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Title: Diagnostic Performance of Clinical Examination Measures and Pain Presentation to Identify Patellofemoral Joint Osteoarthritis

Running head: Identifying Knees with Patellofemoral Joint Osteoarthritis

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Abstract

Objective: Test the diagnostic performance of a comprehensive set of tests and measures to discriminate patellofemoral (PF) from tibiofemoral (TF) osteoarthritis (OA).

Methods: The Clinical Assessment of the Knee Study is a study of knee pain in the general population. The presence of PF crepitus and pain with PF compression were assessed. Anterior knee pain (AKP) was determined from a knee pain map. Pain with stairs and walking on level ground were assessed with the WOMAC. Radiographs were used to define the compartment(s) of the knee affected by OA as: no OA, isolated/predominant PF OA, and isolated/predominant TF OA. In knees with mixed OA, knees with more severe PF OA were included in the isolated/predominant PF group (the same was done for TF OA). We determined the sensitivity (Sn), specificity (Sp), positive and negative predictive values (PPV and NPV), and positive likelihood ratio (LR+) for each test and measure individually, and the combination of these measures, in identifying knees with PF OA from knees with TFJ OA or no OA.

Results: 745 knees were included in the study. No measure had high Sn and Sp. Pain with stairs had the greatest Sn (90%) but poor Sp (15%). The combination of definite crepitus with no pain on walking had the greatest Sp (96%), PPV (53%) and LR+ (1.8) but poor Sn (7%).

Conclusions: Typical clinical examination findings and knee pain patterns commonly thought to represent underlying PF pathology do not discriminate knees with PF OA from knees without OA or TF OA.

Significance and Innovation

- In order to maximize targeted/individualized care and recruit for trials, clinicians/researchers need to be able to discriminate between knees with patellofemoral and tibiofemoral osteoarthritis
- No diagnostic test assessed had a high sensitivity and specificity in discriminating isolated/predominant patellofemoral joint osteoarthritis from those with isolated/predominant tibiofemoral joint osteoarthritis/no osteoarthritis
- Pain with stairs had the greatest sensitivity (90%) but poor specificity (15%)

Knee osteoarthritis (OA) can affect the patellofemoral joint (PFJ) and/or the tibiofemoral joint (TFJ). Contrary to common belief, the PFJ may be a more common site of OA (1, 2) and source of symptoms (3, 4) than OA in the TFJ. PFJ OA also predicts the incidence of TFJ OA (5, 6). Despite this, there is limited evidence for rehabilitation approaches (e.g., bracing, taping, foot orthoses, strengthening, etc.) to decrease pain and improve function in those with PFJ OA. Biomechanical and rehabilitation treatments for PFJ and TFJ OA likely differ. Thus, it would be helpful to discriminate individuals with PFJ OA from those with TFJ OA from clinical examination findings and clinically important pain patterns. Further, to enroll individuals in clinical trials, and avoid the cost of using imaging to screen potential participants, a simple method is needed to discriminate those with PFJ OA from those with TFJ OA.

Anterior knee pain (AKP) and pain ascending and descending stairs are widely believed to be indicative of PFJ pathology. However, we previously reported that these self-reported pain measures have poor diagnostic utility to identify MRI-defined PFJ OA in a large cohort study of older individuals (7). It is possible that the combination of objective clinical examination measures in addition to location of pain and pain with activities will improve the ability to discriminate individuals with PFJ OA from those with TFJ OA. Crepitus (i.e., an audible cracking or grinding with movement of a joint) is associated with MRI features of OA in the PFJ but not the TFJ (8, 9). Additionally, a PFJ compression/glide test may be indicative PFJ pathology.

While there is an increasing body of evidence on the relevance to symptoms of MRI-detected lesions of cartilage and bone in the PFJ (10), abnormalities detected by this imaging modality are common in asymptomatic older adults (11). Plain radiographs are less sensitive but evidence of radiographic PFJ OA is associated with knee pain and functional limitations (3), and remains the more common imaging procedure in routine clinical practice. It is important to know if common tests and measures thought to be related to PFJ OA can be used as diagnostic tests to identify individuals with radiographic PFJ OA.

