Title
Individual magnetic resonance imaging and radiographic features of knee osteoarthritis in subjects with unilateral knee pain: The Health, Aging, and Body Composition Study

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Individual MRI and radiographic features of knee OA in subjects with unilateral knee pain: Health ABC study

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Abstract

Strong associations between radiographic features of knee OA and pain have been demonstrated in persons with unilateral knee symptoms. Our objectives were to compare radiographic with MRI features of knee OA and assess the discrimination between painful and non-painful knees in persons with unilateral symptoms.

283 individuals with unilateral knee pain aged 71 to 80 years from Health ABC, a study of weight-related diseases and mobility, had bilateral knee radiographs, read for KL grade and individual radiographic features, and 1.5T MRIs, read using WORMS. The association of structural features with pain was assessed using a within-person case/control design and conditional logistic regression. Receiver operator characteristics (ROC) were then used to test the discriminatory performance of structural features.

In conditional logistic analyses, knee pain was significantly associated with both radiographic (any JSN grade >=1: OR 3.20 (1.79 – 5.71) and MRI (any cartilage defect:>=2: OR 3.67 (1.49 – 9.04)) features. However, most subjects had MR detected osteophytes, cartilage and bone marrow lesions in both knees and no individual structural feature discriminated well between painful and non-painful knees using ROC. The best performing MRI feature (synovitis/effusion) was not significantly more informative than KL grade >=2 (p=0.42).

In persons with unilateral knee pain, MR and radiographic features were associated with knee pain confirming an important role in the etiology of pain. However, no single MRI or radiographic finding performed well in discriminating painful from non-painful knees. Further work is needed to examine how structural and non-structural factors influence knee pain.

Introduction

Knee osteoarthritis (OA) poses a significant global health burden, ranked 6th among all conditions by the WHO as a cause of moderate and severe disability [1]. Pain is the principal symptom but our understanding of the mechanisms involved in pain is incomplete. While there are well established reproducible methods for grading radiographic structural features in OA [2,3], associations in epidemiological studies between structural features using these methods and symptoms have been modest [4,5]. Even in studies reporting significant associations between structure and symptoms, 51% of those with knee pain for more than one year did not have radiographic knee OA [6]. Equally important, up to 50% of patients with radiographic changes of OA have no symptoms. This suggests that radiographic features of OA have a very limited ability to discriminate between painful and non-painful knees in the general population.

Possible reasons for the modest associations and poor discrimination include: the insensitivity of radiographyto detect structural features of OA; and uncontrolled differences in pain susceptibility and other person level determinants of OA symptoms that confound and obscure structure – pain relationships[7].

Two recent developments address these limitations. MR imaging (MRI) of the knee has enabled the measurement of structural features in three dimensions with direct assessment of cartilage damage and other structural features of OA not seen on radiographs that may cause pain, including effusions, synovitis and edema in subchondral bone [8]. Secondly, to control for person-level confounders, a recent study used examined subjects with unilateral knee pain and performing a within-person matched comparison of structural features of OA between the knee with, and the knee without, pain [9]. In this study, radiographic structural features of OA such as the Kellgren and Lawrence (KL) grade, and the maximum joint space narrowing (JSN) score were very strongly associated with the presence of pain in one knee but not the other, with OR for pain of 9.0 for K-L grade 3 vs. K-L grade 0 knees, for example. Still, in this study half of the subjects had the same K-L grade in the symptomatic and control knees and 31% had a K-L grade of 0 in both knees.

In this study our objectives were to confirm in another cohort the strong association of x-ray findings of OA in a between knee comparison of subjects with unilateral knee pain, to extend this analysis to MRI findings of knee OA, and finally to examine, and compare, the ability of MRI and x-ray findings using marginal models and ROC analysis to discriminate between painful and non-painful knees in all subjects with unilateral pain.

Methods

STUDY POPULATION

The study sample was drawn from the Health, Aging and Body Composition (Health ABC) Study, a prospective cohort study of the effects of weight-related diseases on mobility. The study recruited 3075 black and white men and women aged 70–79 years between April 1997 to June 1998 from the white Medicare beneficiaries and all age-eligible community-dwelling black residents in designated ZIP codes surrounding two field sites, University of Pittsburgh, Pennsylvania and University of Tennessee, Memphis, Tennessee.

Subjects were eligible for Health ABC if they reported no difficulty walking mile, climbing 10 steps, performing basic activities of daily living, no use of special equipment for ambulation, no history of cancer in previous three years and no plan to move from the area for three years. Clinical examination and interview data were collected at baseline then annually.

