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BRIEF REPORT

Relation of MRI-Detected Features of Patellofemoral Osteoarthritis to Pain, Performance-Based Function, and Daily Walking: The Multicenter Osteoarthritis Study

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Objective. The study objective was to determine the relationship of magnetic resonance imaging (MRI)-detected features of patellofemoral joint osteoarthritis to pain and functional outcomes.

Methods. We sampled 1,099 participants from the 60-month visit of the Multicenter Osteoarthritis Study (mean ± SD age: 66.8 ± 7.5 years; body mass index: 29.6 ± 4.8; 65% female). We determined the prevalence of MRI-detected features of patellofemoral joint osteoarthritis (eg, cartilage damage, bone marrow lesions, and osteophytes) and assessed the relationship between these features and knee pain severity, knee pain on stairs, chair stand time, and walking less than 6,000 steps per day. We evaluated the relationship of MRI features to each outcome using logistic and linear regression, adjusting for potential covariates.

Results. Participants with cartilage damage in 3-4 subregions had the highest mean pain severity (22.0/100; 95% confidence interval [CI]: 17.6-26.4 mm). They also showed higher odds of having at least mild pain on stairs (odds ratio [OR]: 3.3; 95% CI: 1.7-6.5) and of walking less than 6,000 steps per day (OR: 2.3; 95% CI: 1.1-4.4) compared with those without cartilage damage. Participants with bone marrow lesions in 3-4 subregions had higher odds of at least mild pain on stairs than those without (OR: 3.3; 95% CI: 2.2-5.2). Participants with osteophytes in 3-4 subregions also had higher odds of walking less than 6,000 steps/day (OR 2.1, 95% CI: 1.3-3.5, respectively).

Conclusion. MRI-detected features of osteoarthritis of the patellofemoral joint are related to pain and functional performance. This knowledge highlights the need to develop treatments for those with patellofemoral joint osteoarthritis to improve pain and maximize function.

INTRODUCTION

Osteoarthritis (OA) of the knee is a common cause of disability in the United States (1) and the world, with knee and hip OA accounting for at least 17 million years lived with disability globally (2). Disability stems from pain, difficulty walking, and difficulty performing functional, home, and community activities. Knee OA affects both the tibiofemoral and the patellofemoral

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compartments. While often overlooked, OA of the patellofemoral joint (PFJ OA) is highly prevalent, present in over 50% of painful knees and those with radiographic involvement (3,4), as well as in 15% to 20% of knees in the general population (5). PFJ OA also often occurs in isolation from tibiofemoral joint (TFJ) OA (6) and is associated with knee pain and functional tasks (7). Furthermore, isolated PFJ OA is related to increased risk of future TFJ OA development (8,9).

Magnetic resonance imaging (MRI) can detect features of PFJ OA that are not seen on radiograph, such as bone marrow lesions (BMLs) and cartilage defects. These MRI-detected features, including cartilage damage, BMLs, and osteophytes, are related to knee pain severity (5,10-12). Although there is some evidence on the relationship of certain types of MRI-detected damage with stair climbing performance (13), whether there is an association between other OA features and stair climbing performance and other functional performance outcomes is not yet known. As stairs and sit to stand commonly load the PFJ, it is logical that structural OA features in the PFJ may be associated with poorer performance on these tasks. Similarly, walking is an important weight-bearing activity that we know little about with regard to the PFJ. Further understanding of how PFJ OA contributes to a person's symptoms and function may also be important for developing clinical trials that could lead to more targeted interventions for PFJ OA.

The purpose of the current study was to determine the cross-sectional relationship of MRI-detected features of PFJ OA to symptoms and performance-measured function. We hypothesized that knees with MRI-assessed structural damage in the PFJ would be associated with increased pain and decreased function, accounting for the presence of concomitant TFJ damage.

METHODS

We performed a cross-sectional analysis using data from the 60-month study visit from the National Institutes of Health–funded Multicenter Osteoarthritis (MOST) study. MOST is a multicenter cohort of 3,026 persons with knee OA or at risk of knee OA at enrollment. Participants were recruited from study centers in Birmigham, Alabama, and Iowa City, Iowa. At enrollment, participants were between 50 and 79 years old, had frequent knee pain or a prior knee injury, or were overweight or obese. Participants were excluded if they had inflammatory or other rheumatoid-like symptoms, were nonambulatory, had significant medical impairments, or were likely to move out of the area within 3 years. Details of the MOST study have been published elsewhere (13). Participants were eligible for the current analysis if they had an MRI of one knee that had been assessed for structural outcomes. The 60-month visit was selected for our sample because it was the first visit that MRI features as well as walking steps per day were collected, in addition to our other outcomes of interest.