The purpose of the current study was to test a comprehensive set of diagnostic tests and measures to discriminate patellofemoral (PF) from tibiofemoral (TF) osteoarthritis (OA) and see if, in doing so, we could improve upon a previous study (7) which used MRI diagnosis and a more limited set of diagnostic tests.

Patients and Methods

The Clinical Assessment of the Knee (CAS-K) Study is a large prospective study of knee pain in the general population in North Staffordshire, United Kingdom (12) . Baseline data was collected from 2002-2003 and all participants were 50 years and over with knee pain. Potential participants were recruited by postal survey and those reporting pain around the knee in the past 12 months were invited to participate in the study. The study protocol was approved by the North Staffordshire Local Research Ethics Committee (project number 1430). Details of the study have been previously published (12).

Clinical Tests and Measures

Details of the methods for clinical tests and measures used in the current study have been described in detail previously (13). Briefly, three research physical therapists based at an academic center for primary care research with 7, 9, and 10 years of experience performed all measures. They were trained in the standardized physical examination with a manual for reference with detailed protocols. Feedback was given during training from two specialist musculoskeletal clinicians. Inter-reader reliability (kappa value) was 0.53 and 0.54 for crepitus and PFJ compression respectively. Coarse crepitus was assessed with the participants positioned sitting on the edge of an adjustable table so the participants' knees were flexed to 90º with both feet on the floor. With the hand over the PFJ, participants were instructed to stand up slowly, putting weight evenly through both legs. The examiner palpated for coarse crepitus under the patella as they rose and then sat back down. Crepitus was graded as none, possible, or definite. A PFJ glide/compression test was performed with participants positioned half-lying on a table with a pillow behind both knees. The examiner gently applied compression to their PFJ, ensuring no mediolateral or caudad/cephalad movement of the patella. Subjects were asked if the maneuver was painful. If there was no pain, compression was applied with a glide of the patella inferiorly as far as it would go, releasing the compressive force once the patella returned to its resting position. The subject was then asked again if the maneuver was painful. Pain was recorded as: none, pain with glide, or pain with compression.

Assessment of Knee Pain

Knee pain map: A knee pain map was used by participants to identify painful areas around the knee (14). Participants were asked to indicate on their own knees ‘‘where your knee hurts.’’ Painful areas indicated by participants were shaded by an assessor on a pre-drawn manikin. A transparent template, with the boundaries

for all 13 sites marked on it, was laid over the completed manikins. Any shading in a site was recorded as 'present'. AKP was considered to be present if pain was present in the prepatellar or infrapatellar regions.

Knee pain with activities: Participants reported pain with ascending or descending stairs and walking on level ground (its absence might rule in PFJ pathology) using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Pain was rated as none, mild, moderate, severe, or extreme.

Radiographic Assessment of Knee OA

Radiographs were obtained and read of the most painful knee. If both knees were painful, one knee was selected at random. Three views of the knee were obtained for each subject: weight-bearing semi-flexed postero-anterior (PA), supine skyline, and lateral views. A Kellgren and Lawrence (KL) score was assigned to the PA and skyline views. TFJ OA was defined by a KL score ≥2 on the PA view and/or the presence of definite osteophytes on the posterior tibial surface of the lateral view. PFJ OA was defined by a KL score ≥2 on the skyline view and/or the presence of a definite superior and/or inferior osteophyte on the patellar surface of the lateral view using a standard atlas (1). Inter-observer reliability for KL scores and osteophytes for the PFJ and TFJ ranged from 0.49-0.76 (unweighted kappa) (1). We categorized knees into having no OA, isolated PFJ OA, isolated TFJ OA, and mixed PFJ/TFJ OA. In knees with mixed PFJ/TFJ OA, we then determined which compartment had the greatest OA severity. Knees with more severe PFJ OA were considered to have isolated/predominant PFJ OA (the same was done for isolated/predominant TFJ OA). If the severity of OA was the same in the PFJ and TFJ, these knees were removed from the study.

