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Magnetic resonance imaging (MRI)-defined cartilage degeneration and joint pain are associated with poor physical function in knee osteoarthritis – the Oulu Knee Osteoarthritis study

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SUMMARY

Objective: The main aim was to investigate the associations between Magnetic Resonance Imaging (MRI)-defined structural pathologies of the knee and physical function.
Design: A cohort study with frequency matching on age and sex with eighty symptomatic subjects with knee pain and suspicion or diagnosis of knee osteoarthritis (OA) and 57 asymptomatic subjects was conducted. The subjects underwent knee MRI, and the severity of structural changes was graded by MRI Osteoarthritis Knee Score (MOAKS) in separate knee locations. WOMAC function subscores were recorded and physical function tests (20-m and 5-min walk, stair ascending and descending, timed up & go and repeated sit-to-stand tests) performed. The association between MRI-defined structural pathologies and physical function tests and WOMAC function subscores were evaluated by linear regression analysis with adjustment for demographic factors, other MRI-features and pain with using effect size (ES) as a measure of the magnitude of an association.
Results: Cartilage degeneration showed significant association with poor physical performance in TUG-, stair ascending and descending-, 20-m- and 5-min walk-tests (ESs in the subjects with cartilage degeneration anywhere between 0.134 [95%CI 0.037–0.238] and 0.224 [0.013–0.335]) and with increased WOMAC function subscore (ES in the subjects with cartilage degeneration anywhere 0.088 [0.012–0.103]). Also, lateral meniscus maceration and extrusion were associated with poor performance in stair ascending test (ESs 0.067 [0.008–0.163] and 0.077 [0.012–0.177]).
Conclusions: After adjustments cartilage degeneration was associated with both decreased self-reported physical function and poor performance in the physical function tests. Furthermore, subjects with lateral meniscus maceration and extrusions showed significantly worse performance in stair ascending tests.

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Introduction

Knee OA is a leading cause of physical disability among elderly people[1]. However, the reported associations between radiographic severity of disease and self-reported and/or objectively measured physical function have been poor[1–5]. Magnetic resonance imaging (MRI) is increasingly important for understanding the associations between structural pathology and OA-related symptoms[6]. Synovitis, osteophytes, large bone marrow lesions (BMLs) and moderate-to-large effusions have been associated with knee pain[1,6–10]. The relationship between MRI-defined structural changes and physical function, on the other hand, has been far less studied with inconsistent findings[8,11–14].

An association between cartilage degeneration and self-reported physical disability has been reported[8,11,12]. Findings from single studies suggest a relationship between multiple structural pathologies (such as meniscal and ligament tears, effusion, synovitis, BMLs and osteophytes) and either self-reported or objectively measured physical function[8,13]. However, also opposite findings suggesting only minor or no relationship between MRI-related structural pathology and functional limitations have been reported[11,13,14]. Knee pain has been reported to be an important determinant of physical disability in knee OA[3,15–17], and this relationship seems independent from radiographic disease stage[3,15,16]. However, even if pain might independently associate physical performance, to our knowledge, there are no studies that have assessed the association between knee pain and physical function adjusted for structural pathology detected on MRI.

The main aim of our study was to investigate the associations between MRI-defined structural joint pathology and both self-reported and objectively measured physical function. We hypothesized that structural pathologies detected on MRI, such as cartilage degeneration, BMLs, effusion and/or synovitis, meniscus damage and ligament tears would show an association with physical performance. As a secondary outcome the relationship between knee pain and physical performance with adjustment for MRI-defined structural pathologies was investigated.

Method

Subjects

Our study is part of the Oulu Knee Osteoarthritis (OKOA) study including symptomatic and asymptomatic subjects. The participants were recruited between October 2012 and April 2014. Each participant gave written informed consent prior to enrollment after receiving detailed information about the study design and methods as well as the subjects' rights for participation. Our study was conducted according to the Helsinki Declaration and approved by The Regional Ethics Committee of the Northern Ostrobothnia Hospital District.

Symptomatic subjects

Eighty volunteers (age range 30–70 years; later during recruitment narrowed to 45–70 years to age-match the symptomatic and asymptomatic groups, however, all 80 included in to the analyses) referred to either Oulu University Hospital or Oulu municipality Health Centers due to knee pain and suspicion of knee OA or planned total knee arthroplasty at the Department of Surgery of Oulu University Hospital were recruited. Knee radiographs of subjects were evaluated according to the Kellgren–Lawrence (K–L) grading[18] by an experienced rheumatologist (JK) blinded to patients details, history and clinical data with an aim to have an equal number of subjects in each K–L group[1–4] and 60% of female subjects. Although previous significant knee joint trauma or surgery were primarily defined as an exclusion criterion, some patients with either a history of significant joint trauma or previous knee joint surgery were included as full patient history was available only after study measurements while the received questionnaires were processed. Subjects with acute trauma were excluded. Also subjects with inflammatory joint disease or other medical condition affecting the knee joint were excluded.

Asymptomatic subjects

Eighty volunteers, 20 to 70 year-old (after pilot examinations narrowed to 45–70 years to age-match the symptomatic group) pain-free subjects were recruited from the colleagues, friends and family members of the research team and by newspaper advertisements. Detailed subject selection is described in our earlier study[10]. Being pain-free was defined as not having repetitive or long-term (more than 2 weeks without interruption) pain in either knee joint. The subjects with previous significant knee joint trauma or surgery, inflammatory joint disease or other medical condition affecting the knee joint were excluded. Our aim was to match the age and sex of asymptomatic subjects with the symptomatic group, however, after inclusion twenty-three (28.8%) asymptomatic subjects had to be excluded because of previous history or present problems in their knee(s) which had not been reported at inclusion. Eventually, 57 women and men without knee pain were approved into the final analyses.

Symptom evaluation

Evaluation of symptoms was performed by questionnaires which were completed by the subjects before undergoing MRI examination (mean time interval 3.4 days with range of 0–41 days). Pain severity was recorded by using 100 mm visual analog scale (VAS). Western Ontario and McMaster Universities Arthritis Index (WOMAC) function subscore[19] was used to estimate self-reported disease-specific physical function.

Physical function tests

The physical function was measured using a standardized test battery[2,20] (mean time interval 0.8 days after undergoing MRI examination with range of 0–12 days). Prior to performance, the subjects were familiarized with the test procedure. Pauses in average 2–3 min between tests were allowed in order to avoid fatigue. The tests were as follows (in the order of performance): 20-m walk test[2,21,22], 5-min walk test[2,22], stair ascending and stair descending tests[2,23,24], Timed Up & Go (TUG) test[2,23] and repeated sit-to-stand test[2,25].

