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RELATION OF MENISCUS PATHOLOGY TO PREVALENCE AND WORSENING OF PATELLOFEMORAL JOINT OSTEOARTHRITIS: THE MULTICENTER OSTEOARTHRITIS STUDY

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Abstract

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AUTHORS CONTRIBUTIONS

All authors were fully involved in drafting the article and all authors approved the final version to be submitted for publication.

COMPETING INTERESTS

AG is the President and shareholder of Boston Imaging Core Lab, LLC. AG is also a consultant for Genzyme, MerckSerono, OrthoTrophix, TissueGene and AstraZeneca. FWR is a CMO and shareholder of BICL, LLC.

AUTHOR CONTRIBUTIONS STATEMENT

All listed authors made substantial contributions to all three sections listed below:
(1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and (3) final approval of the version to be submitted
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Objective—To determine the relationship of meniscal damage to magnetic resonance imaging (MRI) features of compartment-specific patellofemoral joint (PFJ) osteoarthritis (OA) at baseline and 2 years later.

Method—Individuals from a prospective cohort of individuals aged 50-79 with or at risk of knee OA were included. At the 60-month and 84-month study visit, Whole-Organ MRI Score (WORMS) was used to assess meniscal tears and extrusions as well as cartilage damage and bone marrow lesions (BMLs) in the medial and lateral patella and trochlea. Worsening of structural features was defined as any increase in WORMS score from 60 to 84 months. Logistic regression was used to determine the cross-sectional and longitudinal relation of meniscus damage to features of compartment-specific PFJ OA.

Results—Relative to knees without lateral meniscal pathology at baseline, those with grade 3-4 lateral meniscal tear and extrusion had greater risk of worsening of cartilage damage in the lateral PFJ two years later (Risk ratio: 1.7 [95% CI: 1.1-2.7) and (1.7 [1.2-2.5]), respectively. Relative to those without medial meniscal pathology at baseline, those with grades 1-2 (0.6 [0.4-0.9]) and 3-4 (0.7 [0.5-1.0]) medial meniscal tears had lower risk of worsening of BMLs in the medial PFJ two years later.

Conclusion—Meniscal tear and extrusion are associated with increased risk of medial and lateral PFJ OA and more severe meniscal pathology is associated with worsening of PFJ OA two years later. Lateral meniscal pathology appears to be more detrimental to the lateral PFJ.

Keywords

Knee osteoarthritis; MRI; cartilage damage; bone marrow lesion; meniscal tear; meniscal extrusion

INTRODUCTION

Knee osteoarthritis (OA) is a leading cause of disability worldwide[1]. The development and worsening of knee OA is dependent on interactions between several biomechanical and biochemical factors[2]. One of these factors is meniscus damage, which is the focus of the current paper. Meniscal damage, frequent in both athletic and general populations[3, 4], is a major risk factor for development of tibiofemoral joint (TFJ) OA[3–5]. Meniscal damage increases the risk of incident and enlarging bone marrow lesions (BMLs)[6, 7] and the risk of cartilage loss in the TFJ[8]. The patellofemoral joint (PFJ) is frequently affected by OA[9, 10], a potent source of symptoms in knee OA[11], affected earlier than the TFJ and PFJ OA increases the risk of TFJ OA development and progression[9, 10]. However, for the most part, research has focused on risk factors associated with TFJ OA. Although there is ample evidence that meniscus injuries significantly increase the risk of TFJ OA[8, 12], the relationship between meniscus injuries and development of PFJ OA is not well known.

The meniscus is essential for stability and transmission of TFJ loads[13]. When the meniscus is intact, it has a multidirectional stabilizing function, limiting excess motion in all directions[14]. Damage to the meniscus alters normal knee joint mechanics, which can result in decreased contact area and increased contact pressure, potentially leading to initiation of cartilage damage and the development of OA[13, 15, 16]. It is plausible that meniscus damage

mechanically affects transverse plane motion[17]. Stress distribution of the PFJ is affected by tibial rotation, which may alter PFJ contact pressure, and subsequently, result in the development of PFJ OA[18–20]. In individuals following meniscectomy, the combined TFJ and PFJ OA pattern is evident in 18% and associated with worse symptoms, poorer function and worse knee-related quality of life than isolated TFJ OA[21].

