Knee Effusions, Popliteal Cysts, and Synovial Thickening: Association with Knee Pain in Osteoarthritis

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ABSTRACT. ***Objective.*** To evaluate the association of effusions, popliteal cysts, and synovial thickening with knee symptoms in older persons with and without radiographic (XR) osteoarthritis (OA), using magnetic resonance imaging (MRI).

Methods. Subjects with and without knee symptoms were recruited from Veterans Affairs and community sources. All had weight-bearing knee radiographs. Subjects were divided into 3 groups: Knee pain/XROA group had knee symptoms and radiographic OA; No knee pain/XROA group had no knee symptoms and radiographic OA; and No knee pain/no XROA group had no knee symptoms and a normal radiograph. A single knee was imaged using a 1.5 T MR scanner using T1 and T2 weighted and proton density SE imaging sequences. MRI were read for effusion, popliteal cysts, and synovial thickening.

Results. The mean age of subjects was 67.0 years (66.6% male). We studied 381 subjects with Knee pain/XROA, 52 with No knee pain/XROA, and 25 with No knee pain/no XROA. The prevalence of moderate or larger effusions was: Knee pain/XROA 54.6%, No knee pain/XROA 15.6%, and No knee pain/no XROA 11.1%. Popliteal cysts were present in 33.0% of Knee pain/XROA subjects, 28.0% No knee pain/XROA, and 9.1% No knee pain/no XROA. After adjusting for the severity of radiographic OA, there was a difference between those with and without knee pain in prevalence of moderate or larger effusions ($p < 0.001$) and synovial thickening, independent of effusion ($p < 0.001$), but not in the prevalence of popliteal cysts. Further, among those in Knee pain/OA group, synovial thickening was associated with the severity of knee pain.

Conclusion. Effusions and popliteal cysts are common in middle aged and elderly people. After adjusting for the degree of radiographic OA, moderate or large effusions and synovial thickening were more frequent among those with knee pain than those without pain, suggesting these features are associated with the pain of knee OA. In those with knee symptoms, synovial thickening is uniquely associated with the severity of knee pain. (J Rheumatol 2001;28:1330–7)

Key Indexing Terms:
KNEE OSTEOARTHRITIS EFFUSION POPLITEAL CYST SYNOVITIS

Pain is the predominant feature of clinical knee osteoarthritis (OA). However, the cause of pain in knee OA remains enigmatic. Cartilage loss, considered the primary pathological lesion in OA, could occur without pain, as hyaline cartilage contains no pain fibers[1]. Many other structures around the knee have been shown to contain pain fibers including the joint capsule, the periosteum and other bone sites, insertion sites of ligaments and muscles, and possibly the synovium[1]. We showed that periarticular bone marrow lesions identified on magnetic resonance imaging (MRI) are more common in those with symptomatic knee OA than those with asymptomatic OA[2]. However, these lesions were not present in all subjects with symptomatic OA, and given that the joint capsule and bursae have pain fibers, distention of the capsule or inflammation of periarticular structures or synovium could also contribute to the pain of knee OA[3]. The prevalence of effusions, popliteal cysts, and synovial changes in those with and without clinical knee OA is unknown and their association with knee symptoms has not been studied[4]. Low grade synovial inflammation has been described in knee OA[5]. In addition, synovial thickening around the infrapatellar fat pad evaluated using noncontrast enhanced MRI has been shown on biopsy to represent mild chronic synovitis[6].

Joint effusions and popliteal cysts are recognized to

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accompany knee OA[7,8]. MRI studies have revealed knee effusions in OA that increase in prevalence with increasing radiographic severity, ranging from 25% in those with mild radiographic disease to 100% in those with severe radiographic disease[7]. In addition, using ultrasound, popliteal cysts have been detected in 42% of subjects with OA[7]. Studies using MRI have generally used subjects referred for knee symptoms and not those without symptoms. Consequently, there is scant information on the prevalence of effusions and periarticular lesions in asymptomatic persons and middle aged and elderly persons in particular. MRI studies of the spine have shown frequent abnormalities unassociated with symptoms, raising the possibility that this may also be true of the knee[9].