Magnetic resonance imaging (MRI)

Knee MRI was performed using a 3T system (Skyra, Siemens Healthcare Global, Erlangen, Germany) with a 15-channel transmit/receive knee coil. In the symptomatic group the (more) painful knee was imaged, and in the asymptomatic group the knee of the dominant hand side was imaged. The following sequences were included in the protocol: sagittal T2 weighted dual-echo steady-state (DESS), sagittal proton density (PD)-weighted spin echo sequence, sagittal intermediate-weighted 3D SPACE fat-suppressed turbo spin-echo (TSE), coronal PD-weighted TSE and coronal T1-weighted TSE. For assessment of patellofemoral joint, axial images were reconstructed from isotropic DESS images. Coronal fat-suppressed images were reconstructed from the sagittally acquired 3D fat-suppressed SPACE sequence. A detailed description of MRI sequences is presented in Table I.

The presence and severity of structural changes was graded by MRI Osteoarthritis Knee Score (MOAKS)[7] in separate knee locations

(Table II.). Reliability of the MOAKS system has been reported before and agreement by the same readers has been shown to be good to excellent[7]. Weighted kappa values for intra-reader reliability range between 0.68 (Hoffa synovitis) and 0.97 (meniscus morphology) as reported recently in another cohort read by the same readers applying a comparable imaging protocol[26]. The grading was performed by an experienced musculoskeletal radiologist (AG) with 15 years of experience in semi-quantitative MRI analysis of knee OA features, blinded to subject's characteristics, clinical and radiographic data.

Statistical analyses

Means and standard deviations (SDs) for continuous variables and number (n) of cases with percentages (%) for categorical variables were used to describe the demographic data of the symptomatic and asymptomatic groups. The prevalence and severity of structural pathologies detected on MRI was calculated in general and by region (medial and lateral tibia, medial and lateral femur and patellofemoral joint). Definitions for the presence, severity and site-specificity of structural pathologies are presented in Table II.

Because of skewed data distribution, the results of the WOMAC function subscore and the physical performance tests according to the severity of site-specific structural pathologies are presented in medians with interquartile ranges (IQRs). Linear regression analysis was used to assess the associations between WOMAC function subscore and the physical function tests and MRI-defined structural pathologies. For the linear regression analyses, the results of physical function tests and WOMAC function subscore were

Table I
Sequences and their properties used in magnetic resonance imaging

Sequence	Properties							
	Repetition time (ms)/echo time (ms)	Flip angle (°)	Voxel size (mm)	Field of view (mm)	Acquisition matrix	Number of slices	Slice spacing (mm)	Acquisition time (min.)
Sagittal proton density-weighted spin-echo sequence	1680/13.8		0.42 × 0.42 × 3	159	384 × 384	18	3.6	5:41
Sagittal dual-echo steady-state (DESS)	14.1/5	25	0.6 × 0.6 × 0.6	150	238 × 256	160		3:16
Sagittal intermediate-weighted 3-dimensional SPACE fat-suppressed turbo spin-echo (TSE)	1200/26		0.6 × 0.6 × 0.6	147 × 160	236 × 256	176		8:48
Coronal intermediate-weighted turbo spin-echo (TSE)	2800/33		0.36 × 0.36 × 3	140	346 × 384	35	3.3	4:09
Coronal T1-weighted turbo spin-echo (TSE)	650/18		0.41 × 0.41 × 3	130	240 × 320	25	3.3	1:56

Table II
Definitions for the presence, severity and site-specificity of MRI-defined structural pathologies

The presence of any structural change (present/absent) in given region	Size score >0 for cartilage loss, later called cartilage degeneration, defined as cartilage loss for >0% of region of cartilage surface area Size score >0 for bone marrow lesion (BML), defined as BML for >0% of subregional volume Size score >0 for osteophyte, defined as any osteophytes in the given region Meniscus morphology score 2–5 for meniscus tear (including vertical, horizontal, radial, root and complex meniscus tears with an exclusion of signal changes without a tear) Meniscus morphology score 6 or 8 for maceration, defined as either loss of morphological substance of the meniscus (partial maceration) or no remaining visible meniscal substance (complete maceration) Hoffa's synovitis score >0, defined as a at least mild-degree signal hyperintensity in the Hoffa's fat pad Size score >0 for effusion-synovitis, defined as at least small amount of fluid continuous in the retropatellar space ACL score 1 for complete ACL tear* PCL score 1 for complete PCL tear*
The definitions of more severe forms of given structural pathology in MRI†	Severe cartilage degeneration defined as having both score ≥2 (at least 33% of region of cartilage surface area) for the size of any cartilage loss AND score ≥2 (at least 10%) for percentage of full-thickness cartilage loss of the defined region Large BMLs defined as size score ≥2 (i.e., size of BML exceeding 33% of subregional volume) Large osteophytes defined as osteophyte size score ≥2 (i.e., medium and large - sized osteophytes) Moderate-to-severe Hoffa's synovitis defined as Hoffa's synovitis score ≥2 (i.e., at least moderate signal hyperintensity in the Hoffa's fat pad) Moderate-to-large effusion-synovitis defined as effusion-synovitis size score 2–3 (i.e., fluid with slight convexity of the suprapatellar bursa [score 2] or evidence of capsular distention [grade 3])
The site-specificity of given structural pathology in MRI	Site-specificity of cartilage degeneration, BMLs and osteophytes in MRI was defined as i) patellofemoral if there were any changes in at least one of following subregions: anterior medial femur, anterior lateral femur, medial patella or lateral patella ii) medial femoral if there were any changes in at least one of the following subregions: central medial femur or posterior medial femur iii) lateral femoral if there were any changes in at least one of following subregions: central lateral femur or posterior lateral femur the site-specificity of cartilage degeneration and BMLs in MRI was defined as‡ iv) tibial medial if there were any cartilage loss or BMLs in at least one of following subregions: anterior medial tibia, central medial tibia or posterior medial tibia v) tibial lateral if there were any cartilage loss or BMLs in at least one of following subregions: anterior lateral tibia, central lateral tibia or posterior lateral tibia

MRI OA knee score (MOAKS)[10] was used to classify the MRI-related structural pathologies.

* Defined as present or absent in MOAKS.

† The severity of each structural pathology for given location was defined according to the most severe finding in this region (e.g., cartilage degeneration in the medial tibia was defined as severe if there was one severe cartilage lesion in at least one subregion in the medial part of tibial condyle).

‡ In MOAKS osteophytes in tibia are classified only being either medial or lateral.

transformed into a logarithmic scale which corrected the skewness. Partial Eta Squared was used as a measure of effect size (ES), i.e., a measure of the strength of the association between structural pathology and physical performance. ES > 0.02 is considered as small, >0.13 as moderate and >0.26 as large ES[27]. A separate regression model for each location of the given structural feature was used. The results were adjusted for demographic factors (gender, age, BMI)[14,28] and the presence of other MRI-features (severe cartilage degeneration, any BMLs, osteophytes and Hoffa's synovitis) (adjustment model 1). Subsequently, further adjustment for the presence of any pain (defined as VAS > 0 mm) was conducted[9,14,29] (adjustment model 2), because it was considered important to evaluate if the potential association between structural pathology and physical function exists independently from pain[3,4,15,16,31,39]. Analysis of variance for logarithmic-transformed results with *post hoc* tests for multiple comparisons was used to compare physical function between the severity groups of each structural pathology (i.e., severe/large vs mild/small vs no pathology). Furthermore, the associations between the WOMAC function subscore and the physical performance tests with the presence of pain were estimated using linear regression analysis with adjustment for demographic factors and the presence of other MRI-features. In the linear regression analysis, *P* values were corrected for multiple comparisons with an aim to prevent type I error. Because of the extremely high number of the comparisons in the linear regression analysis model, the correction was performed by dividing *P*-value threshold for statistical significance, 0.05, by the count of tests (seven) measuring the physical function (six test for the physical performance and WOMAC function subscore questionnaire) as a compromise. Consequently, *P* values lower than 0.007 are considered statistically significant. Analyses were performed with IBM SPSS software (version 22, SPSS Inc., Chicago, IL, USA).