The mechanism of meniscal pathology and OA in the TFJ is compartment-specific. It has been suggested that mechanical impairment of the meniscus caused by medial or lateral meniscal pathology may alter the weight-bearing capacities of the medial or lateral TFJ, respectively[22]. Recent evidence suggests that lateral PFJ OA is more symptomatic than medial PFJ OA[23, 24]. Thus, understanding compartment-specific risk factors for PFJ OA in individuals with meniscus pathology will assist in developing compartment-specific treatment strategies such as taping and bracing for PFJ OA[25, 26] and identify disease-modifying treatments[26, 27] to prevent or ameliorate PFJ OA. Therefore, this study aimed to: (i) determine the cross-sectional (at one time point) relation of meniscus damage to prevalent compartment-specific magnetic resonance imaging (MRI) features of PFJ OA; and (ii) determine the longitudinal (over 2 years) relationship of meniscus damage to worsening compartment-specific MRI features of PFJ OA over two years.

METHODS

Study population

The Multicenter Osteoarthritis (MOST) Study is an NIH-funded longitudinal, prospective, observational study of 3,026 older adults, aged 50-79 years, who have or are at risk of knee OA. Subjects were recruited from two communities in the US: Birmingham, Alabama, and Iowa City, Iowa. Full details of the study population have been previously published[28]. In the present study, a sample of 1185 knees, which underwent MRI at 60 (current study's baseline) and 84 months (current study's follow-up) were included.

Magnetic resonance imaging acquisition

Knee MRIs were acquired using a 1.0 Tesla extremity MRI unit (OrthOneTM, ONI Medical Systems, Wilmington, MA) with a phased array knee coil to obtain the following sequences: Fat-suppressed fast-spin echo proton density-weighted (PD) 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 mm2 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 mm2 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 mm2 FOV, echo train length 8). Two musculoskeletal radiologists (AG and FR) used the Whole-Organ Magnetic Imaging Score (WORMS) to assess meniscus damage, cartilage morphology and BMLs[29].

Meniscal damage assessment

Meniscal tear and extrusion were assessed from the 60-month study visit MRIs. Sagittal fat suppressed proton density weighted images were used to assess in the posterior and anterior

horns. Coronal STIR images were used for the evaluation of meniscal body, and medial and lateral meniscal extrusion. Meniscal assessment used the WORMS method from 0 to 4: 0, intact meniscus; 1, minor radial or parrot beak tear; 2, non-displaced tear; 3, displaced tear or partial maceration or destruction; and 4, complete maceration or destruction in the anterior, body and posterior horn in the medial and lateral meniscus (Figure 1). Meniscal extrusion was scored using the modified WORMS method from 0-2; where, a score of 0 indicated meniscal extrusion absent; 1, <50%; and 2, >50%. Meniscal extrusion was defined as WORMS score>0[30] (Figure 2). Inter-reader reliability (weighted kappa) of the two readers for meniscal damage and extrusion was 0.60 and 0.80, respectively.

Patellofemoral joint structural damage assessment

The WORMS method was used to define MRI features of PFJ OA based on previously published methods[31–33]. Four PFJ subregions were assessed: medial and lateral patella, and medial and lateral trochlea. The cartilage scale ranges from 0-6, where 0 = normal cartilage morphology; 1 = normal thickness but increased signal on proton density-weighted fat suppressed images; 2 = a single partial thickness focal defect <1 cm in greatest width; 2.5 = a single full thickness focal defect <1 cm in greatest width; 3 = multiple areas of partial thickness (Grade 2) defects intermixed with areas of normal thickness, or a Grade 2 defect wider than 1cm but <75% of the region; 4 = diffuse (≥75% of the region) partial thickness loss; 5 = multiple areas of full thickness loss (Grade 2.5) or a Grade 2.5 lesion wider than 1cm but < 75% of the region; 6 = diffuse (≥75% of the region) full-thickness loss. The bone marrow lesion (BML) scores range from 0-3, where 0 = normal; 1 = <25% of region; 2 = medium, 25 to 50% of region, 3 = large, >50% of region (Figure 3). Any cartilage damage was defined as WORMS score≥2; full thickness cartilage damage as WORMS scores 2.5 (focal), 5 and 6 (diffuse); and any BML as WORMS ≥1 (Figure 3). Worsening of cartilage damage and BMLs were defined as any increase within-grade scoring from 60 (baseline) and 84 (follow-up) months, including within-grade changes in order to increase sensitivity to change[34]. Inter-reader reliability (weighted kappa) for cartilage damage and BMLs was 0.85 and 0.89, respectively.