ASSESSMENT OF MRI-DETECTED PFJ OA FEATURES (EXPOSURE)

MRI acquisition. Knee MRI examinations were performed using a 1.0T extremity system (OrthOne; ONI Medical Systems) with a phased-array knee coil at the 60-month visit. The MOST imaging protocol consisted of the following sequences: i) fat-suppressed fast spin-echo proton density weighted sequences in two planes, sagittal (repetition time/echo time [TR/TE] 4,800 ms/35 ms, 3-mm slice thickness, 0-mm interslice gap, 32 slices, 288 × 192 matrix, 140 mm^2 field-of-view, echo train length 8) and axial (TR/TE 4,680 ms/13 ms, 3-mm slice thickness, 0-mm interslice gap, 20 slices, 288 × 192 matrix, 140 mm^2 field-of-view, echo train length 8) and ii) a short tau inversion recovery sequence in the coronal plane (TR/TE 6,650 ms/15 ms, inversion time 100 ms, 3-mm slice thickness, 0-mm interslice gap, 28 slices, 256 × 192 matrix, 140 mm^2 field-of-view, echo train length 8).

Full-thickness cartilage damage, BMLs, and osteophytes were assessed in one randomly selected knee per participant by two experienced musculoskeletal radiologists (FWR, AG) using the Whole-Organ Magnetic Resonance Score (WORMS) (14). Cartilage damage and BMLs were scored on a scale from 0 (normal cartilage) to 6 (diffuse full-thickness cartilage damage) and from 0 (none) to 3 (large), respectively, in the 4 subregions of the PFJ and the 10 subregions of the TFJ. The size of osteophytes was scored in four locations in the PFJ and six locations in the TFJ from 0 to 7. Presence of full-thickness cartilage damage, BMLs, and osteophytes were defined as WORMS scores of 2.5 or 5-6, >0, and ≥ 2, respectively (14). The Figure exemplifies this scoring (Figure 1).

ASSESSMENT OF PAIN, FUNCTION, AND DAILY WALKING (OUTCOMES)

Knee pain severity was measured on a Visual Analog Scale (VAS), a 100-mm line, where participants mark their level of pain on the line from zero to 100 mm (12). Pain on stairs was assessed using the Western Ontario McMaster Arthritis Index's (WOMAC) pain subscale (13). Those who selected mild, moderate, severe, or extreme pain when going up and down stairs were designated as having at least mild pain on stairs. Function was assessed using the Five Times Sit to Stand Test (15). The number of seconds that it took each participant to rise from a chair and sit back down five times was recorded (15). To measure participants' amount of daily walking, we took the average steps per day while the participant was wearing a StepWatch Activity Monitor (Orthocare Innovations, Mountlake Terrace, WA). The MOST cohort participants were asked to wear the accelerometer for 7 consecutive full days (16). The average number of steps walked per day was calculated for participants who wore the device for at least 10 hours per day for a minimum of 3 days, as this is a valid assessment of average walking steps per day (17). Only subjects who met this criteria were included in the analysis. We