At the year two clinic visit participants with knee pain underwent bilateral radiographic and MRI examinations of the knee. Side-specific knee symptoms were assessed using questions about whether the participant had "pain, aching or stiffness on most days" for at least one month in the past 12 months. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scale was also administered, asking about knee pain during various activities in the past 30 days (15). Each knee was categorized as having significant symptoms, defined as a report of any of the following in that knee: moderate, severe, or extreme (2, 3, or 4) pain during the last 30 days when walking on flat surface, going up or down stairs, at night in bed, standing upright, getting in/out of chair or getting in/out of car; knee pain lasting 1 month in the past 12 months; or knee pain for most days in the past month. Hereafter, we use the term 'knee pain' to refer to knees with significant symptoms as defined here, and 'no knee pain' to refer to knees without significant symptoms. Bilateral knee imaging was obtained in participants with significant symptoms in at least one knee.

IMAGE ACQUISITION

Weight-bearing PA fixed flexion radiographs were obtained of both knees using a positioning frame (Syna-Flexer; Synarc, San Francisco, CA) in order to fix knee flexion between 20° and 30° and external rotation of the feet at 10° [10,11]. Standing skyline views were also obtained of both knees with an angle of flexion of 30 to 40 degrees [12].

The following MRI sequences were performed on both knees using a Signa 1.5T MRI system with a standard unilateral, commercial circumferential knee coil: coronal (T2-weighted fast spin-echo (FSE) (TR 3,500 msec, TE 60 msec) with a slice thickness of 4 mm, a 0.5-mm interslice gap, 2 excitation, FOV 14 cm, and a matrix of 256×256 pixels), sagittal (T2-weighted FSE, including the entire synovial cavity with frequency-selective fat suppression (TR 4,127 msec, TE 60 msec), a 0.5-mm interslice gap, 2 excitation, with the same FOV and matrix), and axial images were obtained and axial (T2-weighted FSE (TR 2,500 msec, TE 60 msec) with a 1-mm interslice gap, 1 excitation, FOV 12 cm, and a matrix of 256×256 pixels.

IMAGE READING

Radiograph films were read by one of two expert readers for K-L grade and individual radiographic features (joint space narrowing (JSN), osteophytes, subchondral attrition, cysts and sclerosis) were scored using the Osteoarthritis Research Society International atlas in the medial and lateral compartment of the tibio-femoral joint and the patello-femoral joint [13] from the PA and skyline projections respectively. The weighted kappas for inter-rater

reliability of ordinal scores were 0.87 for KL grade and 0.75 for osteophytes and 0.90 for JSN.

The MRIs of the knee were read blinded to radiographic scoring by one of 5 trained radiologists using the semi-quantitative whole-organ MRI scoring (WORMS) method of Peterfy et al.[14]. Specifically, 14 sub-regions (anterior, central, and posterior of the medial/ lateral femoral condyles/tibial plateaus and medial/lateral sub-regions of the patella) were each scored separately for cartilage lesion, osteophytes, sub-articular bone marrow lesions (BML), bone cysts and bone attrition. The tibial sub-spinous sub-region, the site of cruciate ligament insertion, was scored for BML and cysts. As these were non-contrast images, synovial thickening and effusion were scored together as 'synovitis/effusion'.

Cartilage lesions were scored 0–6 for severity. As a grade 1 cartilage lesion (signal abnormality) did not reflect a morphological change it was grouped with grade 0 for analysis. Osteophytes were scored 0 – 7 for size; as grade 1 osteophtyes were those considered equivocal, we grouped it with grade 0. BMLs and subchondral cysts were each scored on 0 – 3 scales for lesion size and subchondral bone attrition on a 0–3 scale for severity. Synovitis/effusion scores were grade 0=normal, 1= <33%, 2=33–66% and 3=>66% of the maximum potential distension. Choosing thresholds for lesion scores based on clinical judgment, we categorized each sub-region as normal vs. having any abnormality (lesion present) for each feature and we further classified each sub-region as having a severe abnormality present vs. normal or mild-moderate abnormality present (See Table 1 for cut points used) [15].

Inter-reader reliability in 29 knees for both compartment-specific and total knee scores for all individual MRI features was good, with intra-class correlation coefficients for cartilage damage of 0.71–0.93, 0.84–0.92 for osteophytes, 0.46–0.81 for bone marrow lesions, 0.54 – 0.77 for bone attrition, and 0.45–0.82 for subchondral bone cysts.

DATA ANALYSIS

Consistent with previously used approaches for summarizing or combining WORMS scores of a given feature over different subregions of a knee [16–18], [1920,21], [21,22] we used the highest score for each feature in any of its constituent sub-regions as the score for a compartment and in any compartment for the whole knee. Compartments and the whole knee were then categorized as having any abnormality present and as having a severe abnormality based on the thresholds in Table 1[15]. In a sensitivity analysis, we repeated this classification excluding lesions in the patello-femoral compartment. This did not change our basic findings.

