 2 years later. The other subjects completed their questionnaires on their own in conjunction with the clinical and radiographic assessment. Self-reported outcome was not obtained from 11 patients who had radiographs taken.

We created a definition of a symptomatic knee based on the patient’s self-report from the KOOS questionnaire and consensus among the authors. This operational definition aimed at identifying individuals symptomatic enough to possibly seek medical care [10].

Information on occupational workload and leisure physical activity level was collected for both patients and control subjects. Estimates were made retrospectively by the subject and divided into 5-year periods from the time of surgery until time of assessment. Occupational load was graded as clerical work/unemployed/retired, light labor, moderate labor, or heavy labor. Leisure physical activity level was graded as low, moderate, high (regular sporting activity/jogging, etc., at least twice a week), or very high (top level soccer, etc.). Examples from each category were given in the questionnaire. Patients, who were operated between 1983 and 1985, only estimated their current occupational workload and physical activity level.

Radiographic examination
Skyline view of the patellofemoral joint was obtained with a vertical beam with the subject standing with the knee in ~50 degrees of flexion (fig 1). Standing anteroposterior and lateral images of the knees in ~15 degrees of flexion were obtained of patients and control subjects using a fluoroscopically positioned x-ray beam. A Siemens Basic Radiological System (Siemens GmbH, Erlangen, Germany) was used for patients who were followed up in 1994 and 1995, and for the control subjects. For patients who were assessed in 2000, we used a
Phasix 60 generator (CGR, Liège, Belgium). Two patients did not undergo radiographic examination of the contralateral knee.

The skyline patellofemoral images and frontal knee radiographs were assessed for joint space narrowing (JSN) and osteophytes according to the atlas from Osteoarthritis Research Society International (OARSI) [15]. The presence of these features was graded on a 4-point scale (range 0-3, with 0 = no evidence of bony changes or JSN). We did not score sclerosis, attrition, malalignment, or patellar subluxation. The lateral knee radiographs provided additional information in cases when there was doubt in, e.g., the location of an osteophyte or the presence or absence of JSN. Ten patients (3%) were operated on in the index knee with a high tibial osteotomy for OA. Two of these subjects and 3 additional patients underwent high tibial osteotomy of the contralateral knee. Two patients were treated with knee arthroplasty, of whom 1 in the contralateral knee. When the patient had undergone subsequent tibial osteotomy or arthroplasty for OA, JSN was regarded as grade 3 in the affected tibiofemoral compartment. In these cases, the contralateral and the patellofemoral compartment (if total arthroplasty) were assessed on preoperative images.

One trained observer (ME) read all knee radiographs within a period of 2 weeks with films from patients and controls mixed and with blinding to clinical details. The patellofemoral images from the patients who underwent surgery in 1973 and 1978 have been read by other observers in a previous study [16]. Interrater reliability (kappa statistic) for these readings and present grading was \( \kappa = 0.65 \) for the presence of patellofemoral OA.

We considered radiographic OA to be present in the patellofemoral joint or a tibiofemoral compartment if any of the following criteria was fulfilled: JSN of grade 2 or higher, the sum of the 2 marginal osteophyte grades from the same compartment \( \geq 2 \), or grade 1 JSN in combination with a grade 1 osteophyte in the same compartment. This cutoff approximates grade 2 knee OA based on the Kellgren and Lawrence (K/L) scale [17].

**Statistical analysis**

P-values for binary data in 2 x 2 tables were calculated with Fisher’s exact test and continuous data by Mann-Whitney test or t-test as appropriate. The effects of the evaluated risk factors, using the presence or absence of patellofemoral OA as the dependent variable, were analyzed by means of logistic regression. The multivariate odds ratio (OR) estimates with 95% confidence intervals (95% CIs) were based on the models with all variables entered. We considered a p-value of 0.05 or less significant, and all tests were 2-tailed (SPSS for Windows release 12.0.1, SPSS Inc. 2003).