We examined the association of effusions, popliteal cysts, and synovial thickening with symptom occurrence by comparing the prevalence of these lesions in 3 groups: (1) those with frequent knee symptoms and presence of radiographic OA; (2) those without knee pain and presence of knee OA; and (3) those without knee pain and absence of radiographic knee OA. Any lesions that occurred predominantly in those with knee pain and rarely in those without pain may be associated with pain.

MATERIALS AND METHODS

Participant recruitment. The minimum age for entry into the study was 45 years for men and 50 years for women. Entry age for women was older to lessen the chance of inadvertently obtaining radiographs on pregnant women. Male subjects were drawn from the Veterans Health Study, a prospective cohort study of 2425 men receiving care at regional VA medical centers, designed to evaluate the relationship between chronic diseases and health status outcomes[10]. Female subjects were drawn from clinics at Boston Medical Center and the VA Medical Center, from advertisements in local newspapers, and from a study of women veterans, the VA Women's Health Project (n = 800) that was designed to describe the health status of women veterans using ambulatory services. The human studies committee and the institutional review board approved the protocols. Informed consent was obtained from all subjects.

All subjects were surveyed about knee symptoms. They were asked 2 questions: "Over the past 4 weeks, have you had pain, aching or stiffness in one or both knees on most days?" and "Has a doctor ever told you that you have knee arthritis?" In a followup interview, those answering positively to both questions were asked about other types of arthritis that could cause knee symptoms. If no other forms of arthritis were identified in the interview, then the individual was eligible for recruitment as a person with knee pain. In total, 120 subjects with knee pain were examined by a rheumatologist (DTF), who confirmed that in all cases there was tenderness in or around the knee. We attempted to match those without knee symptoms roughly in age and sex to those with knee symptoms.

We recruited subjects without knee pain from among those who answered in the negative to both the screening questions. In addition to the above questions, which allowed us to classify subjects as with or without knee pain, we also asked subjects to evaluate the severity of pain in each knee, which was scored 0–100 on a 100 mm visual analog scale (VAS).

Radiographic evaluation. Weight-bearing anteroposterior (AP) and skyline radiographs (Buckland-Wright protocol) and weight-bearing lateral radiographs (Framingham Study protocol) were obtained from all subjects[11]. Radiographs were read for the presence of definite osteophytes by one radiologist (DRG) using an atlas[12]. If a definite osteophyte was present in a symptomatic knee on any of the 3 views, the subject was characterized as having radiographic OA (this included the patella). This definition meets American College of Rheumatology criteria for knee OA[13]. Symptomatic individuals without a definite radiographic osteophyte were excluded from study because of small numbers (n = 4), although as noted below many participants with knee symptoms had evidence of minimal radiographic OA. Radiographic severity was measured by Kellgren-Lawrence (K-L) grade on AP view only (for which reproducibility has been reported[14]). Thus, some of those characterized as having radiographic OA had patellofemoral disease, and K-L grade could be less than 2.

MRI evaluation. Each subject underwent MRI of a single knee. In those subjects with knee symptoms, this was the most symptomatic knee. For those subjects without knee symptoms, the dominant knee was selected for imaging. All studies were performed on a GE Signa 1.5 Tesla MR machine (GE Medical Systems, Milwaukee, WI, USA) using a phased array knee coil. An anchoring device was used for the ankle and knee to ensure uniform position between subjects. The imaging protocol included sagittal spin echo proton density and T2 weighted images (TR 2200, TE 20/80) with a slice thickness of 3 mm, a 1 mm interslice gap, 1 NEX, field of view 11–12 cm, and a matrix of 256 × 192; and coronal and axial spin echo fat saturated proton density and T2 weighted images (TR 2200, TE 20/80) with a slice thickness of 3 mm, a 1 mm interslice gap, 1 NEX, field of view 11–12 cm, and a matrix of 256 × 128.