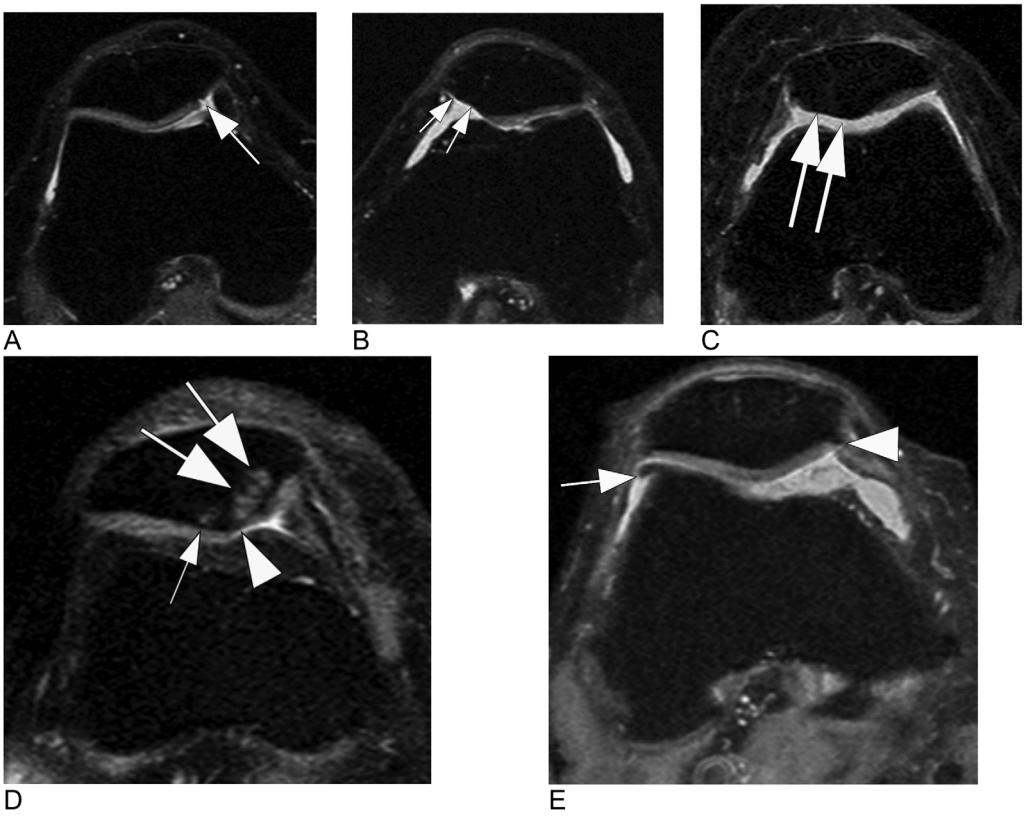

Figure 1. Example of structural PFJ damage. **A**, Focal full-thickness lesion (grade 2.5 by WORMS) at the medial patella facet without associated BML. No PFJ osteophytes are seen. **B**, Diffuse full-thickness cartilage damage grade 5 (arrows) excluding the patella apex, which is also part of the medial patella subregion according to WORMS. No associated BML or osteophyte is seen. **C**, Diffuse wide-spread full-thickness cartilage damage (grade 6 according to WORMS) of the medial patella facet (arrows). **D**, Diffuse grade 3 BML at the medial patella facet (large arrows). In addition, there is superficial cartilage damage at the medial patella facet (arrowhead) and a small BML at the lateral patella (small arrow). **E**, Grade 2 PFJ osteophytes at the medial patella (arrowhead) and the lateral femoral trochlea (arrow). BML, bone marrow lesion; PFJ, patello-femoral joint; WORMS, Whole-Organ Magnetic Resonance Score.

categorized the participants into those who walked more or less than 6,000 steps/day, as this was associated with developing functional limitations in people with knee OA (18).

STATISTICAL ANALYSIS

We created a three-level exposure variable for the number of PFJ subregions affected (0, 1-2, and 3-4) for each type of MRI-detected structural feature. The relationship between the number of PFJ subregions affected and knee pain severity (VAS Pain) and repeated chair-stand time was assessed using analysis of covariance with Tukey pairwise comparisons. Relationship between the number of subregions affected and at least mild pain with stairs and walking <6,000 steps/day was assessed with logistic regression. Mild pain with stairs was chosen because the numbers were too small to assess moderate pain or greater. Knees without any subregion affected were considered the reference category in all models. Separate models were created for each structural feature. All analyses were adjusted for age, sex, body mass index (BMI), history of previous knee injury or surgery, the presence of depressive symptoms (score of more than 16 on the Center for Epidemiological Studies Depression scale) (19,20), and the presence of structural damage (same feature and severity) in the TFJ.

To study the effect of a potential "lesion load," or multiple features present across multiple subregions, we summed the presence of all three features in the four PFJ subregions. This resulted in an exposure score from 0 to 12, with 0 being no feature present in any subregion and 12 being that each feature was present in all four subregions. We collapsed these scores into a four-level exposure variable (0, 1-4, 5-8, and 9-12) and assessed the association to each of our four outcomes.

In sensitivity analyses, all analyses were repeated using only those knees without TFJ Kellgren-Lawrence grades of 3 or 4, to exclude those with moderate to severe OA (21). Analyses were conducted using SAS version 9.4 (SAS Institute Inc.).