**RESULTS**

**Radiographic OA**

Mixed knee OA, i.e., combined patellofemoral and tibiofemoral OA, was present in 57/317 (18%) of the patients’ index (operated) knees. Nine subjects (3%) had isolated patellofemoral OA, and 98 subjects (31%) had radiographic OA confined to the tibiofemoral joint in their index knee. Of the unoperated contralateral knees 13/263 (5%) had mixed OA, 8 subjects (3%) had isolated patellofemoral OA, and 31/263 patients (12%) had isolated tibiofemoral OA. Patellofemoral OA (either in mixed or isolated pattern) was more frequent in index knees than in unoperated contralateral knees (21% vs. 8%, \( p < 0.001 \)). Out of the 317 subjects, bilateral patellofemoral OA was present in 27 (9%) and unilateral in 43 (14%). In the control subjects, 6/68 right knees and 4/68 left knees had patellofemoral OA (isolated or mixed OA pattern).
Subjects with mixed OA pattern had more severe tibiofemoral changes than subjects with isolated tibiofemoral OA, i.e., the sum of all osteophyte and JSN grades from the tibiofemoral joint was 5.0 vs. 3.1 (p < 0.001).

In 37 index knees (of which 16 were lateral meniscectomies) osteophytes only fulfilled the criterion for radiographic patellofemoral OA (i.e., the sum of the medial and lateral osteophyte grade ≥ 2). Of the 29 patellofemoral joints with combined JSN and osteophytes, the JSN was predominately medial in 12 subjects, lateral in 12, and 5 patients had symmetrical narrowing. Nine of the 12 subjects with medial patellofemoral JSN had medial compartment tibiofemoral OA (with JSN); the other had no tibiofemoral JSN. Of those with lateral patellofemoral JSN, 6 had medial, 1 lateral, and 5 had no tibiofemoral JSN.

**Risk factors**

There was an increased likelihood of developing patellofemoral OA (in either mixed or isolated OA pattern) after medial or lateral meniscectomy compared with the control subjects (table 2).

<table>
<thead>
<tr>
<th>Prevalence of PF OA, no. (%)</th>
<th>Crude OR</th>
<th>Adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control subjects†</td>
<td>6/68 (9)</td>
<td>1.0</td>
</tr>
<tr>
<td>Medial meniscectomy</td>
<td>48/250 (19)</td>
<td>2.5</td>
</tr>
<tr>
<td>Lateral meniscectomy</td>
<td>18/67 (27)</td>
<td>3.8</td>
</tr>
</tbody>
</table>

95% CI = 95% confidence interval.
* Adjusted for age, sex, and body mass index.
† Reference category.

The multivariate effects of each investigated risk factor to the development of patellofemoral OA in the patients’ operated knee were analyzed by logistic regression. The presence of tibiofemoral OA was, by far, the strongest factor associated with patellofemoral OA (OR 10.6, 95% CI 4.8 – 23.5). When including tibiofemoral radiographic status in the model, all other risk factors were non-significant.

Excluding radiographic tibiofemoral status as an explanatory variable, the factors significantly associated with patellofemoral OA were age 60 years or older, obesity, and lateral meniscectomy more than medial (table 3).
Table 3  Results of logistic regression analysis of risk factors for radiographic patellofemoral (PF) osteoarthritis (OA), in mixed or isolated OA pattern, in the meniscectomized knee (317 patients of whom 66 developed PF OA).

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Prevalence of PF OA, no. (%)</th>
<th>Crude OR</th>
<th>Adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at followup, years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 50†</td>
<td>19/121 (16)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>50-59</td>
<td>19/98 (19)</td>
<td>1.3</td>
<td>1.5 (0.7 – 3.1)</td>
</tr>
<tr>
<td>≥ 60</td>
<td>28/98 (29)</td>
<td>2.1</td>
<td>2.2 (1.1 – 4.5)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men†</td>
<td>50/251 (20)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Women</td>
<td>16/66 (24)</td>
<td>1.3</td>
<td>1.1 (0.6 – 2.4)</td>
</tr>
<tr>
<td><strong>Body mass index, kg/m²</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 25.0†</td>
<td>23/126 (18)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>25.0-29.9</td>
<td>29/153 (19)</td>
<td>1.0</td>
<td>1.0 (0.5 – 2.0)</td>
</tr>
<tr>
<td>≥ 30.0</td>
<td>14/38 (37)</td>
<td>2.6</td>
<td>2.8 (1.2 – 6.4)</td>
</tr>
<tr>
<td><strong>Localization (compartment)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial†</td>
<td>48/250 (19)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Lateral</td>
<td>18/67 (27)</td>
<td>1.5</td>
<td>2.2 (1.1 – 4.5)</td>
</tr>
<tr>
<td><strong>Type of resection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial†</td>
<td>13/63 (21)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Subtotal</td>
<td>22/99 (22)</td>
<td>1.1</td>
<td>1.6 (0.7 – 3.8)</td>
</tr>
<tr>
<td>Total</td>
<td>31/155 (20)</td>
<td>1.0</td>
<td>1.2 (0.5 – 2.5)</td>
</tr>
<tr>
<td><strong>Type of meniscal tear</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Longitudinal†</td>
<td>23/139 (17)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Degenerative</td>
<td>31/120 (26)</td>
<td>1.8</td>
<td>1.8 (0.9 – 3.5)</td>
</tr>
<tr>
<td>Radial</td>
<td>5/24 (22)</td>
<td>1.3</td>
<td>1.0 (0.3 – 3.3)</td>
</tr>
<tr>
<td>No visible tear or not classified</td>
<td>7/34 (21)</td>
<td>1.3</td>
<td>1.5 (0.5 – 4.0)</td>
</tr>
</tbody>
</table>