Statistical analyses

Logistic regression analyses were used to determine the relation of meniscus damage to compartment-specific prevalence (60-months) and worsening (from 60 to 84 months) of MRI features of PFJ OA. Prevalence ratios were determined for analyses at 60-months and risk ratios were determined for analyses from 60 to 84 months. The maximum score in any meniscus region was used to categorize tears (exposure) as none (grade 0), minor (grades 1-2) and severe (grades 3-4)[30]. Separate models were used for the medial and lateral PFJ (outcomes). Each knee contributed two subregions (e.g., patella and trochlea) for the medial and lateral analyses. Generalized estimating equations (GEE) were used to account for the correlation between two subregions within a knee. Since worsening was defined as any increase in WORMS score, subregions with maximum WORMS score at 60-months were excluded from the longitudinal analyses. A prior history of knee injury or surgery was assessed with two questions: (i) “Have you injured your knee badly enough that limited your ability to walk for at least two days” and (ii) “Have you had any surgery in your knee?” A dichotomous variable was created based on a‘yes’ response to either of the questions and

included as a covariate. All analyses were adjusted for age, sex, body mass index and previous knee injury or surgery. As frontal plane knee alignment could precede meniscus tears, although the exact sequence of development of OA is unknown, in sensitivity analyses we adjusted for frontal plane knee alignment assessed from long limb films.

RESULTS

For the current study, 1185 knees (one knee per subject) were included. The mean age and body mass index was 66.9±7.6 years and 29.7±4.8 kg/m^2, respectively; 62% were females and 16% had history of knee injury or surgery at 60-month study visit.

Prevalence of meniscus tear and extrusion

The prevalence proportions of meniscus tear and extrusion, and patellofemoral joint damage are presented in Table 1 for individuals at the 60-month study visit (the current study's baseline visit).

Relation of meniscus tear to patellofemoral joint structural damage

The cross-sectional analysis revealed that individuals with grade 3-4 medial meniscus tear and those with grade 3-4 lateral meniscus tear had higher prevalence of any cartilage damage in the medial and lateral PFJ, respectively (Table 2). In sensitivity analyses when adjusting for frontal plane alignment, the results were not statistically significant for medial and lateral meniscus tear and prevalence of any cartilage damage in the medial (Risk ratio: 1.0 [95% confidence interval: 0.9-1.1]) and lateral (1.1 [0.9-1.3]) PFJ, respectively. Relative to individuals without medial meniscus tear, those with grade 3-4 medial meniscus tear had lower prevalence of full-thickness cartilage damage and BMLs in the medial PFJ (Table 2). Results were similar in sensitivity analyses when adjusting for frontal plane alignment.

In the longitudinal analysis, those with grades 1-2 and 3-4 medial meniscus tears had lower risk of worsening of BMLs in the medial PFJ compared to those without medial meniscus tear (Table 2). Sensitivity analyses when adjusting for frontal plane alignment revealed that those with grades 1-2 and 3-4 medial meniscus tears had a 40% (0.6 [0.4-0.9]) and 40% (0.6 [0.4-0.9]) reduction in the risk of worsening of BMLs in the medial PFJ relative to those without medial meniscus tear two years later. Relative to those without lateral meniscus tear, those with grades 3-4 lateral meniscus tear had a greater risk of worsening cartilage damage in the lateral PFJ two years later (Table 2) When adjusting for frontal plane alignment in sensitivity analyses results were attenuated (1.5 [0.9-2.4]).