Two readers (CLH, DRG) developed a semiquantitative scale to evaluate knee joint effusions and popliteal cysts. Effusion was read on T2 weighted axial images. The effusion scoring system specified that grade 0 was physiological amount of fluid, grade 1 small (Figure 1A), grade 2 moderate (Figure 1B), grade 3 large (Figure 1C). Grade 3 had evidence of capsular distention with bulging of extensor retinaculum. Popliteal cysts were scored grade 0 for absent, grade 1 for small, grade 2 for moderate, grade 3 for large, on T2 weighted images using axial and sagittal views (Figure 2). One reader (CLH) read all films for effusions and presence of popliteal cysts with a random subset reread for intraobserver reproducibility (weighted kappa for effusions = 0.94, for popliteal cysts = 0.67) and a further random subset was read by second reader (DRG) for interobserver reproducibility (weighted kappa = 0.61 for effusions, for popliteal cysts = 0.59).

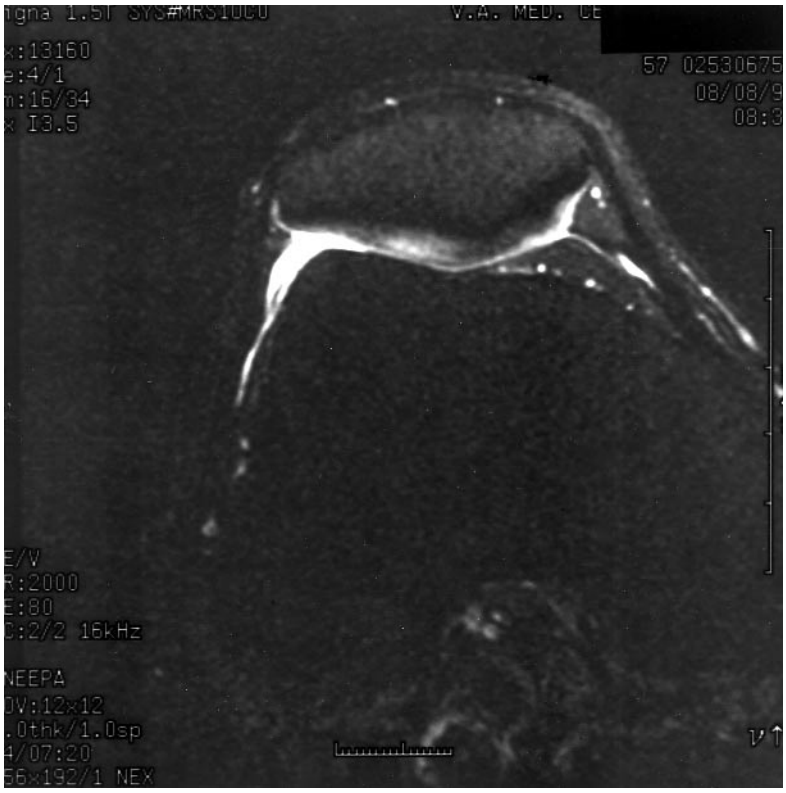
To evaluate synovial thickening and its association with effusion and with knee pain in those with and without effusion, we randomly sampled 150 knees with varying degrees of effusion, oversampling the most informative knees with no or small effusions that had pain or no pain. Synovial thickening was scored in 3 contiguous areas, the infrapatellar fat pad, intercondylar space, and anterior horn of the lateral meniscus, on sagittal T2 and proton density weighted images, using a described method (Figure 3)[6]. The absence of synovial thickening was scored as grade 0 and presence as grade 1. Synovial thickening was read by one reader (DRG). A further random subset of these films was reread for intraobserver reproducibility (kappa for synovial thickening = 0.77).

For reading for this study, MRI of subjects from each of the 3 study groups were ordered randomly, and the reader was unaware of the group status of the subjects.

Definition of study groups. For the purposes of this study, we defined 3 study groups: (1) A person who responded positively to the screening knee symptom question and had a radiograph (XR) showing a definite osteophyte was classified as a subject with Knee pain/XROA (Group 1). (2) Subjects who did not report knee symptoms but had a definite osteophyte on radiograph were grouped as No knee pain/XROA (Group 2). (3) Subjects who did not report knee symptoms and had no definite osteophyte on their knee radiograph were defined as No knee pain/no XROA (Group 3).

Analysis. Only one knee per subject was studied by MRI, and thus analyses were knee- and subject-specific. Differences between proportions were assessed using chi-square, or by Fisher's exact test if expected values were < 5. Differences in continuous measures between the 3 groups were examined using ANOVA. P values reported are 2 sided.

