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Relationship between patient-reported swelling and MRI-defined effusion-synovitis in patients with meniscus tears and knee osteoarthritis

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Abstract

Objective—Synovitis is a prevalent feature in patients with knee osteoarthritis (OA) and meniscal tear and is associated with pain and cartilage damage. Patient-reported swelling is also prevalent in this population. We aimed to investigate the cross-sectional association between patient-reported swelling and effusion-synovitis on magnetic resonance imaging (MRI) in patients with OA and meniscal tear.

Methods—We used baseline data from a multicenter randomized controlled trial, Meniscal Tear in Osteoarthritis Research (MeTeOR). MRI-identified effusion-synovitis, a proxy of effusion and synovitis on non-contrast MRIs, was graded as none/small vs. medium/large. Using MRI-identified effusion-synovitis as the gold standard, we assessed sensitivity, specificity, and positive

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predictive value of patient self-reported swelling in the past week (none; intermittent; constant) to detect effusion and synovitis.

Results—We analyzed 276 participants. Twenty-five percent of participants reported no swelling, 40% had intermittent swelling, and 36% had constant swelling. Fifty-two percent had MRI-identified medium/large effusion-synovitis. As compared with MRI-identified effusion-synovitis, *any* patient-reported swelling (vs. none) had a sensitivity of 84% (95% CI 77%, 89%), specificity of 34% (95% CI 26%, 43%), and positive predictive value of 57% (95% CI 54%, 61%). A history of constant swelling (vs. none or intermittent) demonstrated sensitivity of 46% (95% CI 37%, 54%), specificity of 75% (95% CI 67%, 82%) and positive predictive value of 66% (95% CI 58%, 74%).

Conclusion—We found that the sensitivity and specificity of patient-reported swelling were modest as compared with effusion-synovitis on MRI. These data urge caution against using patient-reported swelling as a proxy of inflammation manifesting as effusion-synovitis.

Introduction

The pathogenesis of osteoarthritis (OA) is increasingly appreciated as a dynamic process involving multiple joint structures (e.g. cartilage, bone, meniscus) with an important role for intra-articular inflammation manifesting as effusion and synovitis. Recent studies have demonstrated that synovitis is associated with pain, incident knee OA, and progression of OA.(1-4) Synovitis is also a prominent feature of meniscal tears even in the absence of OA. (5-7) Of the fourteen million Americans with symptomatic knee OA, up to 91% will have a meniscal tear on magnetic resonance imaging (MRI), highlighting the subset of patients with OA *and* meniscal tear as a clinically relevant and prevalent population.(8, 9)

Knee swelling is a key feature elicited in the clinical history and is commonly reported in patients with knee OA and meniscal tear. However, whether patient-reported swelling accurately predicts the presence of effusion-synovitis on imaging is unknown. As effusion and synovitis identified on imaging may be associated with progression of intra-articular damage,(1) a firmer understanding of the association between patient-reported swelling and the presence of effusion and synovitis on imaging could help clinicians risk stratify patients. This analysis aimed to assess the relationship between self-reported knee swelling and effusion-synovitis on MRI in patients with concurrent meniscal tear and knee OA. We hypothesized that patient-reported swelling would have a positive relationship with MRI-identified effusion-synovitis.

Methods

Sample

We used baseline data from subjects enrolled in the Meniscal Tear in Osteoarthritis Research (MeTeOR) trial, a randomized clinical trial of arthroscopic partial meniscectomy (APM) versus physical-therapy (PT) for management of symptomatic meniscal tears.(10) Three hundred fifty-one subjects were recruited from 7 academic referral centers between June 2008 and July 2011. Recruited males and females were 45 years old, had a non-contrast MRI of the knee with evidence of meniscal tear extending to the meniscal surface, and at

least four weeks of meniscal symptoms (clicking, catching, popping, giving way, pain with pivot or torque, pain that is episodic, and pain that is acute and localized to one joint line). All enrolled patients had evidence of knee OA as determined by either osteophyte and joint space narrowing on plain radiographs, or osteophyte(s) and/or cartilage defect(s) on MRI. Patients with Kellgren-Lawrence (KL) grade 4 knee OA were excluded, as were patients with inflammatory arthritis (i.e. rheumatoid arthritis, psoriatic arthritis, spondyloarthritis) or prior surgery on the index knee. We focused the analysis on data from the index knee. All data domains corresponded to the index knee.