Results

Eighty symptomatic and 57 asymptomatic subjects were approved into the final analyses (Table III). The symptomatic subjects were older in age, had higher BMI and more comorbidities than the asymptomatic subjects.

Cartilage degeneration was highly prevalent (total number of subjects with any cartilage degeneration 128 [93.4%]), especially in the patellofemoral joint ($n = 118$ [86.1%]), however, severe cartilage degeneration was detected almost exclusively in the symptomatic group (number of any severe cartilage degeneration in the

Table III
Characteristics of study subjects

	Symptomatic subjects ($n = 80$)	Asymptomatic subjects ($n = 57$)
Gender		
Female, *n* (%)	49 (61.3)	32 (56.1)
Male, *n* (%)	31 (38.7)	25 (43.9)
Age (years), mean (SD)	59.9 (7.8)	54.6 (14.6)
Body mass index (kg/m$^{2)}$), mean (SD)	29.0 (4.3)	24.7 (3.3)
Comorbidities		
No chronic diseases, *n* (%)	2 (2.5)	13 (22.8)
1 chronic disease, *n* (%)	8 (10.0)	10 (17.5)
2 or more chronic diseases, *n* (%)	70 (87.5)	34 (59.6)
Knee pain, VAS (mm), mean (SD)		
Index knee	37.1 (30.1)	0
Other knee	20.6 (25.7)	0
Duration of knee pain (months), mean (SD)		
Index knee	61.9 (77.3)	0
Other knee	40.2 (68.5)	0
History of knee trauma*,† (yes), *n* (%)		
Index knee	30 (37.5)	3 (5.3)
Other knee	17 (21.3)	4 (7.0)
History of knee surgery† (yes), *n* (%)		
Index knee	19 (24.1)	0
Other knee	16 (20.3)	0
Use of analgetics, *n* (%)		
Paracetamol		
No use	33 (41.3)	57 (100.0)
Few days a month	10 (12.5)	0
Few times a week	24 (30.0)	0
Daily	13 (16.3)	0
NSAID		
No use	35 (43.8)	57 (100.0)
Few days a month	19 (23.8)	0
Few times a week	16 (20.0)	0
Daily	10 (12.5)	0
Weak opioids		
No use	62 (77.5)	57 (100.0)
Few days a month	4 (5.0)	0
Few times a week	8 (10.0)	0
Daily	6 (7.5)	0
Radiographic grades (Kellgren–Lawrence) of index knee, *n* (%)		
0	2 (2.5)	
1	21 (26.3)	
2	20 (25.0)	
3	20 (25.0)	
4	17 (21.3)	

* Mostly minor traumas, e.g., distension, contusion or overuse injury. Two symptomatic subjects had a history of operated meniscus tear and one subject had operated anterior cruciate ligament tear.
† See Method.

symptomatic and asymptomatic group 25 [31.3%] and 1 [1.8%], respectively) (Table IV). The prevalence of both small and large BMLs was notably higher in the symptomatic group (*n* for small BMLs 28 [35.0%] and large BMLs 33 [41.3%] in the symptomatic groups and 1 [28.1%] and 4 [7.0%] in the asymptomatic group, respectively). An example of MRI visualization of BMLs using different sequences applied in our study is presented in Fig. 1. Small osteophytes were common at all locations in the symptomatic subjects, and in the asymptomatic group they were most commonly seen in the patellofemoral joint ($n = 11$ [19.3%]). Large osteophytes were rare ($n = 14$ [10.2%]) and seen only in the symptomatic subjects.

The prevalence of any meniscus tears and meniscus extrusions were 50.0% and 66.3% in the symptomatic group and 31.6% and 19.3% in the asymptomatic group (Table IV). Effusion-synovitis and Hoffa's synovitis were detected in 81.3% and 61.3% of symptomatic subjects and 33.3% and 15.8% of asymptomatic subjects. 21.3% and 15.0% of symptomatic subjects had moderate-to-large effusion-synovitis and moderate-to-severe Hoffa's synovitis, respectively.

MRI associations with WOMAC function subscore

Cartilage degeneration in the medial tibia (ES 0.103 [95%CI 0.018–0.200], medial femur (0.092 [0.013–0.188]) and anywhere (0.075 [0.012–0.183])) were associated with poor self-reported physical function (Table V). Medians and IQRs of the WOMAC function subscores and physical performance tests according to the severity of site-specific cartilage degeneration are presented in Table VI. Subjects with severe cartilage degeneration reported 2.7 to 16.2 times higher median WOMAC function subscores than subjects with small degeneration. Subjects with osteophytes in the lateral tibia, in the medial and lateral femur or in the patellofemoral reported poor physical function (ES range between 0.083 [95%CI 0.015–0.184] to 0.134 [0.010–0.168] in the adjustment model 1) but the associations did not remain significant after further adjustment for the presence of pain (Table V). Results of WOMAC function subscores (medians with IQRs) according to site-specific MRI-defined structural pathologies are shown in Supplementary Table 1.

MRI associations with physical performance tests

Cartilage degeneration anywhere showed moderate association with impaired performance in the physical function tests except for sit-to-stand test (Table VII). Subjects with severe cartilage degeneration (anywhere) needed, in median, 21.0–56.7% longer time to finish TUG-, stair ascending-, stair descending-, 20-m and 5-min. walk-tests compared with subjects with mild degeneration, respectively (Table VI). A moderate association was found between cartilage degeneration in the medial tibia and in the medial and lateral femur and stair ascending test (ESs 0.146 [95%CI 0.004–0.252], 0.128 [0.033–0.232] and 0.161 [0.053–0.268]) and between cartilage degeneration in the medial tibia and femur and stair descending (ESs 0.149 [0.045–0.295] and 0.135 [0.037–0.240]) and 20-m walk tests (0.143 [0.042–0.248] and 0.132 [0.035–0.235]). Cartilage degeneration

Table IV
Prevalence and severity of the MRI-detected site-specific structural pathologies in symptomatic and asymptomatic subjects