To determine if effusions or popliteal cysts were associated with pain severity in those with knee pain, we performed linear regression analyses for those in Group 1 alone, using pain (by VAS) as the dependent variable and testing for effusion or popliteal cyst and radiographic severity (using K-L



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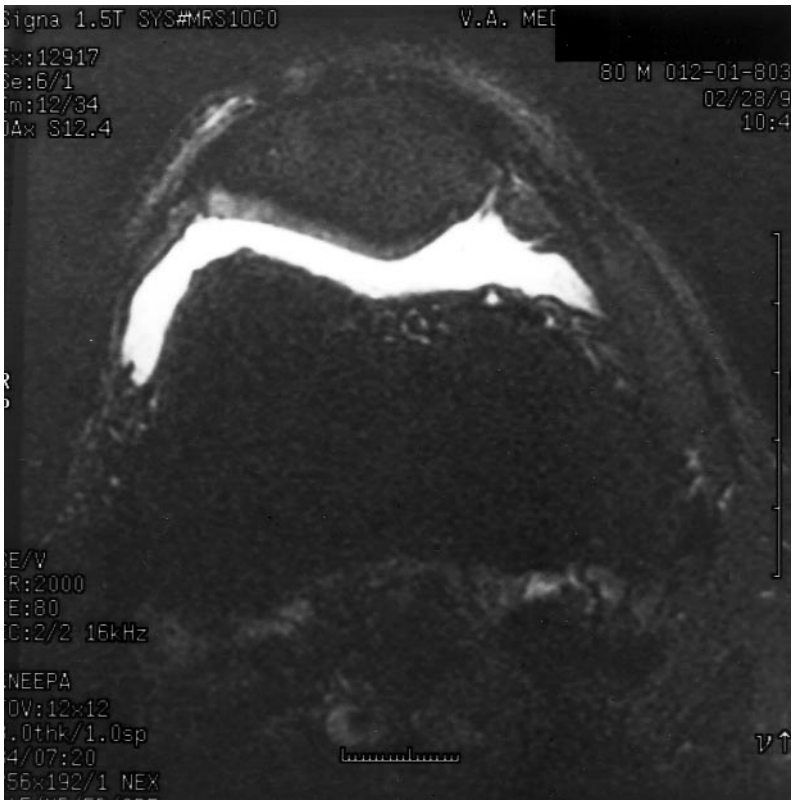

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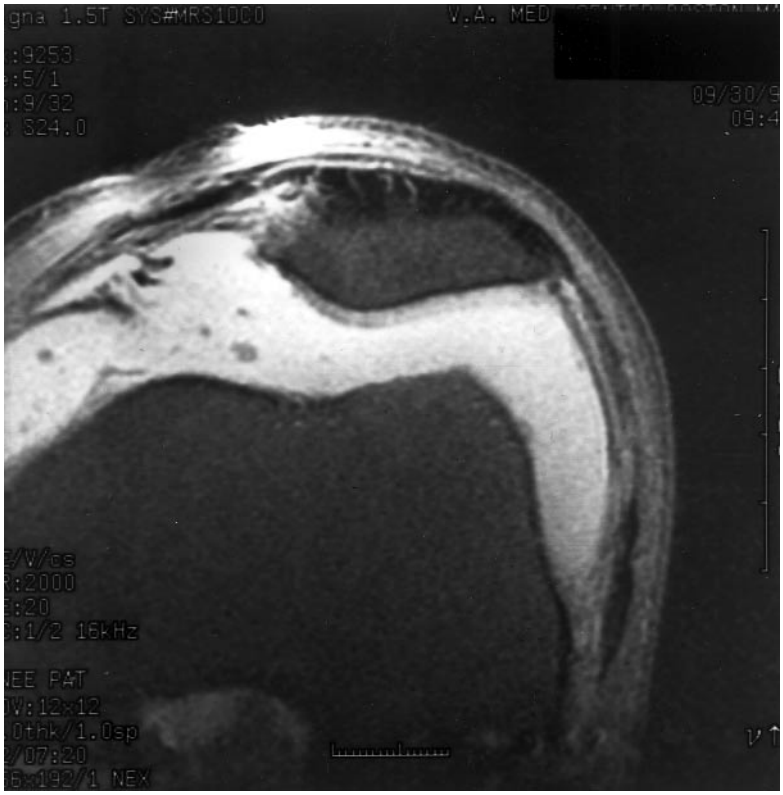

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Figure 1. Axial T2 weighted MR images of (A) small effusion (grade 1), (B) moderate effusion (grade 2), and (C) large effusion (grade 3).