RESULTS

There were 1,099 subjects with complete WORMS readings at the 60-month visit. The mean (SD) age and BMI was 66.8 (7.5)

Table 1. Participant characteristics (N = 1,099)

Sex, n (%) women	716 (65)
Age, y	66.8 (7.5); 55.4-84.9
X-ray data present, n (%)	1,088 (99)
TFJ radiographic OA present, n (%)	411 (37.8)
PFJ radiographic OA present, n (%)	148 (13.6)
BMI, m/kg^2	29.6 (4.8); 16.9-50.6
VAS (N = 1,096)	12.3 (17.2): 0-95
Chair stands, s (N = 1,072)	11.2 (3.4); 4.0-40.9
At least mild pain on stairs, n (%) (N = 1,090)	598 (54.9)
Walking <6,000 steps/d, n (%) (N = 912)	599 (65.7)

Data are presented as mean (standard deviation); range, unless noted.
Abbreviations: BMI, body mass index; OA, osteoarthritis; PFJ, patellofemoral joint; TFJ, tibiofemoral joint; VAS, visual analogue scale.

years and 29.6 (4.8) m/kg^2, respectively, and 716 (65%) participants were women (Table 1). BMLs were the most prevalent structural feature, in 60% of knees (659/1,099), osteophytes were present in 53% (583/1,099), and full-thickness cartilage damage was present in 36.1% (397/1,099) of knees.

Pain. For all three structural features, more subregions affected was related to increased VAS pain (Table 2) when compared with no affected subregions. Participants with full-thickness cartilage damage in 3-4 subregions reported the highest mean pain (22.0/100; 95% CI: 17.6-26.4 mm). This was compared with 14.1 (12.5-15.6 mm) for those with no full-thickness cartilage damage. Participants with BMLs in 3-4 compartments reported a mean pain of 17.0 (14.2-19.9) mm, compared with 11.9 (10.3-13.5) mm for those without BMLs. Participants with osteophytes in 3-4 subregions reported a mean pain of 16.7 (14.1-19.3) mm, compared with 11.0 (9.5-12.5) mm for those without osteophytes.

Chair stand time. There was little variation across the number of involved subregions or structural features with chair-stand time (Table 2), although participants with full-thickness cartilage damage in 3-4 subregions had statistically slower times (12.4; 95% CI: 11.5-13.3 seconds) than those with no cartilage damage (11.5; 95% CI: 11.2-11.8 seconds). Similarly, those with osteophytes in 1-2 and 3-4 regions had slower chair-stand times (11.5 [95% CI: 11.2-11.9 seconds] and 11.9 [95% CI: 11.4-12.4 seconds], respectively) than those without osteophytes (10.8 [95% CI: 10.5-11.1] seconds).

Pain on stairs. Both 1-2 and 3-4 involved subregions of any structural feature was significantly associated with reporting at least mild pain on stairs, compared with no subregions with features (Table 3). In particular, participants with either full-thickness cartilage damage or BMLs in 3-4 subregions had over 3 times the odds of having at least mild pain on stairs compared with those without (OR 3.5 [95% CI: 1.8-6.8] and OR 3.4 [95% CI: 2.2-5.2], respectively).

Daily walking. With respect to daily walking, participants with full-thickness cartilage damage in 3-4 subregions demonstrated higher odds of walking less than 6,000 steps/day (OR 2.3 [95% CI: 1.2-4.6]) (Table 3). Those with osteophytes in 1-2 and 3-4 subregions also had higher odds of walking less than 6,000 steps/day (OR 1.6 [95% CI: 1.1-2.4] and OR 2.1 [95% CI: 1.3-3.5], respectively). The number of subregions affected with BMLs was not related to walking less than 6,000 steps/day.

Lesion load. The analysis that summed all features present across the whole joint (three types across four subregions) yielded similar results to our main analyses (Table 4).

