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The association of meniscal damage with joint effusion in persons without radiographic osteoarthritis: the Framingham and MOST osteoarthritis studies[1]

F. W. Roemer M.D.†‡*, A. Guermazi M.D.†, D. J. Hunter M.B.B.S., Ph.D.§||, J. Niu M.D.||,
Y. Zhang D.Sc.||, M. Englund M.D., M.P.H.¶||, M. K. Javaid M.D.#††, J. A. Lynch Ph.D.#,
A. Mohr M.D.‡‡, J. Torner Ph.D.§§, C. E. Lewis M.D.||||, M. C. Nevitt Ph.D.#
and D. T. Felson M.D., MPH||

† Quantitative Imaging Center (QIC), Department of Radiology, Boston University Medical Center, Boston, MA, USA
‡ Department of Radiology, Klinikum Augsburg, Augsburg, Germany
§ Department of Research, New England Baptist Hospital, Boston, MA, USA
|| Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, USA
¶ Lund University, Lund, Sweden
# Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA, USA
†† Botnar Research Centre, University of Oxford, Oxford, United Kingdom
‡‡ Department of Radiology, Sligo General Hospital, Sligo, Ireland
§§ Department of Epidemiology at the University of Iowa, Iowa City, IA, USA
|||| Division of Preventive Medicine, University of Alabama, Birmingham, AL, USA

Summary

Objective: To assess the cross-sectional association between meniscal status and joint effusion on magnetic resonance imaging (MRI) in knees without radiographic osteoarthritis (OA).

Design: Knees without OA (Kellgren/Lawrence grade 0) from the Framingham and MOST studies were examined by MRI. Meniscal status was assessed with a score of 0−4 in the anterior horn/body/posterior horn of the medial/lateral meniscus and effusion was assessed using a score of 0−3. The odds ratios (ORs) of joint effusion in those with meniscal damage were estimated using a logistic regression model. A sub-analysis was performed for knees without MRI-detected cartilage damage.

Results: Of 1368 knees, 296 (21.6%) showed meniscal pathology in at least one subregion. Effusion was present in 133 (44.9%) of knees with meniscal damage vs 328 (30.6%) in those without meniscal damage. The adjusted OR of effusion in a knee with meniscal damage was 1.8, 95% confidence intervals (CI) [1.4, 2.4]. The OR of effusion for the group with meniscal pathology in two compartments was 5.4, 95% CI [2.1, 14.3]. For knees without any cartilage lesions but with meniscal damage in any compartment the OR was 2.3, 95% CI [1.1, 4.5].

Conclusions: Knees without OA but with meniscal pathology exhibit joint effusion to a significantly higher degree than knees without meniscal damage. The association persists for knees without cartilage damage. The prevalence of effusion is further increased when present in two compartments. Concomitant occurrence of synovial activation and meniscal damage contributes to understanding the pathophysiology of early degenerative joint disease.
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Key words: Meniscal tear, Magnetic resonance imaging, Effusion, Osteoarthritis, Synovium, Knee.

Introduction

The meniscus may tear due to knee trauma or spontaneously due to aging and degenerative processes[1−3]. Mechanical impairment of the meniscus will alter the weight-bearing capacities of a joint and may damage the articular chondral surface of the same compartment as well as the subchondral bone[4,5]. Loss of meniscal function is recognized as a potent risk factor for both the development and progression of knee osteoarthritis (OA)[6,7]. Meniscal tears are commonly observed in conjunction with radiographic OA in the elderly population[8−10], but meniscal damage is also prevalent in younger age groups and even in asymptomatic knees without signs of radiographic OA[11].