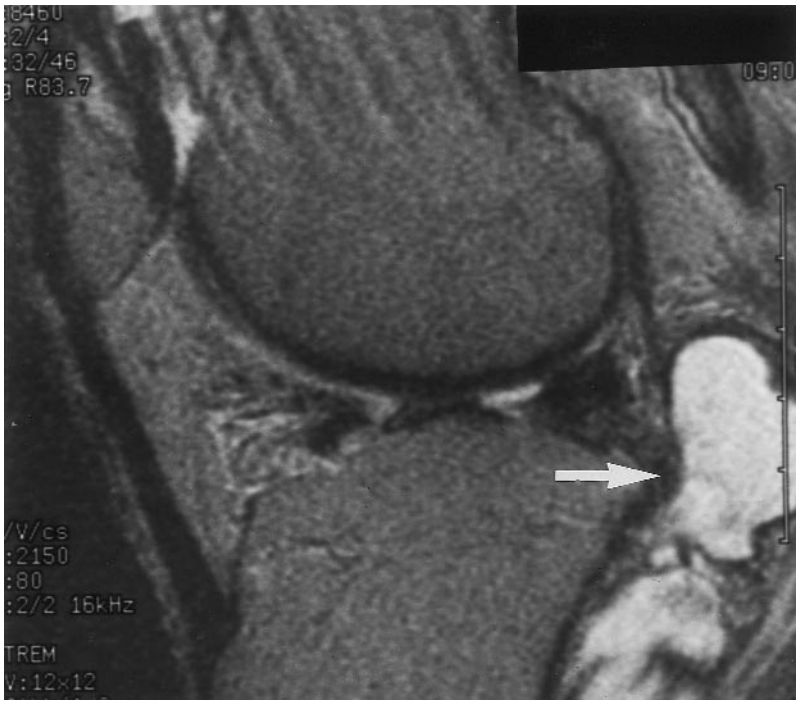

Figure 2. Sagittal T2 weighted MR images of popliteal cyst (grade 3, arrow).

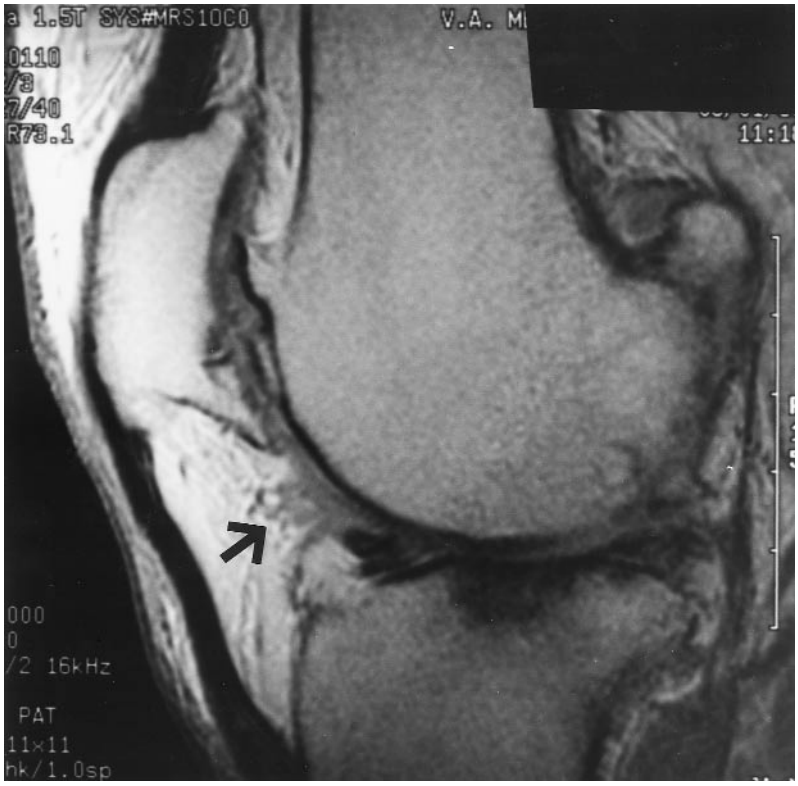

Figure 3. Sagittal proton density weighted MR image of synovial proliferation (arrow).

grade), age, sex, and body mass index (BMI) as independent variables. To evaluate synovial thickening, we performed the same analyses adjusting for radiographic severity, the size of the knee effusion, age, sex, and BMI.