For the current analysis, we used the subsample of MeTeOR with baseline MRIs that were available for central re-reading, reducing the sample to 281 participants. An additional 5 participants were excluded, as they had missing data for the patient-reported swelling scale; thus, we had a final cohort of 276 participants. The MeTeOR study was approved by the Partners HealthCare Human Research Committee. This trial is registered at clinicaltrials.gov (NCT00597012).

Assessments

Demographics including age, sex, and body mass index (BMI kg/m²) were collected at baseline. Patient-reported swelling was assessed via questionnaire and categorized as 1) no swelling; 2) once in the last week; 3) 2-6 times in the last week; 4) 1-2 times a day; 5) several times a day. As some of these categories were sparsely populated, the variable was re-categorized into 0) no swelling; 1) intermittent swelling (categories 2 and 3); and 3) constant swelling (categories 4 and 5). Our group previously reported strong test-retest reliability of using 'swelling' on questionnaires (kappa 0.75) versus providing an expanded description of swelling and found strong agreement between the two question stems.(11) Assessing frequency of swelling in knee OA and meniscal tear has been deemed an important assessment based on input from patients and clinicians.(11, 12) Non-contrast MRIs are frequently used in larger studies due to lower cost and less risk of adverse events. (13) However, non-contrast MRIs cannot distinguish between effusion (fluid within the joint cavity) and synovitis (thickening and enhancement of the synovium); thus, effusion-synovitis is a frequently used proxy for synovitis on non-contrast MRIs.(13) Using T2/IW or PD-weighted fat-suppressed MRI images we assessed baseline effusion-synovitis according to the MRI OA Knee Score (MOAKS) score, a semi-quantitative scoring method for knee OA.(13) All MRIs were re-read centrally by a single reader. The intra- and inter-rater weighted kappa statistics for effusion-synovitis in MOAKS are 0.9 and 0.72 respectively. (13) Effusion-synovitis was categorized as 0) none (physiologic); 1) small (fluid continuous in the retropatellar space); 2) medium (slight convexity of suprapatellar bursa); or 3) large (capsular distention).(13) We dichotomized effusion-synovitis into 1) none to small effusion-synovitis (grade 0-1); and 2) medium to large effusion-synovitis (grade 2-3) because some categories were sparsely populated and for ease of interpretation.

KL radiographic grade was used as an indication of OA severity. The KL grade was categorized as 0) normal; 1) questionable osteophyte; 2) definite osteophyte; 3) <50% joint space narrowing. The Knee injury and Osteoarthritis Outcome Score (KOOS) Pain scale was used to assess overall patient-reported knee pain in the last week, and was transformed to a

0-100, scale with 0 being the least amount of pain and 100 the greatest amount of pain.(12) We assessed the relationships between KOOS Pain and patient-reported swelling and between KOOS Pain and MRI-identified effusion-synovitis.

Sensitivity, Specificity and PPV

Sensitivity, specificity, positive predictive value (PPV), and positive likelihood ratio (LR) were calculated using MRI-identified effusion-synovitis as the criterion standard. We performed analyses using two distinct cut points of patient-reported swelling for a 'positive test': 1) history of *any* swelling (intermittent and constant) and 2) presence of *constant* swelling.