In addition to being a potent risk factor for knee OA, meniscal damage might also be a trigger of synovial activation. Synovial activation in OA is thought to be triggered by release of detritus from joint structures including cartilage[12]. To phagocytose and eliminate this detritus macrophages in the synovial lining proliferate, inducing inflammatory features in the synovium and consequently thickening. In moderate to advanced OA, ligamentous injury, loose bodies or hyaline cartilage deterioration cause synovial activation. In knees without any evidence of OA, damage to knee structures might trigger synovial activation and this activation might, in turn, provide indirect evidence of ongoing structural damage in the joint. Such damage could be present, for example, in the meniscus (Fig. 1). Animal models have also shown that synovial cell response plays an important role in meniscal tear repair[13,14].
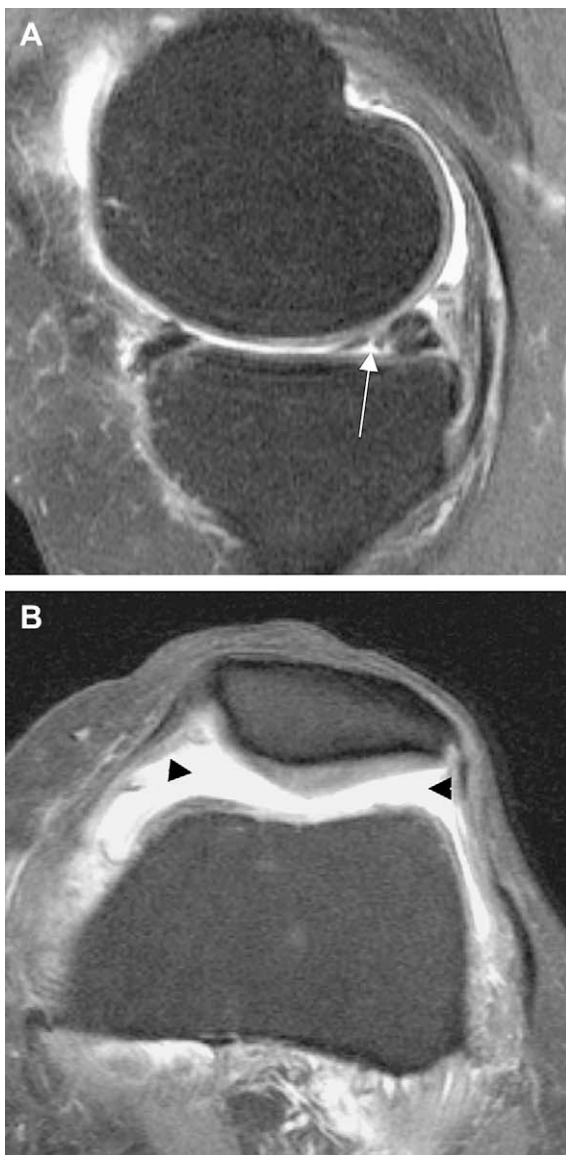
Fig. 1. Example of meniscal tear and concomitant joint effusion. A. Sagittal T2w fat suppressed image. Arrow depicts non-displaced grade-2 meniscal tear in the posterior horn of the medial meniscus. B. Axial T2w fat suppressed image. Grade 2 non-traumatic joint effusion (black arrowheads). Note intact retropatellar cartilage.

Synovial activation of a joint is reflected as synovitis and joint effusion on magnetic resonance imaging (MRI). Direct measures of synovitis are probably ideally obtained from contrast-enhanced MRI assessment of synovial thickness[15,16]. However, joint effusion may be assessed and quantified on non-contrast-enhanced MRI[17−19]. It is not known to what extent meniscal damage in subjects without OA is associated with joint effusion.

This study was performed to analyze the association of meniscal damage and joint effusion in knees without radiographic signs of OA using non-enhanced MRI in a combined patient sample drawn from the Framingham Osteoarthritis Study and the Multicenter Osteoarthritis (MOST) Study. We combined data from two studies in order to have a large number of knees without OA that would permit a robust evaluation of the question.

Methods

SUBJECTS

The study cohort consisted of a combined sample from two large OA studies − the Framingham Osteoarthritis Study and the MOST Study.

FRAMINGHAM SUBGROUP

The Framingham sample was composed of two separate groups, (1) members of the Framingham Heart Study Offspring Cohort and (2) a newly recruited cohort from the town of Framingham, Massachusetts (Community Cohort). Participants in this combined group, designated the *Framingham OA Study Cohort*, were examined between 2002 and 2005.

The Framingham Heart Study Offspring Cohort participants included surviving descendants (and spouses of descendants) of the Original Framingham Heart Study cohort subjects[20]. As part of a study of the inheritance of OA, selected participants were originally examined in 1992−94. Members of this group were identified as potential participants of the current study. All were contacted by telephone and invited to participate in the study. A validated survey instrument[21] supplemented by questions about medication use that would reflect treated rheumatoid arthritis was used to screen potential subjects. Those who screened positively for rheumatoid arthritis were excluded.

The newly recruited participants to the Framingham OA Study Cohort (Community Cohort) were drawn from a random sample of the Framingham, Massachusetts community. Flyers were hung in public areas to increase awareness of the study, which focused on health including bone health, foot health and arthritis. Participants were recruited using random digit dialing and census tract data to ensure inclusion of a representative sample of the community. To be included, subjects had to be at least 50 years old and ambulatory (use of canes and walkers was allowed). Participants with bilateral total knee replacements (TKRs) or a positive screen for rheumatoid arthritis as above[21] were excluded. In neither group was participant selection based on the presence or absence of knee OA or knee pain.