These analyses include only subjects who are discordant for pain between their two knees. The standard analysis for within person comparisons between knees in this type of study design is conditional logistic regression modeling, which derives an odds ratio for the association of the presence of structural abnormalities with pain based on the ratio of the number of subjects with the structural feature in the painful knee only to subjects with the structural feature in the painless knee only. A limitation of this analysis is that subjects whose knees are discordant for pain but concordant for structural features, i.e. with a structural feature in both knees or with the feature in neither knee, are treated as "non-informative" and do not affect the OR estimate.

To determine how well individual structural findings discriminate between painful and non-painful knees in all subjects with unilateral pain, we combined all the knees of those who were informative and non-informative for further analysis. We then evaluated the association between the presence of structural findings and pain in this sample by

calculating the marginal odds ratios. Next we determined the ability of the full range of each of the features to discriminate painful from non-painful knees using receiver operator curves (ROC)[23]. We also compared the areas under the curve for different features, focusing the comparison on radiographic vs. MRI features of the same type. To account for clustering of knees within person we used a cluster resampled bootstrap with 1000 replicates to calculate confidence intervals for differences in the area under the curve (AUC) from the ROC and comparisons between AUC for different features [24].

RESULTS

Of the 636 participants in the Health ABC knee OA study with both radiographic and MRI images in both knees, 283 had unilateral knee pain, 263 had bilateral knee pain and 90 had no pain. Compared with the remainder of the cohort, those with unilateral pain were of similar age, body mass index (BMI) and gender (Table 2). As expected, compared with those with unilateral knee pain, there was more radiographic damage in those with bilateral knee pain and less in those with no knee pain. In those with unilateral knee pain, K&L grade 2 findings were present in 50% of the painful knees and 36% of the non-painful knees, while K&L grade 3–4 was present in 44% of painful and 28% of non-painful knees.

Table 3 shows the presence of each imaging finding in pairs of knees with and without pain and the conditional ORs for the association of each structural feature with unilateral knee pain. For nearly all structural findings, both radiographic and MRI, the presence of an abnormality of any severity somewhere in the knee was significantly associated with knee pain, with ORs ranging from 1.5 to 7.3. The presence of severe radiographic and MRI abnormalities in a knee was also strongly associated with unilateral knee pain compared to less severe or no abnormality, with ORs ranging from 1.9 to 5.3 (all $P < 0.05$). The ORs for association with pain were substantially larger for severe abnormalities compared to defining the same abnormality using a lower threshold for several radiographic findings (K&L grades, osteophytes and sclerosis) and for MRI findings of osteophytes and synovitis/effusion. There were too few instances of severe radiographic attrition and cysts for analysis. Radiographic K-L grade and JSN and MRI cartilage lesions, bone marrow lesions and synovitis/effusion all showed a strong dose-response relationship, with increasing severity associated with greater odds of knee pain (Figure 1).

However, a large proportion of subjects with unilateral knee pain were non-informative for the association of structural damage with pain (Table 3); in other words, while discordant for pain their knees were concordant for the specific structural abnormalities. 72% to 88% of subjects were non-informative for radiographic abnormalities and 66% to 90% were non-informative for MRI abnormalities. As expected, uncommon abnormalities were more likely to be non-informative in terms of subjects not having the abnormality in either knee, while abnormalities that were relatively more common were more likely to be non-informative by having the abnormality in both knees.

In marginal logistic models using all knees of subjects with unilateral pain, all ORs for the association of structural features with pain were attenuated compared to the conditional ORs in Table 3. For example, for severe KL grade the marginal OR was 2.01 (95% CI: 1.58–2.56), and for severe synovitis/effusion was 3.25 (95% CI: 2.21–4.78)).

We then tested the ability of different structural features to distinguish painful vs. non-painful knees in all subjects with unilateral knee pain using ROC curves for the full range of scores (Figure 2). The AUC for each structural feature was low, ranging from 0.54 to 0.60. Further, we found no statistically significant differences between the AUCs for radiographic and MR assessments of the equivalent feature (Table 4). We also compared the best

performing radiographic (K-L grade) and MR (synovitis/effusion) features using this method and no significant difference was found (p=0.42).

Discussion

We confirmed previous studies of persons with unilateral knee pain showing that structural features of knee OA assessed by radiograph are strongly associated with pain in a within-person, matched knee analysis that controls for individual differences in non-structural pain determinants[9]. We extended these findings to MRI-detected structural damage using the same study design and found similarly strong and highly significant associations, such that when these features were present in only one of a subject's knees they were substantially more likely to occur in the knee with pain. These results support an important role for structural abnormalities in the etiology of knee pain. However, to put these findings into a clinical context, we found that for the majority of all the subjects with unilateral knee pain the knee pairs were concordant on specific structural findings, either having the finding in both knees or not having the finding in either knee. Further, in ROC analyses of all knees in subjects with unilateral knee pain we found that neither MRI nor radiographic features of knee OA performed well in discriminating between painful vs. non-painful knees and that there were no differences in performance of the two imaging modalities.