Relation of meniscus extrusion to patellofemoral structural damage

Those with medial meniscus extrusion had greater prevalence of any cartilage damage and full thickness cartilage damage in the medial PFJ compared to those without medial meniscus extrusion (Table 3). When adjusting for frontal plane alignment in sensitivity analyses results were similar. Those with lateral meniscus extrusion had greater prevalence of any cartilage damage and BMLs in the lateral PFJ compared to those without lateral meniscus extrusion (Table 3). When adjusting for frontal plane alignment in sensitivity

analyses no relation was found between lateral meniscus extrusion and cartilage damage (any or full-thickness) or BMLs.

In the longitudinal analysis, relative to those without lateral meniscus extrusion at the 60-month study visit, those with lateral meniscus extrusion had greater risk of worsening cartilage damage in the lateral PFJ two years later (Table 3). When adjusting for frontal plane alignment, results were slightly attenuated (RR=1.5 [1.0-2.3]).

DISCUSSION

Our findings revealed that medial and lateral meniscal pathology are associated with an elevated prevalence of MRI-detected cartilage damage in the medial and lateral PFJ, respectively. Lateral meniscus tear appears to have a greater association with lateral PFJ OA than medial meniscus tear with medial PFJ OA. Relative to knees without lateral meniscus pathology at baseline, knees with lateral meniscus tear or extrusion had roughly twice the risk of worsening cartilage damage over two years in the lateral PFJ. Interestingly, medial meniscus tear at baseline was protective against worsening of BMLs over two years in the medial PFJ, and medial meniscus extrusion had no significant effect on worsening of OA features in the medial PFJ.

The medial meniscus is attached more firmly attached to the tibia and medial collateral ligament relative to the lateral meniscus, which is more mobile and is not robustly anchored to the lateral collateral ligament. Decreased mobility, combined with the increased loading experienced medially, contribute to a higher incidence of medial meniscus injuries in general populations[35–37]. This pattern was reflected in the current study, with a higher prevalence of medial meniscus pathology (40% tears, 44% extrusion) than lateral meniscus pathology (14% tears, 8% extrusion). Although medial meniscus pathology is more common, lateral meniscus pathology appears to be more detrimental to the PFJ. When the meniscus is intact, the medial meniscus sustains maximal loads during internal rotation, whereas the lateral meniscus sustains maximum loads with external rotation[38]. Thus, it is plausible that lateral meniscus pathology has a greater impact on tibial rotational when combined with the decreased stability provided by the convex surface of the lateral tibial plateau[22]. This abnormal tibial motion may, in turn, affect the stress distribution of the medial and lateral PFJ[18–20], leading to PFJ damage. However, further research is needed to explore compartment-specific biomechanical consequences of medial and lateral meniscal pathology.

Frontal plane mal-alignment is a risk factor for TFJ OA and PFJ OA[39–41] and meniscus tears[40, 42]. Presence and severity of medial meniscus tear has been associated with increased peak knee adduction moment, a major determinant of the load passing through medial TFJ, in women without knee OA[43]. Therefore, it is plausible that aberrant frontal plane mechanics may play a role in meniscus pathology and development of knee OA. However, it is unclear whether static frontal plane malalignment precedes meniscus pathology or meniscus pathology directly contributes to altered knee malalignment. When we adjusted for static frontal plane knee alignment, in general, our results were attenuated.

