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Is superolateral Hoffa's fat pad hyperintensity a marker of local patellofemoral joint disease? – The MOST study

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Abstract

Purpose—To determine the relation of superolateral Hoffa's fat pad (SHFP) hyperintensity to cartilage damage and bone marrow lesions (BMLs) in the patellofemoral joint (PFJ) and tibiofemoral joint (TFJ).

Methods—We used data from the 60 and 84-month study visits from the Multicenter Osteoarthritis (MOST) study. SHFP hyperintensity and Hoffa-synovitis were graded from 0 to 3. Cartilage damage and BMLs were scored in the PFJ and TFJ. Structural damage was defined as: any cartilage damage, full-thickness cartilage damage and any BML. Worsening structural damage was defined as any increase in cartilage and BML scores. Logistic regression was used to determine the relation of SHFP hyperintensity and Hoffa-synovitis (>0) to structural damage, adjusting for age, sex and body mass index (BMI).

Results—1,094 knees were included in the study. Compared to knees without SHFP hyperintensity, those with SHFP hyperintensity had 1.2 (95% Confidence Interval (CI), 1.1–1.4),

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Author contributions

All authors contributed to the conception and design of the study, analysis and interpretation of data, drafting the article and revising it critically for important intellectual content, and approved the final version submitted. Dr. Stefanik takes responsibility for the integrity of the work as a whole, from inception to finished article.

Supplementary data

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1.7 (1.3–2.3) and 1.6 (1.3–1.9) times the prevalence of any cartilage damage, full-thickness cartilage damage, and BMLs in the lateral PFJ respectively, and 1.1 (1.0–1.2), 1.3 (1.0–1.8), and 1.2 (1.0–1.4) times the prevalence of any cartilage damage, full-thickness cartilage damage, and BMLs in the medial PFJ. SHFP hyperintensity was associated with worsening BMLs in the medial PFJ (RR: 1.4 (1.0–1.9)). In general, there was no relation between SHFP hyperintensity and TFJ outcomes. Hoffa-synovitis was associated both cross-sectionally and longitudinally with structural damage, regardless of definition, in all compartments.

Conclusion—SHFP hyperintensity may be a local marker of PFJ structural damage.

Keywords

Hoffa's fat pad; Patellofemoral joint; Cartilage; Bone marrow lesions

Introduction

Localized superolateral Hoffa's fat pad (SHFP) hyperintensity is characterized by a focal increase in signal intensity on fluid sensitive magnetic resonance (MR) sequences (including fat-suppressed T2-and proton density-weighted, and STIR) between the posterior superolateral patellar tendon and the lateral femoral condyle. While this finding has previously been termed “SHFP edema”, we prefer to use the term “SHFP hyperintensity” given the lack of histologic confirmation. Thus, we acknowledge that this imaging finding may also include other structural findings beyond edema such as fibrosis or similar. SHFP hyperintensity has gained significant interest during the last decade and has been consistently hypothesized to result from patellofemoral maltracking[1–6]. While most of the initial reports were based on clinical cohorts of rather small size (including up to 90 patients)[4], a recent study based on a large epidemiologic cohort strengthened this hypothesis and showed a cross-sectional association between SHFP hyperintensity and measures of patellofemoral maltracking including patella alta, lateralization of the tibial tuberosity and anterior position of the lateral femoral condyle[7].

Radiologically, SHFP hyperintensity is part of a broad spectrum of Hoffa's fat pad conditions, such as post-arthroscopy changes, Hoffa's disease, or synovial thickening from synovitis[8]. While SHFP hyperintensity is being increasingly discussed in the radiologic literature, its definition and distinction from so-called Hoffa-synovitis may be less known in the field of knee osteoarthritis (OA) research. In fact, while these two entities show similar signal characteristics, they involve different anatomical regions of Hoffa's fat pad. As its name implies SHFP hyperintensity is specifically localized in the superolateral aspect of the Hoffa's fat pad. Hoffa-synovitis, on the other hand, is detected in a more central location. Hoffa-synovitis, a non-specific, albeit sensitive marker of whole knee synovitis has been used as a surrogate marker for a long time and has proven to show cross-sectional associations with structural features of OA and to be predictive of structural progression and OA incidence particularly in the tibiofemoral joint (TFJ) but also in the patellofemoral joint (PFJ)[9–12]. However, previous publications have not addressed whether SHFP hyperintensity is associated with prevalent local structural joint damage in the PFJ. Furthermore it is not known whether SHFP hyperintensity predicts local structural damage longitudinally. Unlike

synovitis, SHFP hyperintensity is not included in any published MR-based semiquantitative whole joint scoring system for knee OA assessment[13–15].