In order assess if a subject had experienced previous knee injury the following question was asked: "Have you ever injured your knee badly enough to limit your ability to walk for at least 3 days?"

Framingham MRI

Based on an agreement with the parent Framingham Heart Study to limit the respondent burden of the Framingham Offspring subgroup, only those who answered affirmatively to the question, "In the past 30 days, have you had any pain, aching or stiffness in either of your knees?" underwent MRI of the knee(s). In these subjects, both knee MRIs were read when acquired. For the community sample, all subjects had bilateral knee MRIs whether or not they had knee symptoms but, because of funding limitations, only the right knee was read. Those participants with MRI contraindications were not scanned, and those with one TKR had only their native knee scanned.

All studies were performed with a 1.5 T MRI system (Siemens, Mountain View, CA) using a phased array knee coil. A positioning device was used to ensure uniform placement of the knees. Imaging sequences included: sagittal (TR 3610 ms, TE 40 ms, 3.5 mm slice thickness, 0 mm interslice gap, 32 slices, 256×256 matrix, 139 mm^2 FOV, echo train length 7), axial (TR 3610 ms, TE 40 ms, 3.0 mm slice thickness, 0 mm interslice gap, 20 slices, 256×256 matrix, 139 mm^2 FOV, echo train length 6) and coronal (TR 3610 ms, TE 40 ms, 3.5 mm slice thickness, 0 mm interslice gap, 30 slices, 256×256 matrix, 139 mm^2 FOV, echo train length 7) T2-weighted turbo spin echo sequences with fat suppression, and a sagittal T1-weighted spin echo

sequence without fat suppression (TR 475 ms, TE 24 ms, 3.5 mm slice thickness, 0 mm interslice gap, 32 slices, 256 × 256 matrix, 139 mm^2 FOV).

Approval for the study was obtained from the Boston University Medical Center Institutional Review Board (IRB).

MOST SUBGROUP

The MOST study is an NIH-funded prospective epidemiological study of 3026 persons aged 50−79 years, with a goal of identifying risk factors for incident and progressive knee OA in a sample with either OA or at high risk of developing it. Those considered at high risk included persons who were overweight or obese, those with knee pain, aching or stiffness on most of the last 30 days, a history of knee injury that made it difficult to walk for at least 1 week, or previous knee surgery.

Subjects were recruited from two US communities, Birmingham, Alabama and Iowa City, Iowa through mass mailing of letters and study brochures, supplemented by media and community outreach campaigns. The study protocol was approved by IRBs at the University of Iowa, University of Alabama, Birmingham, University of California, San Francisco and Boston University Medical Campus.

Subjects were excluded from MOST if they screened positive for rheumatoid arthritis[21], had ankylosing spondylitis, psoriatic arthritis, Reiter's syndrome, had kidney problems requiring hemo- or peritoneal dialysis, a history of cancer (except for non-melanoma skin cancer), had or planned to have bilateral knee replacement surgery, were unable to walk without the help of another person or walker, or were planning to move out of the area in the next 3 years. History of past knee injury was assessed in the same manner than Framingham study.

MOST MRI

MRIs in MOST were obtained in both knees with a 1.0 T dedicated MR system (OrthOne™, ONI Medical Systems, Inc., Wilmington, MA) with a circumferential extremity coil using fat suppressed fast spin echo proton density (PD) weighted sequences in two planes, sagittal (TR 4800 ms, TE 35 ms, 3 mm slice thickness, 0 mm interslice gap, 32 slices, 288 × 192 matrix, 140 mm^2 FOV, echo train length 8) and axial (TR 4680 ms, TE 13 ms, 3 mm slice thickness, 0 mm interslice gap, 20 slices, 288 × 192 matrix, 140 mm^2 FOV, echo train length 8) and a STIR sequence in the coronal plane (TR 6650 ms, TE 15 ms, TI 100 ms, 3 mm slice thickness, 0 mm interslice gap, 28 slices, 256 × 192 matrix, 140 mm^2 FOV, echo train length 8). Only one knee per patient was randomly selected to be read when both knees had been scanned and had available MRI readings.