RESULTS

Three hundred eighty-one subjects with Knee pain/XROA (68.0% male), 52 with No knee pain/XROA (55.8% male), and 25 with No knee pain/No XROA (68.0% male) were recruited. Subjects from the 3 study groups were similar in age. Subjects from the Knee pain/XROA group tended to have higher BMI than those in the other study groups (Table 1) (ANOVA, $p < 0.05$). Persons with symptoms and radiographic OA had a median K-L score of 2, whereas those with no symptoms had median scores of 0, although there was considerable overlap in radiographic severity between the groups with radiographic OA (Groups 1 and 2).

The prevalence of effusion and other findings in those with and without knee pain are shown in Table 2. We found little difference between men and women, therefore the results are combined. We found that among all those without knee pain (Groups 2 and 3 combined), small (62.3%) and moderate (13.2%) effusions were common, although large effusions were not (1.3%). These effusions occurred most frequently in those with evidence of OA by radiograph (Group 2). In those with Knee pain/XROA (Group 1), effusions were highly prevalent, with 37.1% having a small effusion, 36.0% moderate effusion, 18.6% large effusion.

Table 1. Characteristics of subjects.

	Knee Pain		No Knee Pain			
	Knee Pain/XROA, Group 1		No Knee Pain/XROA Group 2		No Knee Pain/No XROA, Group 3	
	Male	Female	Male	Female	Male	Female
Number	259	122	29	23	17	8
Age, yrs, mean (SD)	68.2 (9.4)	65.0 (9.0)	66.8 (9.9)	65.8 (8.4)	63.3 (11.3)	66.6 (8.1)
BMI, kg/m^2, mean (SD)	30.8 (4.9)	32.4 (7.1)	28.5 (4.6)	29.0 (6.5)	28.3 (4.9)	29.0 (5.1)
K-L grade, median (range)	2 (0*–4)	2 (0–4)	0 (0–2)	0 (0–2)	0 (0–1)	0 (0–1)
Pain**, mean (SD)	46.4 (25.5)	42.8 (23.8)	0.9 (1.7)	2.2 (2.3)	0 (0)	1.3 (2.5)

* 72 subjects with Knee pain/OA, who had K-L grade 0 due to normal PA views, were defined as having radiographic OA due to definite osteophytes in patellofemoral joint.
** Pain measured on 100 mm VAS.

Table 2. Prevalence of effusions and soft tissue lesions.

	Knee Pain XROA Group 1, n = 381	No Knee Pain Combined Group 2+3, n = 77	XROA Group 2, n = 52	No XROA Group 3, n = 25
Effusions, %				
Small (grade 1)	37.1	62.3	64.7	55.6
Moderate (grade 2)	36.0	13.2	13.7	11.1
Large (grade 3)	18.6	1.4	1.9	0
Popliteal cyst, grade ≥ 1, %	33.0	20.8	28.0	9.1

Table 3. Prevalence of effusions and cyst by symptoms and K-L grade.

	Knee Pain/ XROA K-L grade ≥ 3 Group 1, n = 107	Knee Pain/ XROA K-L grade ≤ 2 Group 1, n = 267	No Knee Pain/ XROA K-L grade ≤ 2 Group 2, n = 52
Moderate effusion or greater (grade 2 or 3), %	79.6	44.8**	15.4**
Large effusion (grade 3), %	32.7	13.2*	1.9*
Popliteal cyst, %	53.2	23.4	28.0
Synovial thickening, %	100	73.8	52.9

All those in No knee pain/XROA (Group 2) have K/L grade ≤ 2. A random sample of knees in each group were read for synovial thickening. Total for Knee pain/XROA is different from Table 2 due to 7 missing K/L grades. ** $p < 0.001$, * $p = 0.02$, comparing Knee pain/XROA with K/L grade ≤ 2 and No knee pain/XROA.