Our study suggests meniscus extrusion is more strongly related to PFJ OA, at baseline and two years later than a meniscal tear. This may be explained by the relative heterogeneity of the WORMS grading system for meniscal damage, which is mainly based on the presence of meniscal destruction (maceration) and fragment displacement, rather than morphology of meniscal tears, unlike more recent grading systems such as MRI Osteoarthritis Knee Score (MOAKS)[44]. Despite the lack of longitudinal studies, recent literature suggests morphologic types of meniscal tears may be relevant for the progression of knee OA[45]. However, it is known that meniscus extrusion is an independent predictor of cartilage loss in the TFJ[8, 46]. It is plausible that diminished meniscal coverage and height due to meniscal extrusion results in greater alterations in tibial motions than meniscal tear; thus, increasing the damage to PFJ. In addition to biomechanical factors, it is plausible that biochemical factors may contribute to progression of PFJ OA in individuals with meniscal pathology. There is increasing evidence that synovitis plays a critical role in onset and progression of knee OA[47, 48]. It is plausible that synovitis caused by meniscal pathology[49] may be contributing to initiation and worsening of cartilage damage in the PFJ.

This is the first study to report the relation of meniscal pathology to MRI features of PFJ OA. An elevated prevalence of PFJ OA in individuals with meniscus pathology highlights that the TFJ is not the only knee compartment affected by meniscus pathology. A recent systematic review highlighted the effectiveness of exercise therapy for individuals with meniscus lesions[50]. Therefore, in addition to TFJ OA treatments, it is also important to consider treatments specifically designed for PFJ OA[25, 26] for OA management following meniscus pathology and identify PFJ disease-modifying treatments[26, 27]. Englund et al.[51] have previously reported an association between prevalence of meniscus damage and radiographic hand OA, suggesting non-age related systemic factors that may be influencing both the risk of hand OA and meniscus damage. Therefore, it is also important to explore systemic risk factors for PFJ OA and meniscal damage.

There are a number of limitations of our study that should be considered. Firstly, due to the cross-sectional nature of our main results at baseline, we cannot infer causality. Therefore, further research is needed to determine the exact causal pathway of initiation of PFJ OA, and the role of meniscus tear or extrusion. Secondly, we assessed medial and lateral meniscus tears and extrusions separately. We acknowledge that knees may have had a combination of meniscus pathology, and this may have influenced the results. Thirdly, there are a number of independent factors that may contribute to initiation and worsening of structural damage in the PFJ that we did not adjust for in our analyses because the exact temporal relationship is unknown. Fourthly, 1.0 Tesla extremity MRI was used for knee imaging. The lower imaging resolution may increase the possibility of misclassification of meniscal damage or PFJ structural damage. However, 1.0 Tesla extremity MRI image quality is sufficient for semi-quantitative knee OA whole organ assessment and has been validated using a 1.5 Tesla large-bore system[52]. Lastly, we did not adjust for frontal plane alignment in our main analyses because the exact causal sequence of OA development is unknown (i.e., altered frontal plane alignment may precede meniscus damage or be a consequence of it). However, in sensitivity analyses, we adjusted for frontal plane alignment and in general, our results were attenuated. This suggests that frontal plane alignment may be an intermediate variable between meniscus tear and PFJ OA. While a formal mediation analysis was not done and is beyond

the scope of the current analysis, future research to determine the temporal sequence of the development of PFJ OA is warranted.

In summary, the presence of meniscus pathology was associated with an elevated prevalence of MRI-detected cartilage damage in the PFJ. Furthermore, severe lateral meniscus tears and extrusion at baseline were associated with worsening of PFJ OA features two years later. These findings suggest that meniscal pathology not only has deleterious effects on the TFJ but also the PFJ. Further research is necessary to understand the mechanism of OA development in the PFJ following meniscus pathology.

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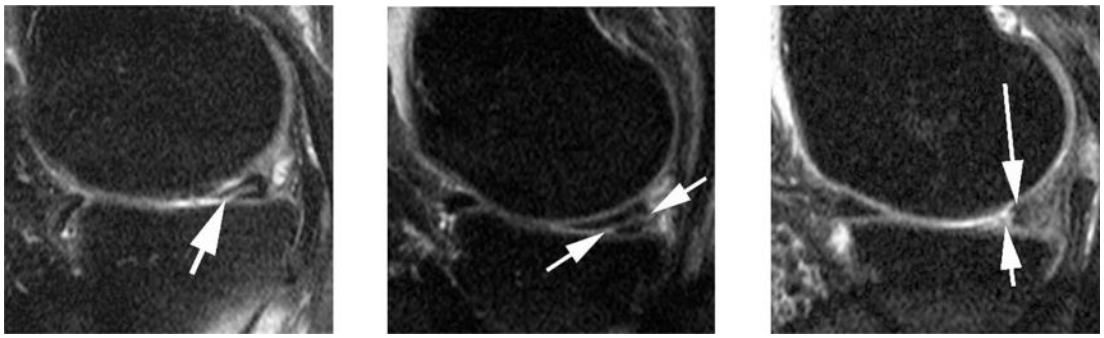

Figure 1.