The within-person, matched knee analysis of discordant pain has the important advantage of controlling for individual differences in non-structural pain determinants, such as factors influencing pain susceptibility, that may obscure structure-pain relationships[9]. Our results are consistent with those of a recent studyto use this approach for knee pain[9], and confirm its potential for uncovering strong, and possibly causal, associations between pain and structural abnormalities detected with knee imaging. These results support a role of for structural abnormalities in the etiology of knee pain and the continued use of MRI and other advanced imaging modalities.

The findings of studies using the within-person matched-knee design appear to conflict with both clinical experience and with previous epidemiological and clinical studies that suggest widespread discordance between structure and pain [4,5]. However, as correctly noted by Neogi and colleagues[9], the apparent conflict reflects different ways of approaching the structure-pain relationship, with one focused on identifying associations and risk factors and the other concerned with diagnostic discrimination and prediction[23]. Only pairs of knees discordant for both pain and also for a given structural finding are used in evaluating the association of structure and pain by means of the conditional odds ratios in the matched knee analysis.

We found that even for knee pairs discordant for pain yet matched on person-level pain determinants, in the majority of subjects the individual structural features did not differ between the painful and non-painful knee, frequently not present in either knee or present in both knees. This suggest that regardless of asymmetry in symptoms, MRI structural findings tend be symmetrical between an individual's knees, as has been observed for structural findings of hand OA[25,26].

Consistent with the above, in analyses that included both knees of all subjects with unilateral pain, the marginal odds ratios for the association of structural features with pain were smaller than the conditional odds ratios estimated in the matched knee analyses. In order for a structural feature to perform well in classifying knees for the presence of pain, the marginal odds ratios for pain would need to be very large, at least an order of magnitude larger than we observed [23]. This was born out in the ROC analyses of all knees of persons with unilateral pain, where neither MRI nor radiographic features of knee OA performed

well in discriminating between painful vs. non-painful knees, with AUCs that were very modest (all were less than 0.61, which is considered poor discriminative ability[27]). This suggests that while common structural features of OA detectable with knee imaging are etiological factors in knee pain, other factors are also likely to make a substantial contribution to determining which knees are painful, even between one individual's two knees. This emphasizes the importance, from a clinical perspective, of continued investigation into non-structural determinants of knee pain.

We further compared the discriminatory performance of the two imaging modalities in ROC analyses, and found no significant differences in AUCs between analogous MRI and radiographic findings (e.g. JSN vs. cartilage loss, attrition on x-ray vs. MRI, etc). MRI findings were more common in general than radiographic findings, especially when defined as present using a low threshold. However, using similar scoring methods, namely the presence or absence of specific features, the greater sensitivity of MRI appeared to provide little extra information over radiographs in predicting the occurrence of knee pain. For findings with a similar prevalence by the two modalities, conditional ORs were no larger for MRI than for x-ray. There were also no consistent differences between imaging modalities in the proportion of knee pairs that were informative vs. non-informative, with both MRI and radiographic features present in both knees or absent in both knees in over two-thirds of subjects with unilateral pain. Consistent with their higher prevalence, MRI findings were more frequently non-informative by being present in both knees of a pair. Further, we found no differences in ability to discriminate between painful and non-painful knees when we compared the AUCs from ROC analyses of analogous MRI and radiographic findings (e.g. JSN vs. cartilage loss, attrition on x-ray vs. MRI, etc). The best performing MRI feature was synovitis/effusion, which does not have a radiographic equivalent; it performed no better than the KL grade of the knee.

These findings may have implications for the use of MRI to investigate the sources of knee pain in individual patients. The ideal structural feature for predicting the presence of unilateral symptoms would have a high frequency in only the painful knees and a low frequency in only the non-painful knee, but also would infrequently be present in both knees of a discordant pair. MRI may be disadvantaged in this regard by its greater sensitivity compared to radiographs, since features that are very common overall may be more likely to exhibit poor discrimination. A high proportion of subjects also had specific radiographic features in both knees, a finding consistent with other studies of unilateral knee pain[28]. Our findings suggest that to realize the potential value of MRI as both a research and clinical tool, future work needs to determine whether certain anatomic locations or combinations of lesions in cartilage, bone, synovium and meniscus are associated with, and predict, knee symptoms [29,30] and how nonstructural factors modify these relationships.