OR = odds ratio, 95% CI = 95% confidence interval.
* Adjusted simultaneously for all other risk factors listed.
† Reference category.

We separately evaluated the effect of the retrospectively estimated knee load in the patients who had such data available (n = 163). Analysis was made in a single model adjusted for age, sex, BMI, and the operated compartment. Subjects with leisure physical activity level estimated as “very high” or “high” had a higher prevalence of patellofemoral OA than did subjects with “low” or “moderate” level of activity (the highest report of the 5-year interval estimates counted) 25% vs. 15% (OR 4.3, 95% CI 1.5 – 11.9). Essentially the same result was obtained when using the median activity level of the estimates (data not shown). Occupational workload did not affect the frequency of patellofemoral OA (p > 0.9).

Intra-operative patellofemoral cartilage status was noted in 70% of the surgical reports. Patellofemoral cartilage changes (superficial fibrillation, etc.) were noted in 16/51 (31%) of those with patellofemoral OA at followup compared with 33/170 (19%) of those without (p < 0.001). There was no effect on the frequency of patellofemoral OA due to type of surgery, i.e., open vs. arthroscopic meniscectomy (p = 0.21).
**Patient-relevant outcome**

The most common outcome 15-22 years after an isolated meniscal injury and resection was having a healthy knee, i.e., being asymptomatic as assessed by the KOOS with no radiographic knee OA (29%), followed by being symptomatic with no definite radiographic OA (21%), having symptomatic tibiofemoral OA (15%), having asymptomatic tibiofemoral OA (14%), and having symptomatic mixed knee OA (12%). Patients with mixed OA scored the worst on the KOOS questionnaire. The differences in mean scores of KOOS between subjects with isolated tibiofemoral OA and mixed knee OA were significant for the subscales: other Symptoms, Sport/Rec, and QOL, but not for Pain (p = 0.18) and ADL (p = 0.3) (fig 2).

**DISCUSSION**

To our knowledge, we are the first to report an increased frequency of patellofemoral OA concomitant with tibiofemoral OA after a meniscal tear treated by surgical resection. There is a paucity of epidemiological studies evaluating risk factors for patellofemoral OA. Meniscectomy has been identified as an important risk factor for tibiofemoral OA [7-9], but little is known of the frequency of OA in the patellofemoral joint in relation to this intervention. Therefore, with a low loss to a 15-22 year followup we studied a well-defined cohort of 317 subjects who had undergone meniscal resection. A standardized skyline radiographic projection of the patellofemoral joint was used as it allows more precise location of change, greater sensitivity in identification of symptomatic subjects, and better reproducibility [18-20].

Tibiofemoral OA with coexisting patellofemoral involvement was a common finding. There are several possible explanations, which likely involve both systemic and local factors. First, we have previously reported on the association between radiographic hand OA and radiographic tibiofemoral OA after meniscectomy, suggesting an interaction between local joint factors and a genetic predisposition to OA [12]. Such a genetic trait for OA may predispose also to meniscus tears, as well as patellofemoral OA [10, 21]. Patellofemoral cartilage changes were noted at the time of index surgery in many of the OA cases. This suggests that pre-radiographic or incipient OA may have been present already at that time. For many of these, mostly middle-aged subjects, the meniscal tear may merely have been the “signal feature” of an already developing OA [10].