Examples of different grades of meniscal damage in using the Whole-Organ Magnetic Imaging Score scoring system. Left side image: A Grade 1-lesion is defined as a minor or parrot-beak tear as shown in this sagittal intermediate- weighted fat suppressed image. Image depicts a horizontal-oblique tear of the posterior horn of the medial meniscus opening to the meniscal undersurface (arrow). Center image: A grade 2 lesion is defined as a non-displaced tear as shown in this example. There is a linear hyper intensity in the medial posterior horn opening to the meniscal undersurface and the posterior meniscal basis (arrows). Right side image: Grade 3 meniscal damage is defined as a displaced tear or partial maceration or destruction as shown in this image. There is partial maceration of the medial posterior horn with missing meniscal substance of the free edge (short arrow). There is only a remnant of normal meniscal substance observed posteriorly (long arrow). Grade 4 meniscal damage is defined as complete maceration or destruction and is not shown.

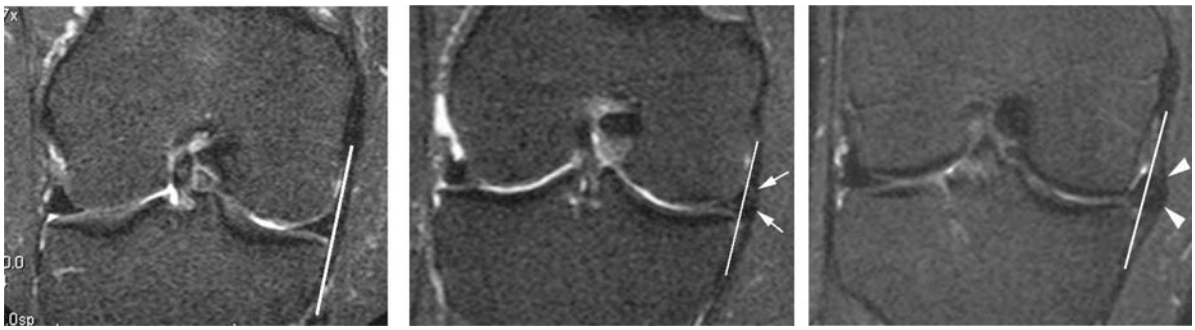

Figure 2.

Examples of meniscal extrusion. Left side image: Coronal STIR image shows grade 0 extrusion of the medial meniscus, which appears aligned to the medial tibial plateau (line). Center image: Example illustrates grade 1 meniscal extrusion (arrows) as seen on coronal STIR image with less than 50% of meniscal body extrusion beyond the tibial plateau (line indicates grade 0 extrusion, i.e. alignment with tibial plateau). Right side image: Grade 2 extrusion (of more than 50% of meniscal body extrusion) is shown in this example (arrowheads). Line indicates alignment with tibial plateau as it would be seen in grade 0 extrusion.