Our study has several limitations that should be noted. All of our subjects were elderly (ages 71–80) and because of a high prevalence of structural findings of knee OA in the elderly some of our findings may not apply to younger age groups in which these abnormalities are less common. However, we were able to replicate the significant structure-pain associations found by others using the same analytical design in subjects of a younger age [9]. It is also well recognized that the symptoms of knee OA fluctuate [31], and our definition of discordant pain may misclassify subjects who develop bilateral pain with further follow-up. Ways of defining unilateral knee pain over several years may produce different results and should be examined in future studies. We used a definition of pain from anywhere in the knee. It is not known if more refined classification of pain in terms of severity, anatomical location of symptoms and/or signs or features of neuropathic pain would improve the correspondence between structural abnormalities and pain. The presence of severe pain in one knee may suppress the experience of lesser pain in the other knee. However, severe knee pain may also

increase pain in the contralateral knee through an increase loading to spare the painful knee or via sensitization of the other knee to be painful with a less noxious stimulus. In addition the MRIs of a subject's two knees may have been assessed by different readers, while a subject's x-ray of both knees was always assessed by the same reader and inter-reader variation in MRI readings may have reduced the strength of associations between MRI features and unilateral knee pain compared to radiographic features. Finally we used classified structural features of OA separately for each feature using the highest grade of damage, we propose that methods of analysis of structural features that take into account combinations of features/sub regions affected may provide better discrimination/prediction and should be explored when analyzing the structural information of the knee.

SUMMARY

In conclusion, among elderly subjects with unilateral knee pain, an individual imaging (MRI or radiographic) feature of OA was infrequently found in just one of a subject's knees, but when this occurred the feature was significantly more likely to be found in the painful than in the non-painful knee, suggesting that in some individuals these findings play an important role in the etiology of knee pain. At the same time, in the majority of subjects with unilateral knee pain the presence of individual radiographic and MRI features of OA did not differ between a subject's two knees, and as a result the two modalities had an equivalent, but poor, ability to discriminate between painful and non-painful knees among all persons with unilateral pain. Further work is required to explore whether new approaches to utilizing information on structural findings of OA from knee imaging better predict knee pain, as well as to identify the important non-structural determinants of knee pain.