Statistical Analysis

We determined the sensitivity (Sn), specificity (Sp), positive and negative predictive values (PPV and NPV), and positive likelihood ratio (LR+; Sn/1-Sp) for PFJ compression test, PFJ crepitus, AKP, pain with stairs (≥ mild), absence of pain with walking (≤ mild), and the combination of these measures in discriminating knees with isolated/predominant PFJ OA from knees with isolated/predominant TFJ OA or no OA. In sensitivity analyses we used a KL score ≥3 (moderate OA) to define PFJ and TFJ OA. We additionally performed analyses removing all knees with mixed OA using both a KL score ≥2 and ≥3 as our OA definitions.

We compared knees with isolated PFJ OA to those with no OA, and compared knees with isolated PFJ OA to those with isolated TFJ OA.

Results

745 knees (one knee per person) were included in the study. The mean (sd) age was 65.2 (8.6) and mean BMI was 29.6 (5.2); 55% were female (Table 1). The prevalence of no OA, isolated PFJ OA, isolated TFJ OA, and mixed was 236 (32%), 178 (24%), 30 (4%) and 301 (40%), respectively. Of 301 knees with mixed OA, 57 and 115 had more severe PFJ and TFJ OA, respectively; 129 had the same severity and were removed from our primary analysis. This left 616 knees eligible for our primary analysis; 381 with no OA or isolated/predominant TFJ OA and 235 with isolated/predominant PFJ OA. Those in the isolated/predominant PFJ OA group were slightly older with higher BMIs and were more likely to be male (Table 1).

The most common diagnostic test measures were pain with stairs (492/566; 87%) and presence of AKP (414/574; 72%) (Table 2); the least common was isolated AKP (48/574; 8%). No measure had high Sn and Sp (Table 2). Pain with stairs had the greatest Sn (90%) but poor Sp (15%). The combination of definite crepitus with no pain with walking had the greatest Sp (96%), PPV (53%) and LR+ (1.8) but poor Sn (7%). No test or combination of test had a LR+ greater than 2.

Using the moderate definition of OA, the prevalence of no OA, isolated PFJ OA, isolated TFJ OA, and mixed was 453 (61%), 99 (13%), 123 (17%) and 70 (9%), respectively. All 70 knees with mixed OA had the same severity in the PFJ and TFJ and were removed from the analysis. This left 675 knees eligible for the sensitivity analysis; 576 with no OA or isolated TFJ OA, and 99 with isolated PFJ OA. When using a moderate definition of OA, no measure had high Sn and Sp (Table 3). In general, Sn and Sp remained unchanged, while PPV decreased and NPV increased compared to results when using a mild OA definition. The combination of definite crepitus with AKP, pain with stairs, and no pain with walking all had LR+ greater than 2. Results comparing knees with isolated PFJ OA to those with no OA and comparing knees with isolated PFJ OA to those with isolated TFJ OA are presented in supplemental tables 1-4. We see a similar pattern in these results as in our main analyses with no test having a high Sn and SP, and in general test combinations that include crepitus

having the greatest LR+. The exception to this was in the comparison of isolated moderate PFJ OA to isolated moderate TFJ OA, pain with compression + no pain with walking had the greatest LR+ (2.8).