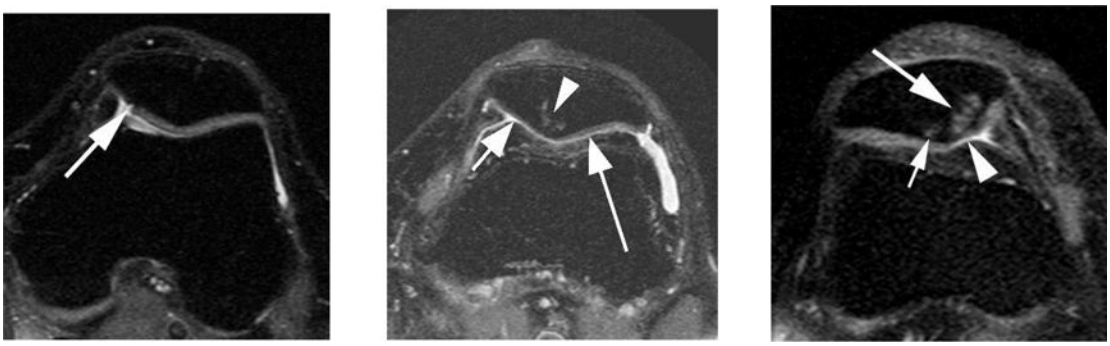

Figure 3.

Examples of patellofemoral structural damage. Left side image: Axial intermediate-weighted fat suppressed image shows a full thickness fissure-like (grade 2.5) cartilage lesion o the medial patella (arrow) without associated bone marrow changes. Center image: Diffuse cartilage thinning (grade 4 in Whole-Organ Magnetic Imaging Score – short arrow) of the medial patella facet and widespread superficial cartilage damage (grade 3) of the medial facet (long arrow) is shown in this example. In addition there is a bone marrow lesion at the patella apex (arrowhead). Right side image: A large grade 3 bone marrow lesion is seen in the medial patella in this example (large arrow). In addition there is a discrete grade 1 BML of the lateral facet (small arrow) and superficial grade 3 damage of the cartilage of the medial patella (arrowhead).

Table 1

Prevalence of Exposure (Meniscus Tear and Extrusion) and Outcomes (Patellofemoral Joint Damage)

Exposure at 60-months	**Medial (n=1185 knees)**	**Lateral (n=1185 knees)**
Meniscus tear n (%)		
Grade 0	709 (59.8)	1020 (86.1)
Grades 1–2	214 (18.1)	89 (7.5)
Grades 3–4	262 (22.1)	76 (6.4)
Meniscus extrusion n (%)	522 (44.1)	100 (8.5)
Patellofemoral Joint Outcomes at 60-months	**Medial PFJ (n=2370 eligible subregions *)**	**Lateral PFJ (n=2370 eligible subregions *)**
Any Cartilage Damage n/N (%)	1291/2305 (56.0)	926/2305 (40.2)
Full-Thickness Cartilage Damage n/N (%)	339/2305 (14.7)	320/2305 (13.9)
Any Bone Marrow Lesion n/N (%)	660/2302 (28.7)	573/2301 (24.9)
Outcomes from 60-84 months		
Worsening of cartilage damage n/N (%)	161/2270 (7.1)	183/2201 (8.3)
Worsening of Bone Marrow Lesions n/N (%)	225/2280 (9.9)	226/2280 (9.9)

* Denominators vary based on some unreadable MRI images and subregions with maximum score at 60 months excluded from worsening analysis