RADIOGRAPHIC ASSESSMENT IN BOTH STUDIES

In both studies, all subjects underwent weight-bearing posteroanterior (PA) fixed flexion knee radiographs using the protocol by Peterfy *et al.* and a plexiglass positioning frame (SynaFlexer™)[22].

A musculoskeletal radiologist and a rheumatologist experienced in reading study films, both blinded to case/control status and clinical data, graded all PA films according to the Kellgren and Lawrence (K/L) scale[23]. If readers disagreed on the presence of radiographic OA, the film readings were adjudicated by a panel of three readers.

Out of the above defined study samples, we excluded all subjects who exhibited any sign of tibiofemoral radiographic OA (K/L grades 1−4) and retained only knees with K/L Grade 0.

MRI ASSESSMENT FOR BOTH STUDIES

In both studies two musculoskeletal radiologists (for the Framingham study FWR and AM; for the MOST study FWR and AG), blinded to clinical and X-ray data, read the MRIs.

Meniscal integrity was graded according to the Whole-Organ MRI Score (WORMS) method[17]. The anterior horn, body segment, and the posterior horn of the medial and lateral menisci were scored separately from 0 to 4: 0 = intact; 1 = minor radial or parrot-beak tear; 2 = non-displaced tear; 3 = displaced tear; 4 = complete maceration or destruction (inter-observer reliability for meniscal scoring in the Framingham study: weighted-kappa 0.70, 95% confidence intervals (CI) [0.64, 0.76]; in the MOST study: weighted-kappa 0.79, 95% CI [0.59, 0.97]). According to the WORMS system meniscal *damage* or *pathology* was defined as a tear, maceration, and (or) destruction (=any grades ≥ 1 on scale above). The readers regarded intrameniscal signal as a meniscal tear only when it communicated with the meniscal inferior or superior margin on at least two slices. Intrameniscal signal alterations that did not fulfill the aforementioned criteria of a tear were scored as no tear (Grade 0).

Joint effusion was graded from 0 to 3 in terms of the estimated maximal distention of the synovial cavity according to the WORMS scoring system: 0 = normal; 1 = <33% of maximum potential distention; 2 = 33−66% of

maximum potential distention; 3 = >66% of maximum potential distention. Joint effusion was defined as any joint effusion score ≥1. (Inter-observer reliability for effusion scoring in the Framingham study: weighted-kappa 0.70, 95% CI [0.62, 0.79]; in the MOST study: weighted-kappa 0.73, 95% CI [0.53, 0.92]).

STATISTICAL ANALYSIS

We first computed the overall prevalence of meniscal damage in the study sample. We then evaluated the association between meniscal damage and presence of joint effusion using logistic regression adjusting for gender, age, body mass index (BMI) and study site, with knees without meniscal damage as the reference group. Before combining the subsamples we examined the data to be sure that results were consistent in both sites. A subanalysis was performed concerning joint effusion present in knees with meniscal pathology in only one or in both, the medial and lateral tibiofemoral compartments. An additional analysis was performed for knees with no cartilage damage (WORMS score ≤ 1) in the tibiofemoral and patellofemoral compartments.

Results

PATIENT DEMOGRAPHICS

The combined study sample included 1368 knees (918 from the Framingham study and 451 from the MOST study) with no signs of radiographic OA (K/L grade 0). Of these, 387 (28.3%) were also free of MRI-defined cartilage damage. On average the subjects in both studies were elderly and overweight, and there were more women than men. Significant differences between the two study samples were found for age and BMI with the MOST participants being slightly younger, more overweight and having experienced more knee injuries in the past. When comparing the subgroups without cartilage damage, no significant demographic differences were observed between the Framingham and MOST participants (Table I). Regarding maximal meniscal damage severity, also no significant demographic differences were observed (Table II). *P* values ranged from 0.10 for age to 0.87 for gender.

MENISCAL STATUS

296 (21.6%) of the knees showed evidence of meniscal damage. Of these, 276 (93.2%) showed damage in only one compartment, and 20 (6.8%) showed damage in both the medial and lateral compartments. Of the 60 knees with meniscal damage and without cartilage lesions only one (1.7%) knee had signs of meniscal damage in both compartments.

Concerning maximal meniscal damage in any subregion, 164 (55.4%) knees exhibited grade 1 tears. 107 (36.2%) showed grade 2 tears, and 25 (8.4%) had grade 3 or 4 tears with only one knee exhibiting a grade 4 meniscal lesion. No significant differences were observed between subjects with grade 1, grade 2 and grade 3−4 meniscal lesions concerning age, BMI and gender (Table II).