		Number of subjects with small or mild lesion		Number of subjects with large or severe lesion	
		Symptomatic subjects ($n = 80$)	Asymptomatic subjects ($n = 57$)	Symptomatic subjects ($n = 80$)	Asymptomatic subjects ($n = 57$)
Cartilage degeneration	Medial tibia	31	11	18	0
	Lateral tibia	45	24	6	1
	Medial femur	43	22	18	1
	Lateral femur	29	5	5	1
	PF joint	69	44	4	1
	Anywhere	53	49	25	1
BML	Medial tibia	9	3	20	0
	Lateral tibia	10	1	7	1
	Medial femur	26	3	14	1
	Lateral femur	5	2	8	1
	PF joint	25	15	7	2
	Anywhere	28	16	33	4
Osteophytes	Medial tibia	47	7	3	0
	Lateral tibia	41	1	0	0
	Medial femur	46	6	10	0
	Lateral femur	39	2	3	0
	PF joint	53	11	8	0
	Anywhere	52	20	14	0
Meniscus tear	Medial	27	14		
	Lateral	19	8		
	Anterior	9	3		
	Posterior	31	13		
	Anywhere	40	18		
	Complex	2	0		
Macerated meniscus	Medial	35	3		
	Lateral	12	1		
	Anywhere	41	4		
Meniscal Extrusion	Medial	47	10		
	Lateral	8	2		
	Anterior	43	4		
	Anywhere	53	11		
ACL Tear		6	0		
PCL Tear		0	0		
Hoffa's synovitis		37	9	12	0
Effusion-synovitis		48	18	17	1

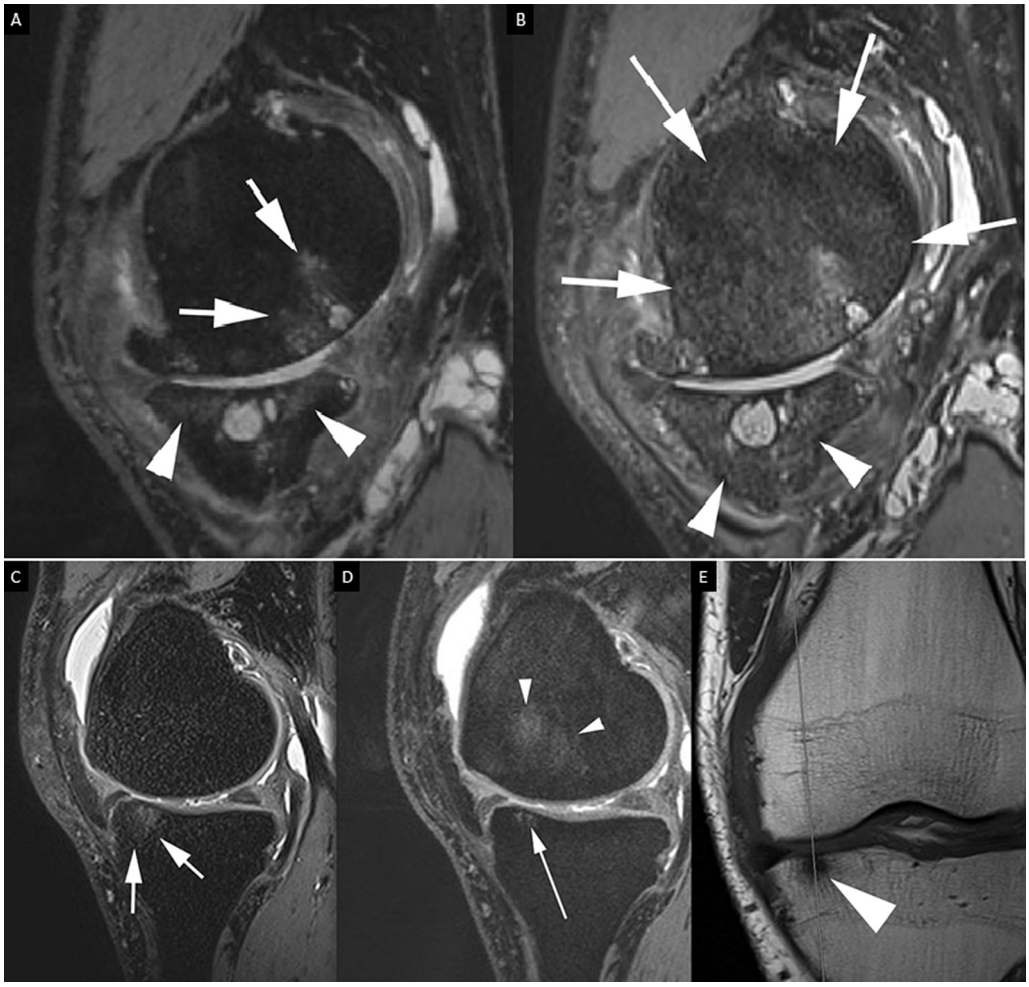

Fig. 1. Direct comparison between different sequences used in the current study. (A) Sagittal DESS image shows cystic portion of femoral and tibial bone marrow lesions (BML) and some ill-defined parts of BML in both, femur (arrows) and tibia (arrowheads). (B) Sagittal SPACE, a 3D T2-weighted FSE fat suppressed fast spin echo sequence, superiorly depicts ill-defined BMLs that are visualized in much larger fashion in femur (arrows) and tibia (arrowheads) compared to DESS. (C) Sagittal SPACE image in another patient shows a BML in the anterior medial tibia (arrows). No bone marrow changes are seen in the femur. (D) Corresponding sagittal DESS shows tibial BML to a much smaller extent compared to SPACE (long arrow). High intensity signal changes in the medial femur represent artifacts as a result of popliteal vessel pulsation and must not be mistaken as bone marrow lesions (small arrowheads). (E) Corresponding coronal T1 weighted image shows tibial BML as a circumscribed hypointensity (large arrowhead). No signal alterations are seen in the femur confirming that signal changes seen in D represent an artifact.

in the medial tibia and medial femur and in the lateral femur showed a small yet significant association with TUG test (Table VII). Also, an association with small effect size was demonstrated between cartilage degeneration in the medial femur and 5-min. walk test and between cartilage degeneration in the lateral femur and sit-to-stand test.

Neither BMLs nor osteophytes showed any significant association with physical performance either in the adjustment model 2 (Table VII) or in the model 1. ESs for the associations between physical function tests and MRI-features in the adjustment model 1 are presented in Supplementary Table 2. Lateral meniscus maceration was associated with poor performance in stair ascending test after adjustments (ES 0.067 [0.008–0.163]) (Table VII). Subjects with and without lateral meniscus maceration used in stair ascending test 14.6 (IQR 2.4)s and 8.5 (1.4)s in median, $P = 0.003$, respectively (Supplementary Table 3). Subjects with lateral meniscus extrusions performed, in median, 100.5% slower in stair ascending test ($P = 0.002$, ES 0.077 [0.012–0.177]). Results of physical performance tests (medians with IQRs) according to site-specific MRI-detected structural pathologies are shown in Supplementary Table 3.

The presence of any pain showed significant association with WOMAC function subscore and all physical function tests with large ES for WOMAC function subscore (ES 0.633 [95%CI 0.622–0.649]) in the adjustment model 2 (Supplementary Table 4). Gender and age had small yet significant association with physical performance, and BMI showed association with both perceived and objectively measured physical function in both adjustment models (Supplementary Tables 4 and 5). Severe cartilage degeneration, osteophytes and Hoffa's synovitis were associated with poor self-reported physical function but only the association with severe cartilage degeneration remained after adjustment for pain. Severe cartilage degeneration also associated with poor performance in all physical function tests with moderate ESs in the stair ascending and descending and 5-min walk tests (ES range between 0.154 [0.106–0.178] and 0.189 [0.117–0.232] in the adjustment model 2).