Table 2

Relationship of Meniscus Tear to Patellofemoral Structural Damage

	Medial PFJ Damage			Lateral PFJ Damage		
	No Medial Meniscus Tear	**Grade 1–2 Medial Meniscus Tear**	**Grade 3–4 Medial Meniscus Tear**	**No Lateral Meniscus Tear**	**Grade 1–2 Lateral Meniscus Tear**	**Grade 3–4 Lateral Meniscus Tear**
60-MO (cross - sectional analysis)						
Any Cartilage Damage						
WORMS ≥ 2 n/N	782/1388	208/412	301/505	781/1985	70/173	75/147
(%)	56.3	50.5	59.6	39.4	40.5	51.0
*Adjusted OR	1.0	0.9	**1.1**	1.0	1.0	**1.2**
(95% CI)	REF	0.8-1.1	**1.0-1.2**	REF	0.8-1.2	**1.0-1.4**
Full-thickness Cartilage Damage						
WORMS ≥ 2.5, 5-6 n/N	224/1388	65/412	50/505	276/1985	17/173	27/147
(%)	16.1	15.8	9.9	13.9	9.8	18.4
*Adjusted OR	1.0	1.1	**0.6**	1.0	0.7	1.2
(95% CI)	REF	0.8-1.4	**0.5-0.9**	REF	0.4-1.2	0.8-1.8
Any Bone Marrow Lesion						
WORMS ≥ 1 n/N	431/1386	116/408	113/508	497/1981	38/174	38/146
(%)	31.1	28.4	22.2	25.1	21.8	26.0
*Adjusted OR	1.0	1.0	**0.8**	1.0	0.9	1.0
(95% CI)	REF	0.8-1.2	**0.6-0.9**	REF	0.6-1.2	0.7-1.3
60-84-MO FOLLOW-UP (longitudinal analysis)						
Worsening Cartilage Damage						
Any increase in WORMS n/N	106/1363	29/405	26/502	150/1896	14/169	19/136
(%)	7.8	7.2	5.2	7.9	8.3	14.0
*Adjusted OR	1.0	0.9	0.7	1.0	1.1	**1.7**
(95% CI)	REF	0.6-1.4	0.4-1.1	REF	0.6-1.8	**1.1-2.7**
Worsening of Bone Marrow Lesion						
Any increase in WORMS n/N	158/1374	29/405	38/501	201/1963	12/174	13/143

	Medial PFJ Damage			Lateral PFJ Damage		
	No Medial Meniscus Tear	**Grade 1–2 Medial Meniscus Tear**	**Grade 3–4 Medial Meniscus Tear**	**No Lateral Meniscus Tear**	**Grade 1–2 Lateral Meniscus Tear**	**Grade 3–4 Lateral Meniscus Tear**
(%)	11.5	7.2	7.6	10.2	6.9	9.1
*Adjusted OR	1.0	**0.6**	**0.7**	1.0	0.7	0.8
(95% CI)	REF	**0.4-0.9**	**0.5-1.0**	REF	0.4-1.2	0.5-1.5

*Adjusted for age, sex, BMI and history of previous knee injury or surgery

Table 3

Relationship of Meniscus Extrusion to Patellofemoral Joint Structural Damage

	Medial PFJ Damage		Lateral PFJ Damage	
	No Medial Meniscus Extrusion	**Prevalent Medial Meniscus Extrusion**	**No Medial Meniscus Extrusion**	**Prevalent Medial Meniscus Extrusion**
60-MO (cross-sectional analysis)				
Any Cartilage Damage				
WORMS ≥ 2 n/N	656/1293	635/1012	825/2111	101/194
(%)	50.7	62.8	39.1	52.1
*Adjusted OR	1.0	**1.2**	1.0	**1.3**
(95% CI)	REF	**1.1-1.3**	REF	**1.1-1.5**
Full-thickness Cartilage Damage				
WORMS ≥ 2.5, 5-6 n/N	158/1293	181/1012	283/2111	37/194
(%)	12.2	17.9	13.4	19.1
*Adjusted OR	1.0	**1.5**	1.0	1.3
(95% CI)	REF	**1.2-1.8**	REF	0.9-1.9
Any Bone Marrow Lesion				
WORMS ≥ 2 n/N	382/1291	278/1011	513/2109	60/192
(%)	29.6	27.5	24.3	31.3
*Adjusted OR	1.0	0.9	1.0	**1.2**
(95% CI)	REF	0.8-1.1	REF	**1.0-1.6**
60-84-MO FOLLOW-UP (longitudinal analysis)				
Worsening Cartilage Damage				
Any increase in WORMS n/N	92/1278	69/992	159/2023	24/178
(%)	7.2	7.0	7.9	13.5
*Adjusted OR	1.0	1.0	1.0	**1.7**
(95% CI)	REF	0.7-1.4	REF	**1.2-2.5**
Worsening of Bone Marrow Lesion				
Any increase in WORMS n/N	132/1278	93/1002	204/2090	22/190
(%)	10.3	9.3	9.8	11.6
*Adjusted OR	1.0	0.9	1.0	1.1
(95% CI)	REF	0.7-1.2	REF	0.7-1.7

*Adjusted for age, sex, BMI and history of previous knee injury or surgery