Second, OA disease activity primarily in the tibiofemoral joint may be associated with activation of cytokine and protease cascades that act locally on all joint tissues and compartments, or even systemically [22]. In our cohort medial facet patellofemoral OA (which is unusual) seems to be relatively frequent (most meniscectomies were medial with frequent medial tibiofemoral OA). Altered loading patterns may act locally on the patellofemoral joint due to malalignment caused by unicompartmental tibiofemoral OA [4]. Furthermore, the OA may increase knee joint laxity or be associated with quadriceps weakness increasing the risk for patellofemoral disease. Neurogenic pathways may also affect joint metabolism [23].

Although low subject numbers warrant caution in interpretation, lateral meniscectomy in particular appears to be associated with osteophytosis of the patellofemoral joint. In a previous report on this population [11], lateral meniscectomy was more frequently associated with radiographic OA of the tibiofemoral joint compared with medial meniscus resection, in line with other studies [24-26]. This was suggested to depend on increased cartilage stress due to the loss of the mechanically more important lateral meniscus [27, 28]. The high prevalence...
of OA changes in the patellofemoral joint after lateral meniscectomy could thus be secondary to the increased OA frequency in the tibiofemoral compartment.

A limitation associated with the present study is that no long leg films to measure knee alignment were obtained. Other limitations are inherent with any historical cohort study. However, the loss to followup was low. By excluding subjects with cruciate ligament injury, the cohort is enriched in subjects with degenerative meniscal injuries, i.e., lesions that may occur in absence of an overt knee trauma. The radiologist’s written statement from the preoperative knee radiographs (normally frontal and lateral projections only) was used to exclude subjects with radiographic OA at time of index surgery. In 31 patients (10%) the preoperative radiographic statement or films were not available. Therefore, the odd subject with radiographic patellofemoral or tibiofemoral OA at baseline may have been included in the cohort, although the relatively young age at surgery makes it unlikely.

Our results corroborate observations that risk factors for patellofemoral OA and tibiofemoral OA are typically the same [4-6]. In agreement with other investigators we found obesity to be a risk factor for developing patellofemoral OA [6, 29-30]. Using retrospective estimates of body weight, made from the subjects operated in 1973 and 1978 (data not shown), we did not find any evidence that individuals first developed OA and then become sedentary and obese, although the strength of our conclusion is limited by the cross-sectional nature of the BMI data. Patellofemoral OA has been linked to elite weight lifting, running, and tennis, which suggests that high physical knee loading is a risk factor [31, 32]. Nevertheless, within the limitations associated with restricted subject numbers and retrospective estimates, our study suggests an association between continued high knee load after the meniscectomy and increased risk of patellofemoral OA.

The importance of patellofemoral OA to symptoms and functional limitations has been called to attention [3], but the focus in epidemiological studies of knee OA remains on investigating tibiofemoral OA. We find that subjects with a mixed radiographic OA pattern have the worst patient-relevant outcome. It is unlikely that the small increase in severity of radiographic changes in the tibiofemoral joint in subjects with concomitant patellofemoral OA is a major contributor [33, 34], suggesting that patellofemoral involvement may be more important.

Conclusions
In conclusion, mixed patellofemoral and tibiofemoral OA is common after meniscectomy, not only isolated tibiofemoral OA. Patellofemoral OA is a contributing cause of knee symptoms and reduced knee-related quality of life in a meniscectomy population and relevant to the management of knee complaints of this group of patients.

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Competing Interest Statement
We declare no competing interests.

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Ethical Approval
The ethics committee of the Faculty of Medicine, Lund University, approved the study and informed consent was obtained from all participating subjects.

Figure Legends
Figure 1  Knee positioning to obtain skyline patella radiographs.

Figure 2  Knee injury and Osteoarthritis Outcome Score (KOOS) according to the radiographic pattern of osteoarthritis (OA) 15-22 years after meniscectomy. P values indicate the significance of the difference between subjects with the different patterns of radiographic OA. Patients with isolated patellofemoral (PF) OA are not shown due to the low subject number (n = 7). See Patients and Methods for the definition of radiographic OA. TF = tibiofemoral, NS = not significant, ADL = activities of daily living, Sport/Rec = function in sports and recreation, QOL = knee-related quality of life.
REFERENCES