Association between pain and pain pattern with self-reported physical function and objectively measured physical performance

Subjects who reported presence of any pain (VAS > 0 mm) had significantly worse self-reported physical function (ES 0.634

Table V
The effect sizes (es) for the associations between site-specific MRI-detected structural pathologies and WOMAC function subscores

	Adjustment Model 1*			Adjustment model 2†		
	WOMAC function subscore			WOMAC function subscore		
Structural Pathology	ES‡	95% CI	P§	ES‡	95% CI	P§
Cartilage Degeneration						
Tibia medial	**0.122**	**0.030–0.224**	**<0.001**	**0.103**	**0.018–0.200**	**0.001**
Tibia lateral	0.001	<0.001–0.018	0.921	0.001	<0.001–0.016	0.931
Femur medial	**0.077**	**0.007–0.169**	**0.006**	**0.092**	**0.013–0.188**	**0.002**
Femur lateral	0.024	<0.001–0.088	0.213	0.006	<0.0010–0.466	0.666
Patellofemoral	0.008	<0.001–0.051	0.613	0.010	<0.001–0.058	0.524
Anywhere	**0.075**	**0.006–0.166**	**0.007**	**0.088**	**0.012–0.183**	**0.003**
Bone Marrow Lesions						
Tibia medial	0.035	<0.001–0.107	0.103	0.066	0.003–0.154	0.013
Tibia lateral	0.006	<0.001–0.046	0.664	0.037	<0.001–0.111	0.093
Femur medial	0.043	<0.001–0.120	0.062	0.057	<0.001–0.141	0.025
Femur lateral	0.005	<0.001–0.041	0.727	0.048	<0.001–0.127	0.046
Patellofemoral	0.029	<0.001–0.098	0.150	0.017	<0.001–0.074	0.342
Anywhere	0.036	<0.001–0.109	0.096	0.029	<0.001–0.098	0.152
Osteophytes						
Tibia medial	0.053	<0.001–0.135	0.031	0.027	<0.001–0.094	0.173
Tibia lateral	**0.083**	**0.015–0.184**	**0.001**	0.003	<0.001–0.047	0.571
Femur medial	**0.134**	**0.010–0.168**	**<0.001**	0.056	<0.001–0.139	0.027
Femur lateral	**0.085**	**0.011–0.179**	**0.003**	0.004	<0.001–0.039	0.754
Patellofemoral	**0.114**	**0.025–0.214**	**<0.001**	0.032	<0.001–0.102	0.131
Anywhere	0.060	0.001–0.146	0.019	0.004	<0.001–0.035	0.796
Meniscus Tear						
Medial	0‖		0.976	0.003	<0.001–0.047	0.575
Lateral	0‖		0.991	0.007	<0.001–0.062	0.346
Anterior	<0.001	<0.001–0.004	0.912	0.001	<0.001–0.030	0.763
Posterior	<0.001	<0.001–0.001	0.965	0.016	<0.001–0.040	0.161
Anywhere	<0.001	<0.001–0.007	0.888	0.017	<0.001–0.084	0.146
Complex tear	0.004	<0.001–0.052	0.479	0.001	<0.001–0.037	0.734
Meniscus Maceration						
Medial	0.029	<0.001–0.107	0.053	0.015	<0.001–0.081	0.167
Lateral	0.001	<0.001–0.032	0.755	0.001	<0.001–0.023	0.793
Anywhere	0.020	<0.001–0.091	0.108	0.006	<0.001–0.058	0.403
Meniscus Extrusion						
Medial	0.036	<0.001–0.119	0.030	0.029	<0.001–0.107	0.054
Lateral	0‖		0.991	0‖		1.000
Anterior	0.013	<0.001–0.076	0.202	0.003	<0.001–0.048	0.562
Anywhere	0.048	0.002–0.136	0.013	0.033	<0.001–0.113	0.041
ACL tear	0.017	<0.001–0.085	0.138	0.006	<0.001–0.058	0.398
Hoffa's Synovitis	0.059	0.001–0.144	0.020	0.009	<0.001–0.055	0.560
Effusion-Synovitis	0.029	<0.001–0.098	0.153	0.030	<0.001–0.081	0.152

* Linear regression analysis with adjustment for gender, age, BMI, and the presence of severe cartilage degeneration, any BMLs, any osteophytes and any hoffa's synovitis.
† Linear regression analysis with adjustment for gender, age, BMI, and the presence of severe cartilage degeneration, any BMLs, any osteophytes, any hoffa's synovitis and the presence of any pain.
‡ Partial Eta Squared used as a measure for the effect size (ES). ES > 0.02 is considered as small effect size, >0.13 as moderate and >0.26 as large effect size[27].
§ *P* Values < 0.007 are considered statistically significant (**highlighted**) after correction for multiple comparisons (see Method/Statistical analysis).
‖ ES marked as 0 if both the ES and the upper limit of the 95% CI are <0.001.

[0.622–0.649]) and they performed worse in every physical function tests, and these differences remained significant after adjusting the results for the demographic factors and MRI-features (ES range 0.088 [0.030–0.142] - 0.139 [0.015–0.185], respectively) (Supplementary Table 6). The presence of pain independently accounted for 76.6% variance in WOMAC function scores, and for 25.5–30.8% variance in physical function tests.

Discussion

The main finding of our study is that cartilage degeneration, lateral meniscus maceration and lateral meniscus extrusion were associated with poor physical performance when adjusted for demographic factors, other MRI-features, and further with pain. Osteophytes were associated with poor self-reported physical performance after adjustment for demographic factors and other MRI-features but the association did not remain after further adjustment for pain. Knee pain showed significant association with both poor self-reported physical function and poor performance in the physical function tests independently from MRI-defined structural pathologies.

We have earlier reported of the associations between MRI-related structural pathologies and pain – the another main symptom of knee OA in this study population[10]. The findings were somewhat different showing that, instead of cartilage degeneration, Hoffa's synovitis and osteophytes had significant association with pain, and medial knee pain was associated with medially located structural pathologies (e.g., cartilage loss in the medial tibia, osteophytes in the medial tibia and medial femur, medial meniscus maceration and anterior meniscus extrusions)[10]. These differences might be interpreted as consequence of different mechanisms underlying pain and physical function.