Acknowledgments

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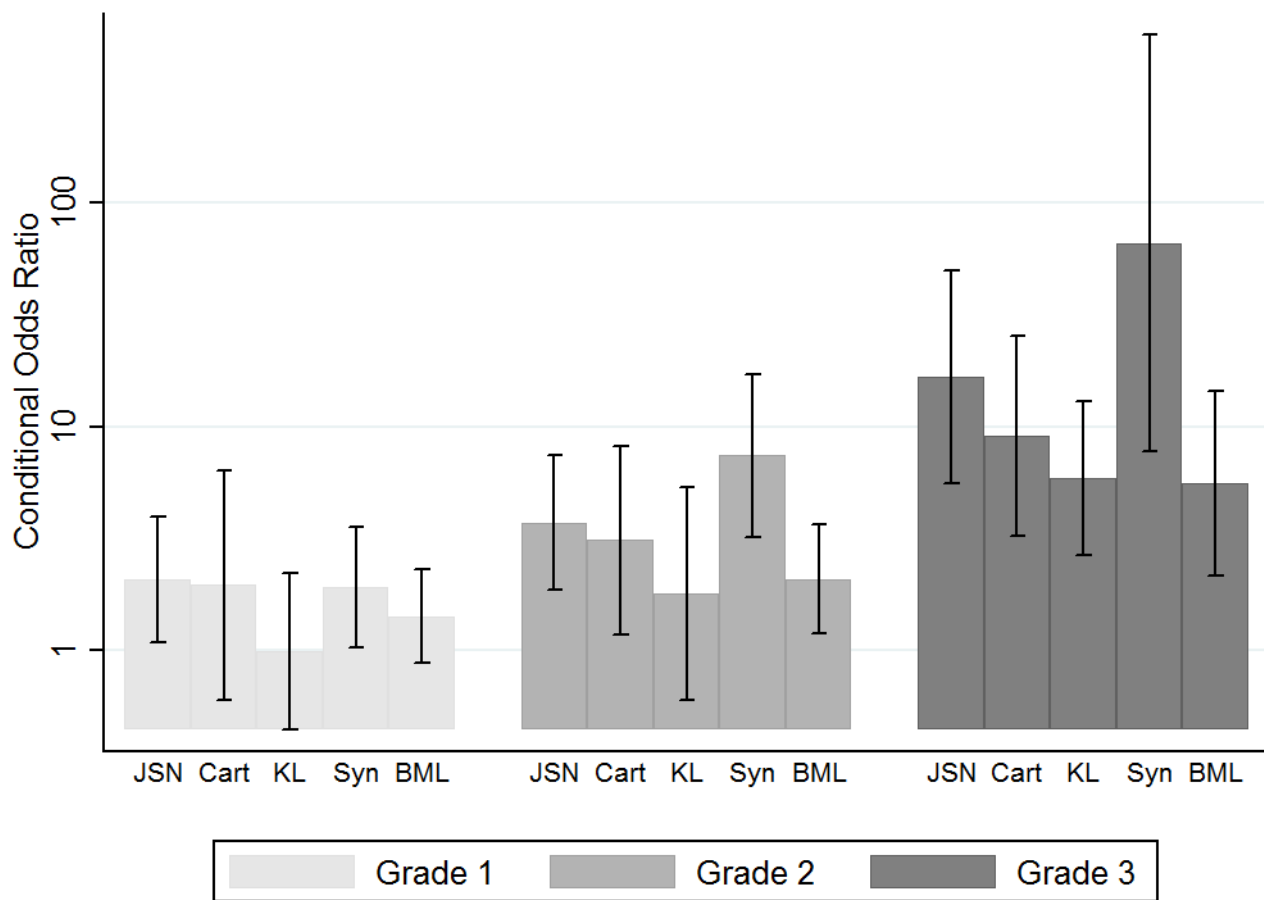
Figure 1. Conditional OR (95% CI) for association of grade of structural damage with the painful knee in subjects with unilateral knee pain
For all ORs, the referent category is a score of 0 for the feature. JSN= Radiographic OARSI grade of Joint Space Narrowing; CART = MRI WORMS grade of cartilage lesion (referent = grade 0/1; 1= grade 2; 2= grade 3/4; 3= grade 5/6); KL = Radiographic Kellgren and Lawrence grade (1=1; 2=2; 3=3/4); SYN= MRI WORMS synovitis/effusion grade BML= MRI WORMS Bone marrow lesion.
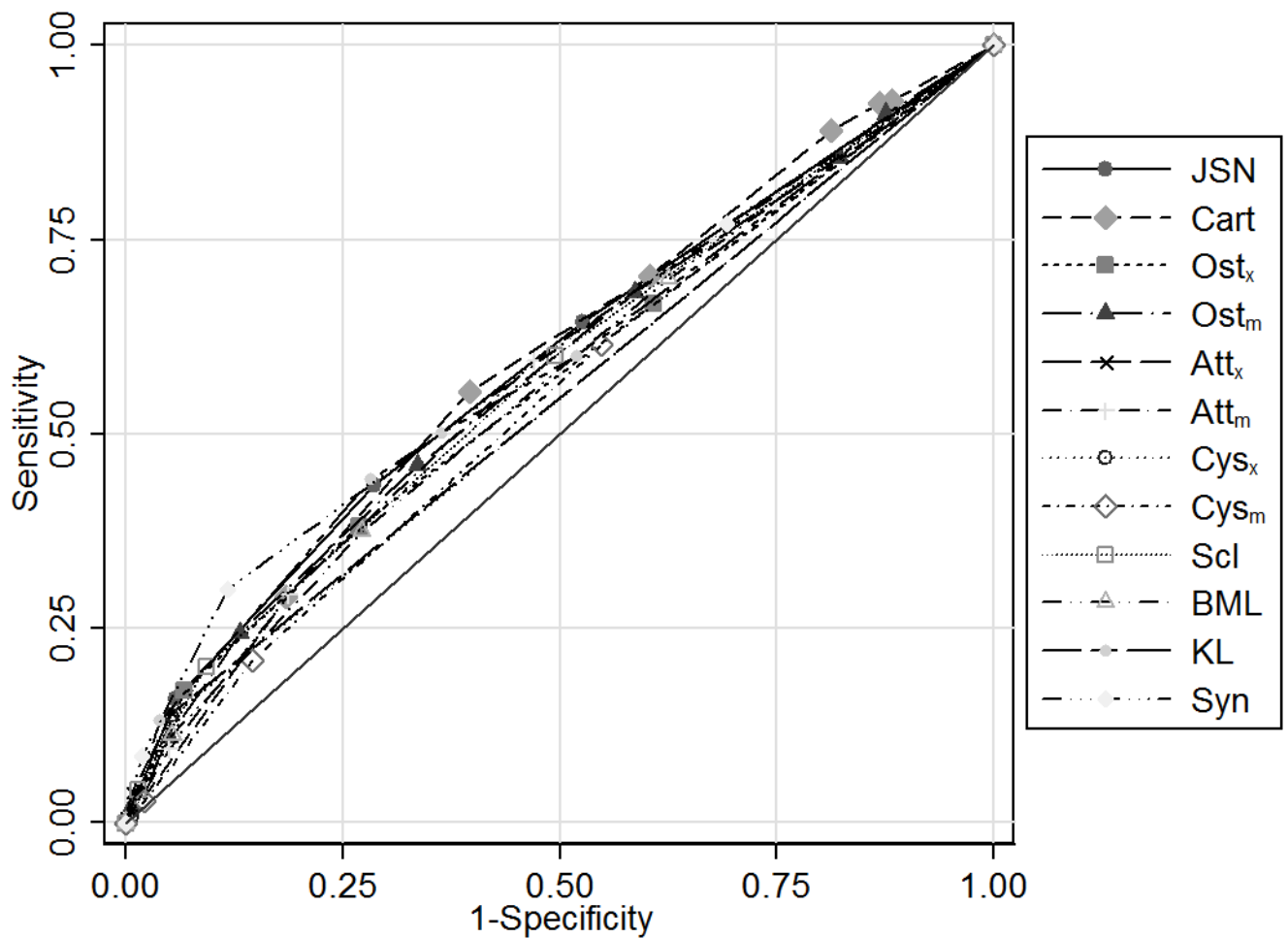
Figure 2. ROC curves for radiographic and MR based measurements of structural features of OA to predict knee pain in patients with unilateral knee pain
With Area under the curve: JSN: joint space narrowing (0.59); Cart: cartilage lesion (0.59); Ost_x: radiographic osteophyte (0.57); Ost_m: MR osteophyte (0.58); Att_x: radiographic attrition (0.54); Att_m: MR attrition (0.58); Cys_x: radiographic cyst (0.54); Cys_m: MR subchondral cyst (0.55); Scl: radiographic sclerosis (0.58); KL: Kellgren and Lawrence grade (0.58); BML: MR bone marrow lesion (0.56); Syn: synovitis (0.60).