Analyses excluding knees with TFJ KL grades of 3-4. When we removed knees with TFJ KL grades of 3-4 from our analyses, the results were similar (Supplementary Tables 1 and 2). One exception was that there was a significant effect of the

Table 2. Relationship of number of PFJ subregions affected to pain and functional performance (continuous variables)

No. of Subregions Affected	Cartilage Damage (n = 1,096)	BMLs (n = 1,096)	Definite Osteophytes (n = 1,096)
Adjusted Mean VAS Pain (0-100 mm)			
0	14.1 (12.5-15.6)	11.9 (10.3-13.5)	11.0 (9.5-12.5)
1-2	14.8 (13.0-16.7)	15.7 (14.1-17.2)*	11.0 (9.3-12.7)
3-4	22.0 (17.6-26.4)**	17.0 (14.2-19.9)*	16.7 (14.1-19.3)**
Adjusted Mean Time to Complete Five Chair Stands (s)			
0	11.5 (11.2-11.8)	11.2 (10.9-11.6)	10.8 (10.5-11.1)
1-2	11.1 (10.8-11.5)	11.3 (11.0-11.6)	11.5 (11.2-11.9)*
3-4	12.4 (11.5-13.3)***	11.5 (10.9-12.1)	11.9 (11.4-12.4)*

* Significant difference from 0, $P < 0.05$.
** 3-4 group different from others $P < 0.05$.
*** 3-4 group different from 1-2 group $P < 0.05$.
All models adjusted for age, sex, BMI, history of previous knee injury or surgery, the presence of depressive symptoms, and the presence of the same structure type in the TFJ.
Abbreviations: BMI, body mass index; BML, bone marrow lesion; PFJ, patellofemoral joint; TFJ, tibiofemoral joint; VAS, visual analogue scale.

Table 3. Relationship of number of PFJ subregions affected to pain and function (dichotomous variables)

	Full-Thickness Cartilage Damage		BMLs		Definite Osteophyte	
No. of Subregions Affected	n/N (%)	Adjusted* OR (95% CI)	n/N (%)	Adjusted* OR (95% CI)	n/N (%)	Adjusted* OR (95% CI)
At Least Mild Pain on Stairs						
0	344/695 (49.5)	1.0 (REF)	184/433 (42.5)	1.0 (REF)	224/509 (44.0)	1.0 (REF)
1-2	211/340 (62.1)	1.6 (1.2-2.1)	318/523 (60.8)	2.1 (1.6-2.7)	225/371 (60.7)	1.4 (1.0-1.9)
3-4	43/55 (78.2)	3.5 (1.8-6.8)	96/134 (71.6)	3.4 (2.2-5.2)	149/210 (71.0)	1.6 (1.0-2.4)
Walking Less Than 6,000 Steps/Day						
0	186/581 (32.0)	1.0 (REF)	124/374 (33.2)	1.0 (REF)	118/420 (28.1)	1.0 (REF)
1-2	100/286 (35.0)	1.0 (0.7-1.4)	153/429 (35.7)	0.97 (0.7-1.3)	118/318 (37.1)	1.6 (1.1-2.4)
3-4	27/45 (60.0)	2.3 (1.2-4.6)	36/109 (33.0)	0.76 (0.5-1.2)	77/174 (44.3)	2.1 (1.3-3.5)

***** Adjusted for age, sex, BMI, history of previous knee injury or surgery, the presence of depressive symptoms, and the presence of the same structure type in the TFJ.
Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio; PFJ, patellofemoral joint; REF, reference; TFJ, tibiofemoral joint.

presence of osteophytes on pain with stair climbing, which was not evident in the full sample. When the lesion load analysis was limited to knees without TFJ KL grades of 3 or 4, the results were also similar to the main analyses, but the effects on mean VAS pain severity and pain and odds of pain on stairs were higher, and the odds of walking less than 6,000 steps a day were lower than in the full sample (Supplementary Table 3). These results indicate that MRI-detected structural features in the PFJ are related to pain and function in the absence of radiographic TFJ OA.

DISCUSSION

MRI-detected PFJ OA structural features are common in the general population and in painful knees (3-5), but knowledge of the relationship of these features to pain and functional outcomes is limited. As hypothesized, we have demonstrated that MRI-detected PFJ OA features are associated with increased pain and poor performance-based functional outcomes. Although all three features were associated with at least one outcome, there were differences in the relationship of each feature type to the outcomes, and there appeared to be a dose–response relationship to the number of subregions affected. When only 1-2 subregions were involved, the relationship between the structural feature and clinical outcomes varied. For example, it appears that BMLs are related to pain severity when present in at least one subregion, whereas full-thickness cartilage damage may need to be more widespread. Overall, participants with more subregions affected had increased symptoms and poorer physical function. When each of the three structural features was present in 3-4 PFJ subregions, there was a relationship with worse outcomes. Participants with full-thickness cartilage damage or osteophytes in multiple PFJ subregions had higher pain severity and increased odds of walking less than 6,000 steps per day.