Sowers *et al.*[8] reported 15–30% decrease in walking and stair climbing performance in subjects with full-thickness cartilage defects in the medial tibia and medial femur. Also, increasing WOMAC function scores were significantly associated with cartilage defects in their study[8]. Link et al.[11] reported significant differences in WOMAC function scores in subjects with or without cartilage

Table VI
Results of physical function tests (medians and interquartile ranges [IQRs]) according to site-specific cartilage degeneration

Cartilage degeneration			WOMAC Function Subscore (mm)		Sit-to-stand [s]		Timed Up&Go [s]		Stair ascending [s]		Stair descending [s]		20 m walk [s]		5 min walk [m]	
Location	Severity*	*n*	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Medial tibia	none	77	0.81	12.2	10.5	1.3	5.71	1.27	7.94	1.25	7.4	1.38	9.68	1.33	515.5	1.24
	small	42	14.05	22.56	11.91	1.29	6.33	1.34	9.28	1.4	8.5	1.46	10.47	1.4	476	1.37
	severe	18	42.46	38.79	13.64	1.33	8.42	1.3	12.44	1.67	11.86	2.03	12.76	1.24	402	1.4
Lateral tibia	none	61	1.64	17.6	10.71	1.39	5.96	1.3	8.19	1.36	7.76	1.49	9.93	1.35	511	1.3
	small	69	12.76	32.96	11.8	1.32	6.56	1.31	8.71	1.47	8.36	1.64	10.13	1.34	480	1.26
	severe	7	39.63	57.8	15.83	1.83	10.95	3.26	20.47	3.05	19.43	3.01	14.19	1.78	345	1.6
Medial femur	none	53	0.09	5.22	9.94	1.32	5.68	1.3	7.89	1.27	7.25	1.39	9.01	1.31	521	1.27
	small	65	10.22	25.06	11.57	1.27	6.24	1.26	8.59	1.42	7.96	1.45	10.46	1.22	485	1.28
	severe	19	36.84	32.76	13.69	1.36	8.28	1.31	12.45	1.7	12.36	1.93	12.74	1.34	393.92	1.41
Lateral femur	none	97	2.07	18.29	10.56	1.27	5.85	1.29	8.14	1.33	7.45	1.42	9.72	1.38	516.5	1.29
	small	34	19.98	38.06	13.07	1.31	6.95	1.36	10.25	1.66	10.29	1.63	11.33	1.31	452	1.3
	severe	6	52.99	60.19	16.62	2.14	11.22	3.15	20.62	2.63	20.89	2.79	15.92	2.12	332.26	1.64
PF joint	none	19	0.09	13.41	9.84	1.35	5.64	1.3	7.88	1.36	6.7	1.61	8.89	1.33	558	1.34
	small	113	7.25	27.62	11.56	1.32	6.31	1.33	8.7	1.45	8.18	1.57	10.29	1.3	489	1.27
	severe	5	35.82	50.85	15.83	1.53	9.35	2.03	13.47	2.34	13.41	2.8	13.17	2.1	376	1.76
Anywhere	none	9	0	7.4	8.88	1.36	4.88	1.42	7.88	1.49	6.7	1.87	8.86	1.33	568	1.33
	small	102	2.7	18.03	10.92	1.27	5.89	1.25	8.29	1.3	7.57	1.37	9.75	1.32	509	1.26
	severe	26	38.24	39.65	13.64	1.34	8.42	1.42	12.44	1.83	11.86	2.05	12.76	1.36	402	1.42

* Definition: see Table II.

lesions, and weak but still significant associations between WOMAC function subscale and tibial cartilage volume determined from MRI was reported by Wluka *et al.*[12] in subjects with knee OA. Our results are in line with these findings. However, also opposite results with no association between cartilage lesions and poor physical performance have been reported[14].

The underlying mechanisms for the association between cartilage degeneration and poor physical function are not clear. Considering pain as an important mediator for physical disability it is important to notice that cartilage is not innervated with nociceptive fibers. However, cartilage loss has been reported to be associated with knee pain[1,8,10,11,31,32]. This might be due to increased loading resulting in subchondral BMLs and concomitant changes in synovium which are known to be associated with pain and may result in increased sensitivity to impact stresses during physical activity[1,12,30]. Decreased physical activity due to OA-related pain has been associated with impaired physical performance in subjects with knee OA[17,31,32], and on the other hand, remaining physically active and sustaining good knee function seems to help to maintain good cartilage quality[33].

In contrast to our original hypothesis, BMLs and osteophytes were not associated with poor physical performance when adjusted for demographic factors, other MRI-features and pain. However, our findings confirm the results of some earlier studies[11,14,34–36]. On the contrary, Sowers *et al.* reported significant association between both BMLs and osteophytes and increased walking and stair climbing times[8]. It is notable that in their study only crude *P* values are presented with no adjustment for the demographic factors and/or other significant MRI-features or pain which may explain the differences between our results. We have earlier shown in this study population that osteophytes were strongly associated with knee pain[10] and thus, it is also worth to notice that if knee pain is an intermediate between osteophytes and physical function, including it into the regression analysis model as a confounder may have lead to a false negative finding, i.e., lost of a true positive association. As such, there was a significant association between osteophytes and self-reported physical function when the presence of pain was left out of the analyses. Furthermore, based on observations from large longitudinal cohorts it may be discussed that the structural pathology itself may not be the main determinant of functional impairment but the rate of structural progression instead may be of greater significance[37] that may also explain our findings.

Both presence[8,13] and absence[11,14] of association between meniscus tears and poor physical function have been reported. In our study meniscus tears did not associate with physical performance or self-reported disability. However, we found that lateral meniscus maceration, i.e., substance loss that is considered to be more severe morphological change than any tears, was associated with poor performance in stair ascending test after adjustments for demographic factors, other MRI-features and pain. Furthermore, we found small yet significant association between lateral meniscus extrusions and poor performance in stair ascending test after adjustments. An association between meniscus extrusions and maceration and OA-related symptoms may be due to altered biomechanical loading following the loss of meniscal function[38]. It can be discussed, that, as with cartilage degeneration, meniscus changes might not only be a risk factor for physical disability in knee OA subjects but also a consequence of OA-related physical inactivity[13]. As suggested by Lange and colleagues[13] a vicious cycle that exists between reduced activity levels and overall mobility impairment may contribute to the progression of OA, and excess pain and disability limits individuals' ability to participate in physical activity. To our knowledge, this is the first study to report relationship between meniscus extrusion and physical function.

Knee pain has been reported to be an important determinant of physical disability in knee OA[3,4,15,16,31,39], and this relationship seems independent from radiographic disease stage[3,15,16]. Additionally, we found an association between knee pain and physical function independently from MRI-related structural pathology. Especially for the perceived function (WOMAC function subscore) the magnitude of the effect of presence of any pain was large. The differences found perceived and objectively measured physical function may reflect the different constructs of function they capture[40–42]. Overall, the underlying mechanisms between pain and physical function, however, are not clear. It has been suggested that pain may lead to avoidance of physical activity and accompanying muscle wasting, weakened physical fitness and thus poor physical performance[2,13,15,28]. OA patients with regular physical activity report less intense pain[17] and have better physical function[32]. From a clinical point-of-view, these data suggest that adequate controlling of pain can be considered important to maintain physical function despite the underlying structural abnormalities.