Popliteal cysts were seen in 20.8% of those without knee pain and 33.0% of those with knee pain (Table 2). Popliteal cysts were more common among those with radiographic OA. Popliteal cysts communicate with the knee joint, and we found an association between the presence of effusion and presence of popliteal cyst. In those with moderate or larger effusion, 43.2% had a popliteal cyst compared to 22.7% in those with small or absent effusion ($p < 0.001$, chi-square). Further, there was a weak positive correlation between the size of effusion and the size of the cyst ($r = 0.30$, $p < 0.001$).

Synovial thickening was more prevalent with increasing effusion, from 45.0% in those with no effusion to 80.0% in those with a large (grade 3) effusion ($p = 0.001$, chi-square). In addition, the presence of synovial thickening was more likely with increasing K-L grade, from 24.0% in those with K-L grade 0 to 78.3% in those with grade 3/4 ($p < 0.001$, chi-square).

To test the association of these lesions with knee pain, we compared the prevalence of these findings in Groups 1 and 2 (Knee pain/XROA vs No knee pain/XROA). Moderate and large effusions (grade 2/3) were significantly more common among those with Knee pain/XROA compared to No knee pain/XROA ($p < 0.005$, chi-square). Popliteal cysts were no more common among those with Knee pain/XROA compared to those with No knee pain/XROA. This was also true of larger popliteal cysts (grade > 2).

To further assess the relationship between effusions/popliteal cysts, lesions, and pain, we restricted the sample to those with K-L grade ≤ 2, as none of the No knee pain/XROA subjects had radiographic grades > 2 (Table 3). (Subjects with Knee pain/OA, who had K-L grade 0 due to normal PA views, were defined as having radiographic OA due to definite osteophytes in the patellofemoral joint.) There remained a significant difference between the Knee pain/XROA and No knee pain/XROA subjects in the prevalence of either moderate or greater and large effusions alone ($p < 0.001$, $p = 0.02$, respectively). However, there was no difference between the groups in the prevalence of popliteal cysts.

We evaluated the association of effusion with knee pain by attempting to determine whether pain was specifically associated with synovial thickening or effusion. As effusions and synovial thickening are closely associated, we looked at the prevalence of synovial thickening among persons without clinically important knee effusions. Among those with small (grade 1) or no knee (grade 0) effusion, we found that those with knee pain had a prevalence of synovial thickening of 73.6% compared to 21.4% of those without knee pain ($p < 0.001$, chi-square).

Next, we restricted our analyses to those with Knee pain and XROA (Group 1) to test whether any lesion was associated with knee pain severity as assessed by VAS pain score. After adjustment for radiographic severity, there was no difference in VAS pain scores in those with different grades of effusions. Nor, in a similar analysis, was there an association of presence of popliteal cyst with pain severity. However, there was a significant difference in VAS pain scores in those with synovial thickening compared to those without synovial thickening, after adjustment for radiographic severity, size of effusion, age, sex, and BMI. The mean pain score in those with synovial thickening after adjustment for radiographic severity and size of effusion was 47.2 mm (standard error 6.0), compared to 28.2 mm (SE 2.8) in those without synovial thickening ($p = 0.006$).

DISCUSSION

Our study shows that effusions and popliteal cysts observed on MRI are common in older individuals, with 13.0% of asymptomatic people having at least a moderate effusion and 20.8% having evidence of a popliteal cyst. We also found that the presence of moderate and large effusions with capsular distention and synovial thickening were significantly more common among those with knee pain, compared to those without knee pain, suggesting that these lesions may contribute to the pain associated with knee OA.