Discussion

In order to recruit individuals for clinical trials and to prescribe the most effective interventions for individuals with PFJ or TFJ OA, clinicians and researchers need to be able to discriminate between these two phenotypes of knee OA. We found that among persons aged over 50 years with knee pain, typical clinical examination findings and knee pain patterns (pain location and with activities) that are commonly thought to represent underlying PFJ pathology do not discriminate knees with PFJ OA from TFJ OA/no OA. The results of the current study are consistent with our previous studies in the MOST cohort using MRI criteria for knee OA and pain location and with activities (7) and with Peat et al. (15). Using radiography with both a lateral and skyline view to diagnose PFJ OA (1), and also adding objective measures from a clinical examination, we found no test with a LR+ greater than 2. It was hypothesized that adding objective measures from the clinical examination may improve our ability to discriminate those with PFJ OA from those with TFJ OA/no OA. However, when using moderate severity as an OA definition, definite crepitus combined with AKP, pain with stairs, and no pain with walking all had LR+ greater than 2. Similar results were also seen when removing knees with mixed OA (supplemental tables). However, we would caution the interpretation of these results, as they do not replicate what is typically seen in a clinical or research recruitment setting. In these settings, we cannot exclude these individuals; and, we need to be able to identify those with primary PFJ OA from all those with knee pain that may or may not have TFJ involvement.

Contrary to our findings, others have found a relationship between crepitus and PFJ MRI features of OA. Schiphof et al. found among females without OA, using a proposed MRI definition, that the presence of crepitus was associated with cartilage damage (odds ratio (OR): 5.5 (95% confidence interval (CI) 3.8-7.9), osteophytes (OR: 2.6 (2.0-3.4), cysts (OR: 2.8 (2.0-4.0), and bone marrow lesions (OR: 3.7 (2.7-5.0) in the PFJ (9). They also found a relation between a history of patellar pain and all the above features except osteophytes. No relation was found between crepitus and patellar pain with these features in the TFJ. The post-test probabilities of crepitus, patellar pain and the combination of the two were 64.3, 54.7 and 71.8%, respectively.

However, Crema et al. found a relationship between crepitus and osteophytes in both the PFJ and TFJ (8). While these previous studies report an association between crepitus and PFJ OA, we found crepitus to have low sensitivity (24%), and high specificity (82%). This highlights the need to be cautious in using crepitus as a diagnostic indicator of mild PFJ OA, despite high odds ratios for the association between crepitus and PFJ OA features on MRI. However, using a moderate definition of OA, the greatest positive likelihood ratios were found when crepitus was combined with anterior knee pain, pain with stairs, and no pain with walking. Consistent with our results, Schiphof et al. also found no relation between a patellar compression test and PFJ OA features on MRI.

Our findings highlight the need for improved understanding of knee pain pathophysiology and ways to appropriately target compartment-specific biomechanical or rehabilitation interventions in OA. When recruiting participants for clinical trials for PFJ OA, researchers need to be cautious in the tests and measures that are used for recruitment strategies. Based on the results of the current study, definite crepitus combined with no pain with walking has the lowest false positive rate (4%; Sp=96%). Using this combination will most likely yield participants that actually have PFJ OA. Further research is needed to determine the best recruitment strategies for PFJ trials. It is recommended that investigators who recruit subjects with PFJ OA publish detailed information on their recruitment strategies and the % yield (e.g., those that met inclusion criteria that actually had PFJ OA).

We recognize limitations to our current study. While lateral and skyline radiographs identify the most cases of PFJ OA (1), it may not detect early OA changes seen on MRI. Despite this, we find similar results to a previous study using MRI criteria to define PFJ and TFJ OA. Additionally, MRI may be too sensitive and the clinical significance of early MRI lesions is unknown. Also, evidence of changes on imaging may represent historic joint damage, which may no longer be relevant to symptoms, and this remains a challenge for diagnostic studies in OA. We recognize pain is a subjective experience that varies greatly between individuals and is influenced by psychosocial factors for which we did not account. However, in performing analyses evaluating diagnostic tests, we hoped to replicate how simple tests may be used by clinicians in order to

diagnose PFJ OA. We do recognize that the reliability of clinical exam measures may influence our results as misclassification of exam measures may occur (13).

In summary, typical clinical exam findings and knee pain patterns commonly thought to represent underlying PF pathology do not discriminate knees with PF OA from knees without OA or TF OA. Clinicians and researchers should be cautious using these clinical tests and measures to identify individuals with PFJ OA, both in an everyday clinical setting or in a research setting when defining PFJ OA.