Our study has both strengths and limitations. The results of physical function tests and WOMAC function subscores according

Table VII
The effect sizes (ES) for the associations between site-specific MRI-detected structural pathologies and physical function tests in the adjustment model 2*

Structural Pathology	Sit-to-stand			Timed-Up-and-Go			Stair Ascending			Stair Descending			20-m Walk			5-min Walk		
	ES†	95% CI	P‡	ES†	95% CI	P‡	ES†	95% CI	P‡	ES†	95% CI	P‡	ES†	95% CI	P‡	ES†	95% CI	P‡
Cartilage Degeneration																		
Tibia medial	0.032	<0.001–0.103	0.126	**0.119**	**0.028–0.220**	**<0.001**	**0.146**	**0.004–0.252**	**<0.001**	**0.149**	**0.045–0.255**	**<0.001**	**0.143**	**0.042–0.248**	**<0.001**	**0.150**	**0.047–0.256**	**<0.001**
Tibia lateral	0.039	<0.001–0.113	0.084	0.047	<0.001–0.126	0.047	0.073	0.005–0.164	0.009	0.043	<0.001–0.121	0.064	0.052	<0.001–0.133	0.034	0.033	<0.001–0.104	0.120
Femur medial	0.045	<0.001–0.124	0.054	**0.102**	**0.019–0.200**	**0.001**	**0.128**	**0.033–0.232**	**<0.001**	**0.135**	**0.037–0.240**	**<0.001**	**0.132**	**0.035–0.235**	**<0.001**	**0.119**	**0.028–0.220**	**<0.001**
Femur lateral	**0.087**	**0.011–0.182**	**0.003**	**0.091**	**0.013–0.186**	**0.002**	**0.161**	**0.053–0.268**	**<0.001**	**0.101**	**0.018–0.200**	**0.001**	0.053	<0.001–0.135	0.032	0.070	0.004–0.159	0.010
Patellofemoral	0.048	<0.001–0.128	0.046	0.014	<0.001–0.067	0.413	0.053	<0.001–0.135	0.034	0.046	<0.001–0.125	0.053	0.003	<0.001–0.033	0.820	0.016	<0.001–0.072	0.359
Anywhere	0.061	0.001–0.147	0.019	**0.134**	**0.037–0.238**	**<0.001**	**0.224**	**0.013–0.335**	**<0.001**	**0.191**	**0.075–0.300**	**<0.001**	**0.149**	**0.047–0.255**	**<0.001**	**0.179**	**0.067–0.287**	**<0.001**
Bone Marrow Lesions																		
Tibia medial	0.026	<0.001–0.091	0.193	0.031	<0.001–0.100	0.138	0.019	<0.001–0.008	0.295	0.019	<0.001–0.079	0.295	0.040	<0.001–0.116	0.073	0.005	<0.002–0.042	0.717
Tibia lateral	0.021	<0.001–0.082	0.268	0.008	<0.001–0.050	0.615	0.046	<0.001–0.125	0.053	0.029	<0.001–0.096	0.161	0.001	<0.001–0.011	0.949	<0.001	<0.001–0.001	0.973
Femur medial	0.034	<0.001–0.106	0.113	0.003	<0.001–0.034	0.803	0.004	<0.001–0.037	0.784	0.005	<0.001–0.029	0.718	<0.001	<0.001–0.087	0.993	0.001	<0.001–0.038	0.919
Femur lateral	0.036	<0.001–0.109	0.099	0.001	<0.001–0.014	0.939	0.007	<0.001–0.047	0.661	0.005	<0.001–0.043	0.718	<0.001	<0.001–0.002	0.993	0.001	<0.001–0.018	0.919
Patellofemoral	0.053	<0.001–0.136	0.032	0.018	<0.001–0.075	0.321	0.002	<0.001–0.026	0.880	<0.001	<0.001–0.002	0.994	0.002	<0.001–0.026	0.876	<0.001	<0.001–0.007	0.980
Anywhere	0.038	<0.001–0.113	0.086	0.060	0.001–0.145	0.020	0.035	<0.001–0.108	0.106	0.028	<0.001–0.095	0.174	0.040	<0.001–0.116	0.074	0.021	<0.001–0.083	0.266
Osteophytes																		
Tibia medial	0.010	<0.001–0.056	0.545	0.011	<0.001–0.059	0.504	0.015	<0.001–0.070	0.391	0.016	<0.001–0.072	0.370	0.038	<0.001–0.112	0.084	0.025	<0.001–0.089	0.202
Tibia lateral	<0.001	<0.001–0.012	0.850	0.003	<0.001–0.049	0.519	0.001	<0.001–0.040	0.694	0.001	<0.001–0.039	0.696	<0.001	<0.001–0.012	0.845	0.001	<0.001–0.035	0.740
Femur medial	0.024	<0.001–0.088	0.218	0.009	<0.001–0.055	0.554	0.022	<0.001–0.084	0.250	0.003	<0.001–0.032	0.826	0.012	<0.001–0.061	0.477	0.028	<0.001–0.096	0.161
Femur lateral	0.005	<0.001–0.030	0.730	0.001	<0.001–0.018	0.922	0.029	<0.001–0.097	0.163	0.025	<0.001–0.091	0.202	0.006	<0.001–0.046	0.665	0.001	<0.001–0.019	0.915
Patellofemoral	0.016	<0.001–0.072	0.361	0.004	<0.001–0.036	0.790	0.013	<0.001–0.064	0.450	0.017	<0.001–0.073	0.353	<0.001	<0.001–0.006	0.982	0.002	<0.001–0.025	0.883
Anywhere	0.004	<0.001–0.037	0.778	0.004	<0.001–0.035	0.799	0.003	<0.001–0.030	0.845	0.002	<0.001–0.024	0.888	0.002	<0.001–0.023	0.896	0.007	<0.001–0.049	0.631
Meniscus Tear																		
Medial	<0.001	<0.001–0.005	0.898	<0.001	<0.001–0.004	0.911	0.007	<0.001–0.061	0.365	0.001	<0.001–0.038	0.728	0.010	<0.001–0.069	0.260	0.001	<0.001–0.039	0.696
Lateral	0.003	<0.001–0.049	0.533	0.003	<0.001–0.049	0.528	0.001	<0.001–0.027	0.777	0.002	<0.001–0.046	0.587	0.008	<0.001–0.064	0.314	0.007	<0.001–0.061	0.348
Anterior	0.001	<0.001–0.037	0.730	0.003	<0.001–0.049	0.533	0.002	<0.001–0.045	0.604	0.019	<0.001–0.089	0.121	0.014	<0.001–0.078	0.180	0.013	<0.001–0.076	0.197
Posterior	<0.001	<0.001–0.020	0.806	0.001	<0.001–0.037	0.735	0.001	<0.001–0.021	0.801	0.001	<0.001–0.038	0.718	0.010	<0.001–0.069	0.260	<0.001	<0.001–0.010	0.860
Anywhere	0.016	<0.001–0.083	0.155	0.002	<0.001–0.049	0.602	0.004	<0.001–0.053	0.473	0.005	<0.001–0.056	0.427	0.001	<0.001–0.040	0.689	0.003	<0.001–0.049	0.525
Complex tear	0§		0.984	<0.001	<0.001–0.010	0.860	0.001	<0.001–0.029	0.767	0.002	<0.001–0.044	0.634	0.001	<0.001–0.041	0.663	0.001	<0.001–0.028	0.769
Meniscus Maceration																		
Medial	0.017	<0.001–0.084	0.144	0.001	<0.001–0.032	0.753	0.005	<0.001–0.056	0.426	<0.001	<0.001–0.001	0.961	0.001	<0.001–0.035	0.743	<0.001	<0.001–0.001	0.956
Lateral	0.028	<0.001–0.105	0.060	0.029	<0.001–0.107	0.052	**0.067**	**0.008–0.163**	**0.003**	0.042	0.001–0.128	0.020	0.013	<0.001–0.076	0.201	0.042	0.001–0.127	0.020
Anywhere	0.013	<0.001–0.077	0.198	<0.001	<0.001–0.016	0.827	<0.001	<0.001–0.002	0.945	0.001	<0.001–0.041	0.669	<0.001	<0.001–0.008	0.877	<0.001	<0.001–0.007	0.885
Meniscus Extrusion																		
Medial	<0.001	<0.001–0.002	0.936	0.001	<0.001–0.026	0.776	0.016	<0.001–0.083	0.157	<0.001	<0.001–0.008	0.874	0.003	<0.001–0.048	0.552	0.003	<0.001–0.049	0.524
Lateral	0.048	0.002–0.136	0.013	0.019	<0.001–0.088	0.121	**0.077**	**0.012–0.177**	**0.002**	0.032	<0.001–0.113	0.043	0.002	<0.001–0.044	0.608	0.021	<0.001–0.093	0.100
Anterior	0.001	<0.001–0.038	0.721	<0.001	<0.001–0.019	0.808	0.002	<0.001–0.042	0.658	0.004	<0.001–0.053	0.480	0.001	<0.001–0.036	0.739	0.003	<0.001–0.050	0.513
Anywhere	<0.001	<0.001–0.006	0.892	0.003	<0.001–0.047	0.569	<0.001	<0.001–0.012	0.851	0.001	<0.001–0.030	0.763	0.007	<0.001–0.061	0.351	0§		0.978
ACL tear	0.002	<0.001–0.046	0.583	0.005	<0.001–0.054	0.446	0.004	<0.001–0.053	0.483	0.002	<0.001–0.043	0.640	0§		0.997	0.001	<0.001–0.024	0.785
Hoffa's Synovitis	0.004	<0.001–0.038	0.766	0.005	<0.001–0.043	0.705	0.023	<0.001–0.086	0.240	0.023	<0.001–0.087	0.232	0.006	<0.001–0.047	0.661	0.010	<0.001–0.058	0.517
Effusion-Synovitis	0.063	0.002–0.150	0.017	0.047	<0.001–0.126	0.048	0.058	<0.001–0.143	0.025	0.045	<0.001–0.124	0.057	0.032	<0.001–0.103	0.126	0.018	<0.001–0.077	0.312