We performed sensitivity analyses to further investigate the relationship between patient-reported swelling and MRI-identified effusion-synovitis. First, we examined the relationship between patient-reported swelling and effusion-synovitis after stratifying by OA severity based on KL grade (those with KL grade 0 and 1 vs. grade 2 and 3). We also stratified by patient-reported pain based on KOOS Pain dichotomized at the cohort mean (≤ 46 for less pain and >46 for greater pain), as well as BMI dichotomized to obese (BMI ≥ 30) and non-obese (BMI <30). Lastly, we stratified by sex. We additionally dichotomized MRI-identified effusion-synovitis as none (grade 0) vs. any (grade 1-3) and re-investigated the relationship between patient-reported swelling and MRI-defined effusion-synovitis. The Breslow-day test was used to assess for homogeneity between the strata.

Results

The study sample consisted of 276 participants (1 affected knee per person). Twenty-five percent of patients reported no swelling, 40% reported intermittent swelling, and 36% reported constant swelling. Mean age was similar among the swelling categories ranging from 58 to 59 years old. Females constituted 69% of participants reporting constant swelling, 51% of participants reporting intermittent swelling, and 47% of participants reporting no swelling. The KOOS Pain score was greater in patients with constant swelling (54 points) than in those with intermittent swelling (45 points) and no swelling (38 points) ($p<0.01$; Table 1).

A total of 133 (48%) patients had no or small effusion-synovitis (grade 0-1), and 142 (52%) patients had medium or large effusion-synovitis (grade 2-3) (1 participant was missing data on effusion-synovitis). Medium or large effusion-synovitis was identified in 34% of patients with no swelling, 50% with intermittent swelling, and 66% with constant swelling ($p<0.01$). Table 2. The KOOS pain score was 48 points in those with medium or large effusion-synovitis and 45 in those with no or small effusion-synovitis ($p=0.07$).

Using patients who reported any swelling (those with intermittent and constant swelling) to calculate sensitivity, specificity, and PPV, swelling had a sensitivity of 84% (95% CI 77%, 89%), specificity of 34% (95% CI 26%, 43%), PPV of 57% (95% CI 54%, 61%), and positive LR of 1.3 (95% CI 1.1, 1.5) as compared with the gold standard, MRI-identified effusion-synovitis. Using a more stringent cut point of *constant* swelling (vs. intermittent and no swelling), sensitivity was 46% (95% CI 37%, 54%), specificity 75% (95% CI 67%,

82%), PPV 66% (95% CI 58%, 74%), and positive LR 1.8 (95% CI 1.3, 2.6) for effusion-synovitis on MRI (Table 2).

In sensitivity analyses, the associations between self-reported swelling and MRI-documented effusion-synovitis were largely similar after stratifying by KL grade, patient-reported KOOS Pain score, BMI, or sex (test of homogeneity for all $p > 0.05$). Dichotomizing effusion-synovitis as none vs. any led to qualitatively similar results, though some categories were under-populated.

Discussion

Our findings indicate that patient-reported swelling did not perform well as a proxy for MRI-identified effusion-synovitis. *Any* reported swelling had a sensitivity of 84% for MRI-defined effusion-synovitis but lacked specificity (34%). Conversely, more frequent swelling (constant) was more specific for effusion-synovitis, 75%, but lacked sensitivity (46%). Neither cut point for patient-reported swelling resulted in a strong PPV for MRI defined effusion-synovitis (range 57-66%). Likelihood ratios were small. These results suggest that patient-reported swelling is not an especially useful clinical marker of MRI-identified effusion-synovitis.

Weak associations between patient-reported symptoms and structural abnormalities have been identified in other studies and conditions.⁽¹⁴⁾ An evaluation of hip pain and radiographic hip OA using the Framingham Osteoarthritis Study reported that radiographic hip OA had a sensitivity of 27% and specificity of 91% for groin or anterior thigh pain.⁽¹⁴⁾ Similar results were reported in the Osteoarthritis Initiative (OAI) with frequent hip pain having a sensitivity of 9% and specificity of 94% for radiographic hip OA.⁽¹⁴⁾ One study also using data from the OAI demonstrated an association of patient-reported swelling and knee pain with extension and effusion-synovitis on MRI.⁽¹⁵⁾ However, this study did not assess the performance characteristics of patient-reported symptoms and MRI findings, precluding a direct comparison with our work. We stratified by KL grade, KOOS Pain score, BMI, and sex but found that patient-reported swelling was not strongly associated with effusion-synovitis on imaging in any of these distinct strata. Our study demonstrated a significant difference in pain among the patient-reported swelling categories, with those indicating more frequent swelling also reporting greater pain. This relationship was not seen with MRI-identified effusion-synovitis, for which there was no difference in pain levels between those with no or small effusion-synovitis and those with medium or large. This suggests that the relationship between various patient-reported measures may be stronger than the association between patient-reported symptom measures and structural findings on imaging.