Table 4. The relation of PFJ OA lesion load to clinical outcomes: Sum of features present across the joint (three types across four subregions)

	VAS Pain	Time to Complete Five Chair Stands	At Least Mild Pain on Stairs		Walking < 6,000 Steps/Day	
Lesion Load	Mean (95% CI)	Mean Time (95% CI)	n/N (%)	Adjusted* OR (95% CI)	n/N (%)	Adjusted* OR (95% CI)
0	10.9 (8.8-13.0)	11.1 (10.7-11.6)	94/248 (37.9)	1.0 (REF)	57/210 (27.1)	1.0 (REF)
1-4	11.6 (10.2-13.1)	11.2 (10.9-11.5)	318/575 (55.3)	1.5 (1.1-2.1)	169/481 (35.1)	1.3 (0.9-1.9)
5-8	14.5 (12.2-16.7)	11.3 (10.8-11.8)	147/216 (68.1)	2.1 (1.4-3.3)	63/175 (36.0)	1.2 (0.7-2.0)
9-12	17.5 (13.2-21.8)	12.2 (11.2-13.1)	39/51 (76.5)	2.9 (1.4-6.2)	24/46 (52.0)	2.5 (1.2-5.3)

* Adjusted for age, sex, BMI, history of previous knee injury or surgery, the presence of depressive symptoms, and TFJ lesion load.
Abbreviations: BMI, body mass index; CI, confidence interval; OA, osteoarthritis; OR, odds ratio; PFJ, patellofemoral joint; REF, reference; TFJ, tibiofemoral joint; VAS, visual analogue scale.

It is important to consider the relationships among PFJ OA features with and without coexistent TFJ OA. We attempted to address this by adjusting the analyses for the presence of similar features in the TFJ and by excluding knees with severe TFJ damage, thereby increasing the confidence that our findings reflect a true association between PFJ OA features and clinical outcomes. When we removed participants with moderate–severe TFJ OA from the analysis, the strength of the association of PFJ OA features to pain and functional outcomes—most notably the presence of pain with stair climbing—was even stronger. These findings are consistent with prior evidence of isolated PFJ damage contributing to pain with stair climbing (13).

PFJ OA features appear to be important clinically, whether present in isolation or with TFJ OA features, and health care providers may be reminded to consider the PFJ as a source of their patient's pain and functional limitations. Future randomized controlled trials are needed to determine the best approach to address patients with clinical presentations that suggest PFJ OA. While exercise is the recommended first course of care for people with knee OA in any compartment (22,23), it is possible that exercise that modifies mechanical load or slowly develops a load tolerance could be especially useful in the beginning stages of PFJ OA. If these patients present with pain at first, new treatment approaches could impact the progression to functional limitations. Besides exercise, knee brace use can decrease BML volume in the PFJ over time, likely as a result of changes in mechanical load, and may be related to decreased pain (24). Adopting measures such as these early in the course of care may prevent or slow the progression of disease or interrupt the development of TFJ OA, which could limit the need for more invasive interventions.

Strengths of our study include the use of valid and reproducible exposure and outcome measures in a large, well-described cohort with rigorous study procedures. We adjusted all analyses for potential confounding variables, including TFJ OA features, and performed additional analyses removing knees with moderate to severe TFJ OA. A limitation of our study was that the mean pain severity for our participants as a whole was low. However, most participants had at least mild pain on stairs and walked less than 6,000 steps per day, indicating at least some functional impairment. Finally, although we understand that clinicians may not have access to MRI for their patients, the knowledge of how structural damage in the PFJ is related to certain clinical signs and symptoms may encourage them to consider the PFJ as a contributing factor to their clinical presentation.

In conclusion, we found that MRI-detected PFJ OA features were associated with poor clinical outcomes, and this relationship appeared to strengthen as the number of involved subregions increased. These associations should be examined with longitudinal data and through randomized clinical trials to investigate potential interventions for people who report clinical symptoms consistent with PFJ OA, with the goal of reducing pain and disability.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Stefanik had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Maxwell, Neogi, Crossley, Macri, White, Nevitt, Lewis CE, Torner, Stefanik.

Acquisition of data. Neogi, Guermazi, Roemer, Nevitt, Lewis, Torner.

Analysis of data. Maxwell, Neogi, Crossley, Macri, White, Guermazi, Roemer, Nevitt, Lewis, Torner, Stefanik.

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