JOINT EFFUSION IN K/L 0 KNEES AND ITS ASSOCIATION WITH MENISCAL DAMAGE

Joint effusion (any grade) was present in 461 (33.7%) knees in the combined study sample (K/L grade 0 knees). 328 (30.6%) knees without meniscal damage and 133 (44.9%) knees with meniscal damage exhibited joint effusion. 119 (43.1%) knees with unicompartmental meniscal damage and 14 (70.0%) knees with pathology in two compartments showed joint effusion. The large majority of joint effusions were small (Table III).

Table I
Demographic overview of the subjects in the Framingham and MOST studies

	Both studies combined (N = 1368)	Framingham study (N = 918)	MOST study (N = 450)
All subjects without radiographic OA (K/L grade = 0)			
Age	61.9 ± 8.2	62.6 ± 8.4	60.6 ± 7.5*
% women	57.5	56.8	59.1
BMI	28.5 ± 5.2	28.2 ± 5.4	29.0 ± 4.5*
% previous knee injury	12.1	9.3	17.6*

	Both studies (N = 387)	Framingham Study (N = 274)	MOST Study (N = 113)
Subjects with no radiographic OA and no cartilage damage on MRI			
Age	60.7 ± 7.9	60.7 ± 8.0	60.6 ± 7.6
% women	58.5	57.6	60.8
BMI	27.9 ± 4.9	27.8 ± 5.2	28.1 ± 4.0
% previous knee injury	9.5	6.8	16.0*

*Statistically significant defined as $P < 0.05$.   BMI body mass index K/L Kellgren/Lawrence.

The adjusted odds ratio (OR, 95% CI) of any joint effusion in knees with meniscal damage was 1.8 (1.4, 2.4) using knees without meniscal damage as the reference. The OR of joint effusion for the subgroup with damage in only one compartment was 1.7 (1.3, 2.2) and 5.4 (2.1, 14.3) for the group with pathology in two compartments (Table IV).

JOINT EFFUSION IN K/L GRADE 0 KNEES WITHOUT CARTILAGE DEFECTS AND ITS ASSOCIATION WITH MENISCAL DAMAGE

Joint effusion (any grade) was present in 60 (15.7%) knees in the subgroup without MRI-detected cartilage damage. 45 (14.0%) knees without meniscal damage and 15 (25.0%) knees with meniscal damage exhibited joint effusion.

The adjusted OR (95% CI) of any joint effusion in a knee with meniscal damage was 2.3 (1.1, 4.5), with knees without meniscal damage as the reference group (Table V).

Discussion

In a large sample of middle-aged and elderly adults with no signs of radiographic OA from two large OA studies, we examined the association of meniscal damage and joint

Table II
Demographic overview concerning the distribution of meniscal damage severity

	1, N = 164 (55.4%)	2, N = 107 (36.2%)	3–4, N = 25 (8.4%)
Maximal meniscal damage in knees with meniscal damage (N = 296)			
Age	63.5 ± 8.8	65.8 ± 8.8	63.8 ± 8.5
BMI	28.0 ± 5.2	28.1 ± 4.7	29.8 ± 5.7
Women, %	41.5	41.1	36.0

BMI body mass index.

Table III
Prevalence of joint effusion and relation to meniscal damage

Meniscal damage	Joint effusion		
	0 (%)	1 (%)	2–3 (%)
Absence (N = 1072)	744 (69.4)	295 (27.5)	33 (3.1)
Presence (N = 296)	163 (55.1)	109 (36.8)	24 (8.1)
Present in one compartment (N = 276)	157 (56.9)	96 (34.8)	23 (8.3)
Present in both compartments (N = 20)	6 (30.0)	13 (65.0)	1 (5.0)

effusion. A significant association was observed that was also confirmed for the subgroup without cartilage damage.

Our findings suggest that synovial activation reflected as joint effusion on MRI may be triggered by meniscal pathology, which is supported by the findings of previous work on animal models. These studies described marked synovial stimulation during the healing phase of meniscal tears or enhancement of repair through synovial activation[13,14,24]. However, we cannot comment on whether tears and effusion are truly subsequent events or if effusion might precede meniscal damage or might even have a damaging effect on meniscal composition, which will ultimately result in a tear. Only a longitudinal study with multiple visits over short periods of time might clinically be able to show the train of events.