This study has several limitations. Effusion-synovitis identified on non-contrast MRI is a frequently used proxy for effusion and synovitis in clinical studies given the lower cost and the lower risk of adverse effects with non-contrast scans. However, non-contrast MRI cannot differentiate between effusion and synovitis.⁽¹³⁾ Clinician assessment of effusion on physical exam was not recorded as part of the trial. Thus, we cannot evaluate the relationship between clinical exam evidence of effusion, MRI-identified effusion-synovitis and patient

reported swelling. We recognize that it would be useful to minimize the role of participant subjectivity. Further study using clinical exam or musculoskeletal ultrasound could leverage safe bedside modalities for assessing synovitis. Our patient population had concurrent OA and meniscal tear; thus, we are unable to discern whether OA, meniscal tear, or a combination of both drives patient-reported swelling or effusion-synovitis noted on MRI. MRI and assessment of patient-reported swelling was not done on the same day. As the presence of effusion-synovitis is dynamic, this may have weakened associations. Our study is strengthened in that it is a large multicenter study with rich demographic and imaging data, focusing on a prevalent population of patients with both meniscal tear and knee OA.

In conclusion, in a population of patients with OA and meniscal tear we found that the sensitivity and specificity of patient-reported swelling were modest as compared with effusion-synovitis on MRI. We caution against clinical use of patient-reported swelling as a measure or proxy of synovitis in this population.

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Significance

- We found that the sensitivity and specificity of patient-reported swelling were modest as compared with effusion-synovitis on MRI in patients with knee osteoarthritis and meniscal tear
- This relationship did not differ despite stratification based on sex, radiographic severity of OA, body mass index, or patient-reported pain

Table 1

Baseline characteristics and association of patient-reported swelling and MRI-identified effusion-synovitis.

	0 No swelling (n=68)	1 Intermittent Swelling (n=110)	2 Constant Swelling (n=98)	P value
Age, mean (SD)	59 (9)	58 (7)	58 (6)	0.53
Female, n (%)	32 (47)	56 (51)	68 (69)	0.005
BMI, mean (SD)	30 (6)	29 (5)	31 (7)	0.04
KL grade, n (%)				
0	22 (32)	22 (20)	18 (18)	0.21
1	13 (19)	24 (22)	28 (29)	
2	16 (24)	35 (32)	21 (21)	
3	17 (25)	29 (26)	31 (32)	
KOOS Pain Score, mean (SD)	38 (15)	45 (14)	54 (15)	<0.0001

BMI; body mass index. KL; Kellgren-Lawrence.

KOOS; Knee Injury and Osteoarthritis Outcome Score.

Table 2

Severity of effusion-synovitis by frequency of patient-reported swelling, and sensitivity, specificity, and positive predictive value of patient-reported swelling for effusion-synovitis.

	Effusion-Synovitis			
	None/small	Medium/large		
No swelling, n	45	23		
Intermittent swelling, n	55	54		
Constant swelling, n	33	65		
	Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value (95% CI)	Positive Likelihood Ratio (95% CI)
Any swelling *	84% (77%, 89%)	34% (26%, 43%)	57% (54%, 61%)	1.3 (1.1, 1.5)
Constant swelling	46% (37%, 54%)	75% (67%, 82%)	66% (58%, 74%)	1.8 (1.3, 2.6)

* Intermittent and constant swelling. CI; confidence interval.