Although cartilage has no neural elements, studies have shown that intracapsular elements contribute to pain. Creamer, *et al* randomized 20 OA knees to local anesthetic or placebo injection[15]; in 6/10 knees injected with local anesthet-

ic, there was a reduction in pain after 1 hour compared to 2/10 knees injected with placebo, suggesting an intracapsular cause of pain in a substantial percentage of subjects. In addition, other workers have injected OA knees with small doses of morphine, with prolonged pain relief compared with placebo[16]. Our study also suggests that intracapsular elements contribute to knee pain in OA, as we observed an increased prevalence of moderate or larger effusions with associated capsular distention and of synovial thickening in those with knee pain compared to those without pain. These results suggest that there may be 2 independent intracapsular contributors to pain: capsular distention and synovitis. Finally, among those with knee pain, synovial thickening was associated with the degree of pain after adjustment for both radiographic severity and size of effusion.

The cross sectional nature of our study precludes us from making any assumptions about the causation of effusion and synovial thickening on the pain of knee OA. Further longitudinal studies will be helpful in this regard. However, we have found a clear association between effusion and synovial thickening and pain in knee OA. In addition, although we observed intraobserver and interobserver agreements for MRI reading that were substantial beyond chance[17], these levels were still not optimal. It highlights the inherent difficulty of reading MRI scans due to the necessity of reading features across multiple cuts, giving kappa values lower than for reading radiographs. Previous knee MRI studies have generally not reported intra and interobserver reliability[4,6,7]; however, one study of knee MRI reading resulted in kappa levels substantially lower than ours, generally between 0.0 and 0.4 for interobserver agreement[18]. These difficulties are likely to give rise to some misclassification; however, it is likely to bias the results toward the null. In addition, there is the potential for misclassification of early symptomatic OA in the No knee pain/no XROA group, as radiographs are not sensitive enough to detect changes of early OA and the screening question asks about pain over the past 4 weeks. This is also likely to bias results toward the null. In addition, there is the possibility that our sample may not be representative of OA in the general community, particularly for men, in which most of the sample subjects were from the VA system, with likely higher rates of disability and comorbidity than the general elderly US population.

Although we did not use gadolinium in this study to allow us to distinguish synovial inflammation, we were able to find evidence of synovial thickening in and around the infrapatellar fat pad, using a similar MRI evaluation as Fernandez-Madrid and colleagues[6]. In knee OA they found that synovial thickening in this area, detected on noncontrast MR imaging, represented chronic mild synovitis when biopsied[6]. In knees with radiographic OA, they found degrees of synovial thickening at each K-L grade similar to ours[7]. In addition, they showed a nonsignificant increase in synovial thickening in those with symptomatic knee OA, compared to asymptomatic knees[7]. However, the numbers in each group were smaller than ours, and there was no evaluation of the severity of pain.

There are few studies of the prevalence of knee effusions in normal populations. A community study in Sudbury, Massachusetts, showed an effusion in one or both knees in 22.3% of men and 17.3% of women aged 45 years and older[19]. Effusions were measured by clinical examination using the "bulge" sign. There were no significant differences in knee effusions between those who had evidence of arthritis (OA or rheumatoid arthritis) on hand radiographs and those who did not, although no knee radiographs were obtained. We found that 13.0% of subjects over 40 years without knee symptoms had at least a moderate effusion on MRI, which is lower than the Sudbury population; however, that they did not differentiate between those with and without knee symptoms may explain this difference.

MRI studies have shown the prevalence of popliteal cysts is between 5% and 19%; however, these studies used subjects referred for MR imaging for knee symptoms and included few, if any, older subjects[20,21]. Our study revealed a high prevalence of popliteal cysts (20.8%) among asymptomatic older people. The subjects with popliteal cysts on MRI were not examined to determine whether the cysts were clinically detectable. However, of the 16 popliteal cysts identified in this group, only 5 were of moderate or large size, suggesting that most would not be clinically detectable. Another MRI study found that popliteal cysts were most common among those with knee effusions and degenerative joint disease[20].

We observed that small and moderate effusions and popliteal cysts are common among middle aged and elderly subjects using MR imaging. Popliteal cysts occurred with similar prevalence among those with radiographic knee OA regardless of symptoms, and do not appear to be associated with pain. Moderate or larger effusions and synovial thickening were significantly more common in those with knee pain and evidence of radiographic OA than in those with a comparable grade of radiographic severity without pain, suggesting that these lesions may contribute to knee pain in OA. Our finding that synovial thickening was related to the severity of knee pain suggests that it may contribute importantly to the cardinal feature of OA — pain.

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