* Linear regression analysis with adjustment for gender, age, BMI, and the presence of severe cartilage degeneration, any BMLs, any osteophytes, any hoffa's synovitis and the presence of any pain.
† Partial Eta Squared used as a measure for the effect size (ES). ES > 0.02 is considered as small effect size, >0.13 as moderate and >0.26 as large effect size[28].
‡ *P* Values < 0.007 are considered statistically significant (**highlighted**) after correction for multiple comparisons (see Method/Statistical analysis).
§ ES marked as 0 if both the ES and the upper limit of the 95% CI are <0.001.

to MRI-defined features were adjusted for gender, age, BMI and the presence of severe cartilage lesions, any BMLs, osteophytes, Hoffa's synovitis and pain considered having significant influence on physical performance resulting to a model that at best accounted for 83.1% variance of self-reported physical functioning. Also, with the exception for BMLs, all covariates showed significant association with either self-reported physical function or performance in at least some physical performance tests. On the other hand, due to adjustment for multiple covariates, the models may also have resulted in diluting some significant associations. Furthermore, other factors that may have influenced physical performance, such as other illnesses[29,43], which were significantly more frequent in the symptomatic subjects, muscle strength[2,14], use of analgesics or fear-avoidance behavior[44,45], were not taken into account. Also, in general, the controls are best recruited from the same source population as the cases, which unfortunately did not happen in our study, which may have served as a potential source of bias. However, failure in matching the study groups on age and BMI should not induce any obvious bias as these factors were included in the regression models. The cross-sectional nature of this study allowed us to examine only the associations between structural features and physical function, which may not have been truly causal but rather reflecting the severity of another underlying structural pathology and/or involvement of some unmeasured symptom- and/or performance-modifying factors, such as physical activity. Also, although the physical function tests were performed mainly at the same day or day after undergoing MRI, and the mean latency between filling the questionnaires and MRI examination was 3.4 days, in which time it is unlikely to have any changes in MRI-features, it is possible that in some subjects (the range of delay 0–41 days) the delay between these measurements may have affected the results. Finally, it is worth to note that the missing association between most MRI-features and physical disability in this study should not be interpreted as a true negative finding without criticism because of limited number of subjects studied (type II error).

In summary, cartilage degeneration showed significant association with both self-reported and objectively measured physical function with moderate-to-small effect sizes. Lateral meniscus maceration and lateral extrusions associated with increased stair ascending time. Osteophytes were associated with decreased self-reported physical function after adjustment for demographic factors and other MRI-features, but the association didn't remain after further adjustment for pain. Knee pain showed a significant association with poor physical function independently from MRI-defined structural pathology.

Author contributions

P. Kaukinen participated in design and conception of the study, literature review, analysis and interpretation of the data and wrote the first draft of the article.

J. Podlipská participated in design and conception of the study, acquiring the data, analysis and interpretation of the data, critical revision of the article for the important intellectual content, and final approval of the article.

A. Guermazi participated in analysis and interpretation of the data, critical revision of the article for the important intellectual content, and final approval of the article.

J. Niinimäki participated in analysis and interpretation of the data, critical revision of the article for the important intellectual content, and final approval of the article.

P. Lehenkari participated in analysis and interpretation of the data, critical revision of the article for the important intellectual content, and final approval of the article.

F. W. Roemer participated in analysis and interpretation of the data, critical revision of the article for the important intellectual content, and final approval of the article.

M. T. Nieminen participated in analysis and interpretation of the data, critical revision of the article for the important intellectual content, and final approval of the article.

J. M. Koski participated in analysis and interpretation of the data, critical revision of the article for the important intellectual content, and final approval of the article.

S. Saarakkala participated in design and conception of the study, analysis and interpretation of the data, critical revision of the article for the important intellectual content, and final approval of the article.

J. P. A. Arokoski participated in design and conception of the study, analysis and interpretation of the data and critical revision of the article for the important intellectual content, and final approval of the article.

Conflict of interests

P. Kaukinen: Activities related to the present article: grant from Finland State Research Funding. Activities not related to the present article: payment for lectures including service on speakers bureaus from MEDA Oy, Pfizer Oy. Other relationships: disclosed no relevant relationships.

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Supplementary data

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