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Table 1. Baseline characteristics

	All knees (n=745)	Isolated/predominant PFJ OA (n=235)	Isolated/predominant TFJ OA and no OA (n=381)
Mean Age, years	65.2 (8.6)	65.9 (8.8)	64.3 (8.5)
Sex (% female)	55	48.9	59.1
Mean BMI, kg/m^2	29.6 (5.2)	29.6 (4.7)	29.1 (5.1)

Table 2. Diagnostic utility of clinical examination measures, location of pain and pain with activities to identify knees with isolated/predominant mild PFJ OA (compared to knees with no OA and isolated/predominant mild TFJ OA)

	Prevalence*	Sensitivity	Specificity	PPV	NPV	LR+
Clinical Exam Measures						
Definite crepitus	123/616 (20%)	24%	82%	46%	64%	1.3
Pain with PFJ compression	308/615 (50%)	56%	53%	43%	66%	1.2
Knee Pain Location						
AKP	414/574 (72%)	74%	29%	39%	64%	1.0
Isolated AKP	48/574 (8%)	10%	92%	44%	62%	1.3
Pain with Activities						
Pain with stairs	492/566 (87%)	90%	15%	40%	70%	1.1
No pain with walking	168/571 (29%)	26%	69%	35%	60%	0.8
Combined Measures						
Definite crepitus + AKP	94/574 (16%)	20%	86%	46%	63%	1.4
Pain with PFJ compression + AKP	219/574 (38%)	43%	65%	43%	65%	1.2
Definite crepitus + pain with stairs	105/566 (19%)	23%	84%	48%	63%	1.4
Pain with PFJ compression + pain with stairs	261/565 (46%)	52%	58%	44%	65%	1.2
Definite crepitus + no pain with walking	30/571 (5%)	7%	96%	53%	62%	1.8
Pain with PFJ compression + no pain with walking	50/570 (9%)	10%	92%	42%	62%	1.3
AKP + pain with stairs	339/528 (64%)	67%	38%	40%	65%	1.1
AKP + no pain with walking	105/534 (20%)	20%	81%	39%	62%	1.1

*Denominators vary based on missing data for clinical exam and pain measures

Table 3. Diagnostic utility of clinical examination measures, location of pain and pain with activities to identify knees with isolated moderate PFJ OA (compared to knees with no OA and isolated moderate TJF OA)

	Prevalence*	Sensitivity	Specificity	PPV	NPV	LR+
Clinical Exam Measures						
Definite crepitus	132/675 (20%)	33%	83%	25%	88%	1.9
Pain with PFJ compression	336/674 (50%)	70%	54%	21%	91%	1.5
Knee Pain Location						
AKP	455/630 (72%)	77%	29%	16%	87%	1.1
Isolated AKP	55/630 (9%)	6%	91%	11%	84%	0.7
Pain with Activities						
Pain with stairs	542/622 (87%)	92%	14%	16%	91%	1.1
No pain with walking	186/627 (30%)	24%	69%	12%	84%	0.8
Combined Measures						
Definite crepitus + AKP	99/630 (16%)	28%	87%	27%	87%	2.2
Pain with PFJ compression + AKP	239/630 (38%)	53%	65%	21%	88%	1.5
Definite crepitus + pain with stairs	112/622 (18%)	34%	85%	28%	88%	2.3
Pain with PFJ compression + pain with stairs	286/621 (46%)	67%	58%	21%	91%	1.6
Definite crepitus + no pain with walking	34/627 (5%)	10%	95%	26%	86%	2.0
Pain with PFJ compression + no pain with walking	57/626 (9%)	11%	91%	18%	85%	1.2
AKP + pain with stairs	377/583 (64%)	72%	37%	17%	88%	1.1
AKP + no pain with walking	118/589 (20%)	20%	80%	15%	85%	1.0

*Denominators vary based on missing data for clinical exam and pain measures