Table 1

Thresholds used in defining the presence of any abnormality and severe abnormality in any compartment of the knee for radiographic and MRI derived measures of structural damage

Pathologic features	Scale range	Any Abnormality	Severe Abnormality
Radiographic:			
Joint space narrowing	0–3	1	2
Osteophytes	0–3	1	2
Sclerosis	0–3	1	2
Attrition	0–3	1	2
Cysts	0–3	1	2
KL grade	0–3	1	3
MRI:			
Cartilage damage (CRT)	0–6	2[1]	5[1]
Osteophytes (OST)	0–7	2[2]	4[2]
BMLs	0–3	1[3]	2[3]
Cysts	0–3	1[3]	2[3]
Attrition	0–3	1[4]	2[4]
Synovitis/effusion	0–3	1[5]	2[5]

[1] Abnormal: any partial thickness or full thickness defect. Severe: full thickness defect > 1cm maximum width.

[2] Abnormal: a small horizontal or curved spur. Severe: large horizontal spur or moderate size curved spur.

[3] Abnormal: presence of one or more lesions of any size. Severe: lesions occupy 25% of a sub-region.

[4] Abnormal: Mild or worse deviation from expected bony contour. Severe: moderate or worse deviation.

[5] Abnormal: any distension of joint capsule. Severe: 33% of the maximum potential distension.

Table 2

Description of study participants

Participant and knee characteristics	Full cohort (n=636)	Participants with discordant knee pain (n=283)	Participants without discordant knee pain† (n=353)	p-value
Age (years), median (IQR)	73 (71,76)	73 (71,76)	73 (71,76)	0.787
BMI (kg/m²), mean (SD)	28.1 (4.6)	28.0 (4.4)	28.2 (4.7)	0.318
Sex				
Female, %	64.5%	60.4%	67.7%	0.057
Male, %	35.5%	39.6%	32.3%	
Race, % white	53.1%	56.5%	50.4%	0.125
Painful knee				
Left, % painful	64.3%	51.6%	74.5%	<0.0005
Right, % painful	62.9%	48.4%	74.5%	<0.0005
KL grade				
Non-painful knee †	n=373		n=90	
0, %	53.1%	48.1%	68.9%	
1, %	15.6%	15.5%	15.5%	
2, %	8.0%	8.1%	7.8%	0.001
3, %	20.1%	24.4%	6.7%	
4, %	3.2%	3.9%	1.1%	
Painful knee †	n=546		n=263	
0, %	36.3%	39.9%	32.3%	
1, %	11.5%	9.9%	13.3%	
2, %	6.4%	6.0%	6.9%	0.379
3, %	31.7%	31.1%	32.3%	
4, %	14.1%	13.1%	15.2%	

†Participants not used in the analysis comprise of 263 with bilateral knee pain and 90 with no pain. For participants with bilateral knee pain, the highest KL grade was used.

‡Participants used in the analysis are tested against those not used, using the 2-tail t-test for continuous normal data, the Wilcoxon rank-sum test for continuous non-normal data and the chi-square test for categorical data.

Table 3

Presence of at least one radiographic or MRI any and severe structural lesion within the whole knee in 283 participants with unilateral knee pain