MRI diagnosis of meniscal pathology is reliable and well-accepted in clinical practice, and has been reported to have a sensitivity and specificity in the range of 80–95% compared with a reference standard of arthroscopic inspection and probing[25,26]. Our findings suggest that meniscal tears are common in knees without radiographic OA. About a fifth of the knees (all K/L grade 0) exhibited meniscal damage in our study sample, while in the whole population-based Framingham study sample of middle-aged and elderly persons (irrespective of radiographic OA status and symptoms) about one-third of knees had meniscal damage[10]. In addition, a recent study that examined a small cohort of asymptomatic postmenopausal women reported meniscal tears in nearly half of the knees[27].

We found that one-third of the knees in our sample showed joint effusion. In another large study examining the probability of radiographic OA in elderly patients with knee pain, the subgroup without radiographic OA (K/L = 0 and 1) exhibited palpable joint effusion in 21%[28]. The amount of moderate to gross effusion in that study was higher than in our cohort, which showed large grade

Table IV
Cross-sectional association of joint effusion (all grades ≥1) with meniscal damage (any grades ≥1 in any subregion) on MRI for all knees without radiographic OA (K/L grade = 0)

Meniscal damage	Joint effusion		Adjusted OR*
	0 (%)	1–3 (%)	
Absence (N = 1073)	744 (69.4)	328 (30.6)	1.0 (reference)
Presence (N = 296)	163 (55.1)	133 (44.9)	1.8 (1.4, 2.4)
Present in one compartment (N = 276)	157 (56.9)	119 (43.1)	1.7 (1.3, 2.2)
Present in both compartments (N = 20)	6 (30.0)	14 (70.0)	5.4 (2.1, 14.3)

*Adjusting for age, sex, BMI, and study site.

Table V
Cross-sectional association of joint effusion (all grades ≥ 1) with meniscal damage (any grades ≥ 1 in any subregion) on MRI for knees without cartilage damage only (N = 381)

Meniscal damage	Joint effusion		Adjusted OR*
	0 (%)	1−3 (%)	
Absence (N = 321)	276 (86.0)	45 (14.0)	1.0 (reference)
Presence (N = 60)	45 (75.0)	15 (25.0)	2.3 (1.1, 4.7)

*Adjusting for age, sex, BMI, and study site.

2 and 3 effusions in only 4%. These discrepant findings are explained by the higher sensitivity of MRI for the detection of joint effusion compared to physical examination. Secondly, the two study samples are only marginally comparable despite having no radiographic OA. Hayes *et al.* detected joint effusion in about 10% of the knees in their mixed study sample concerning OA status and meniscal tears in 27%[29]. This group used a different effusion definition which might further explain the discrepant number to our findings. A large study assessing inflammation in painful knee OA using ultrasound found a prevalence of effusion in 44% of the examined knees[30]. There are no comparable population-based studies available that describe non-traumatic joint effusion in a population without knee OA. In the subgroup without any cartilage damage joint effusion was observed in several knees that exhibited no concomitant meniscal damage. One reason explaining this finding is that intrameniscal pathology that did not fulfill the criteria of damage or other intraarticular lesions might have been present in these knees. It also has been shown that a large number of radiographically normal knees exhibit some intraarticular pathology on MRI[31].

There are several limitations to our study that bear mention. Some other underlying conditions that may trigger non-traumatic effusion despite meniscal damage must be considered in the differential diagnosis. The most common reasons for non-traumatic effusion beside OA are infection, rheumatic disease, crystal induced arthropathies, other more rare rheumatic conditions and tumor[32−34]. Patients were screened for rheumatoid arthritis with a validated screening tool and those who screened positive were excluded prior to participation in the study. The MRI analysis did not suggest a knee tumor or signs of a septic joint that might be attributable to effusion. A limitation of the WORMS method of semiquantitative meniscal scoring is that it does not differentiate between a meniscal tear and partial resection or maceration. Also mucoid degeneration, a common finding of unknown clinical relevance is not scored in WORMS.

In summary, we found a prevalence of meniscal damage in about one-fifth and effusion in about one-third of knees. After adjusting for age, gender, BMI and study cohort we found a significant association of joint effusion for knees with meniscal damage when compared to knees without damage. Also, the presence of joint effusion was even more frequent when meniscal tears were present in both tibiofemoral compartments. As meniscal tears are a potent risk factor for the development of OA[35] the presence of an isolated joint effusion might place subjects also at greater risk for subsequent OA. The described association of meniscal damage and concomitant joint effusion should warrant further longitudinal investigation to help understand the role of synovial activation in early knee OA.

Conflict of interest

Acknowledgments

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