Feature	Imaging	Severity of grade[1]	Occurrence of structural findings									Odds ratios from Conditional logistic model		
			Any knee[2]	Neither knee		Knee without pain only		Knee with pain only		Both knees		OR	95% CI	p
				n	(%)	n	(%)	n	(%)	n	(%)			
KL grade	X-ray	Any	56.0%	99	(35.0%)	14	(5.0 %)	37	(13.1%)	133	(47.0%)	2.64	1.43,4.89	<0.001
		Severe	36.2%	147	(51.9%)	11	(3.9%)	56	(19.8%)	69	(24.4%)	5.09	2.67, 9.71	<0.001
JSN	X-ray	Any	58.5%	86	(30.4%)	15	(5.3%)	48	(17.0%)	134	(47.3%)	3.20	1.79,5.71	<0.001
		Severe	47.5%	141	(49.8%)	19	(6.7%)	61	(21.6%)	62	(21.9%)	3.21	1.92,5.37	<0.001
Cartilage	MR	Any	89.8%	15	(5.3%)	6	(2.1%)	22	(7.8%)	240	(84.8%)	3.67	1.49,9.04	0.005
		Severe	47.5%	107	(37.8%)	19	(6.7%)	64	(22.6%)	93	(32.9%)	3.37	2.02,5.62	<0.001
Osteophyte	X-ray	Any	63.8%	76	(26.9%)	18	(6.4%)	35	(12.4%)	154	(54.4%)	1.94	1.10,3.43	0.022
		Severe	32.5%	165	(58.3%)	10	(3.5%)	42	(14.8%)	66	(23.3%)	4.20	2.11,8.37	<0.001
	MR	Any	83.9%	22	(7.8%)	19	(6.7%)	28	(9.9%)	214	(75.6%)	1.47	0.83,2.63	0.19
		Severe	39.8%	132	(46.6%)	21	(7.4%)	56	(19.8%)	74	(26.1%)	2.67	1.61,4.40	<0.001
Attrition	X-ray	Any	9.7%	239	(84.5%)	4	(1.4%)	29	(10.2%)	11	(3.9%)	7.25	2.55,20.62	<0.001
		Severe	2.3%	272	(96.1%)	0	(0)	9	(3.2%)	2	(0.7%)	/	/	/
	MR	Any	53.1%	90	(31.8%)	25	(8.8%)	60	(21.2%)	108	(38.2%)	2.40	1.51,3.83	<0.001
		Severe	24.0%	185	(65.4%)	15	(5.3%)	45	(15.9%)	38	(13.4%)	3.00	1.67,5.38	<0.001
Cyst	X-ray	Any	9.5%	236	(83.4%)	8	(2.8%)	32	(11.3%)	7	(2.5%)	4.00	1.84,8.68	<0.001
		Severe	0.7%	279	(98.6%)	2	(0.7%)	2	(0.7%)	0	(0)	/	/	/
	MR	Any	58.1%	78	(27.6%)	31	(11.0%)	50	(17.7%)	124	(43.8%)	1.61	1.03,2.52	0.037
		Severe	17.7%	204	(72.1%)	20	(7.1%)	38	(13.4%)	21	(7.4%)	1.90	1.11,3.27	0.020
Sclerosis	X-ray	Any	54.8%	93	(32.9%)	20	(7.1%)	50	(17.7%)	120	(42.4%)	2.50	1.49,4.20	0.001
		Severe	14.7%	217	(76.7%)	9	(3.2%)	40	(14.1%)	17	(6.0%)	4.44	2.16,9.16	<0.001
BML	MR	Any	66.3%	55	(19.4%)	30	(10.6%)	51	(18.0%)	147	(51.9%)	1.70	1.08,2.67	0.021
		Severe	32.3%	145	(51.2%)	32	(11.3%)	61	(21.6%)	45	(15.9%)	1.91	1.24,2.92	0.003

Feature	Imaging	Severity of grade[1]	Occurrence of structural findings									Odds ratios from Conditional logistic model		
			Any knee[2]	Neither knee		Knee without pain only		Knee with pain only		Both knees		OR	95% CI	p
				n	(%)	n	(%)	n	(%)	n	(%)			
Synovitis/effusion	MR	Any	73.1%	50	(17.7%)	15	(5.3%)	37	(13.1%)	181	(64.0%)	2.47	1.35, 4.49	0.003
		Severe	20.9%	186	(65.7%)	12	(4.2%)	64	(22.6%)	21	(7.4%)	5.33	2.88, 9.88	<0.001

[1] See table 1 for definitions of 'any' and 'severe' structural abnormality.

[2] For any knee, proportion derived from 566 knees.

Table 4

Performance of radiographic vs. MR detected structural features using Receiver operator characteristics area under the curve.

Radiographic feature		MR feature		P-value for Difference
Area under the curve	95% CI	Area under the curve	95% CI	
JSN		Cartilage lesion		
0.59	0.55–0.64	0.59	0.54–0.64	0.97
Osteophytes				
0.57	0.52–0.61	0.58	0.53–0.63	0.49
Attrition				
0.55	0.52–0.57	0.58	0.53–0.62	0.16
Subchondral cysts				
0.54	0.52–0.57	0.55	0.50–0.59	0.86
KL		Synovitis/effusion		
0.58	0.54–0.63	0.60	0.56–0.64	0.42

P-value from difference in area for ROC curve using bootstrapping (1000 replicates) comparing radiographic with MR features.