The aim of our study was to determine whether SHFP hyperintensity is associated with local structural damage in the PFJ in subjects with or at risk of OA. For this we sought to compare presence of SHFP hyperintensity and Hoffa-synovitis and their associations with prevalent cartilage damage and bone marrow lesions (BMLs) in the PFJ and TFJ. Furthermore, we sought to analyze whether SHFP hyperintensity predicts worsening of local structural damage in the medial and lateral PFJ. We hypothesize that SHFP hyperintensity will be cross-sectionally and longitudinally related to structural damage in the PFJ, but not the TFJ. While in contrast Hoffa-synovitis will be associated with structural damage in all compartments, both cross-sectionally and longitudinally.

Methods

Study sample

Subjects were participants in the Multicenter Osteoarthritis (MOST) study, a prospective epidemiologic study aimed at identifying risk factors for incident and progressive knee OA. The study included 3,026 people at baseline aged 50–79 years who had or were at high risk of developing OA. They were recruited from two U.S. communities, Birmingham, Alabama, and Iowa City, Iowa, through mass mailing of letters and study brochures, supplemented by media and community outreach campaigns. MOST study subjects were recruited and enrolled between June 2003 and March 2005[16]. Written informed consents were obtained from all patients.

Subjects considered at high risk for developing knee OA included those who were overweight or obese; had knee pain, aching, or stiffness on most of the past 30 days; had a history of knee injury that made it difficult to walk for at least 1 week, or had previous knee surgery[17–21]. In the present study, we used data from the 60 and 84-month study visits where all eligible subjects had knee MRI assessed for other structural features of knee OA (Fig. 1).

MR image acquisition

One knee per subject was randomly selected for evaluation. Knee MRIs were obtained at the 60-month study visit using a 1.0-T dedicated extremity unit (OrthOne; GE Healthcare-*formerly ONI Medical Systems*, Wilmington, Mass) with a circumferential extremity coil. Choice of pulse sequences for the parent MOST study was based on a time-efficient sequence protocol developed by Roemer *et al.*[22]. The following sequences were obtained: fat-suppressed fast spin echo proton density-weighted sequences in two planes, sagittal (repetition time (TR) 4,800 ms, echo time (TE) 35 ms, 3 mm slice thickness, 0 mm interslice gap, 32 slices, 288 × 192 matrix, 140 mm^2 field of view (FOV), echo train length 8) and axial (TR 4,680 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 6,650 ms, TE 15 ms, inversion time 100 ms, 3mmslice thickness, 0mminterslice gap, 28 slices, 256 × 192 matrix, 140mm^2 FOV, echo train length 8). Examinations were performed

at the University of Alabama at Birmingham and the University of Iowa City by using identical MR units.

MR image interpretation

Two musculoskeletal radiologists (A.G. and F.W.R., with 17 and 14 years of experience, respectively, in standardized semiquantitative MR assessments of knee OA), who were blinded to radiographic OA severity and clinical data, evaluated cartilage morphology, BMLs, and Hoffa-synovitis using the Whole-Organ Magnetic Resonance Score (WORMS) system[15].

Cartilage damage and BMLs were assessed in ten TFJ subregions (five medial and five lateral) and four PFJ subregions (two medial and two lateral) according to WORMS system. Cartilage morphology was graded as follows: grade 0, normal thickness and signal; grade 1, normal thickness but increased signal intensity on T2-weighted images; grade 2, partial thickness focal defect less than 1 cm at its greatest width; grade 2.5, full-thickness focal defect less than 1 cm at its greatest width; grade 3, multiples areas of normal thickness or a grade 2.0 defect greater than 1 cm but less than 75% of the subregion; grade 4, diffuse (≥75% of the subregion) partial-thickness loss; grade 5, multiple areas of full-thickness loss or a grade 5 lesion wider than 1 cm but less than 75% of the subregion; and grade 6, diffuse (≥75% of the subregion) full-thickness loss. BMLs were assessed from 0 to 3 based on the extent of regional involvement: grade 0, none; grade 1, less than 25% of the region; grade 2, 25–50% of the region; and grade 3, more than 50% of the region[15]. We used three definitions of prevalent structural damage: Any cartilage damage (WORMS score of ≥2), full-thickness cartilage damage (WORMS score 2.5, 5 and 6) and any BML (WORMS score of ≥1). Worsening of cartilage damage and BMLs from 60 to 84 months was considered to be present if there was any increase in WORMS score, including within-grade changes. Subregions with maximal scores at 60 months were removed from the longitudinal analysis. In addition, subregions were excluded if their MRI was of poor quality.

Infrapatellar/intercondylar synovitis was graded using a 0–3 scale, based on size of hyperintense T2 signal within the Hoffa's fat pad on sagittal images, as follows: grade 0, normal; grade 1, mild; grade 2, moderate; grade 3, severe (Fig. 2)[13]. A knee was considered to have Hoffa-synovitis if either infrapatellar or intercondylar synovitis was >0. In addition, another musculoskeletal radiologist (M.J., who was not involved in reading the other features, with 6 years of experience in standardized semiquantitative MR assessments of knee OA) graded SHFP hyperintensity on the lateral-most sagittal fat-suppressed proton density-weighted MR images (Fig. 2), using a 0–3 scale, based on the size of hyperintensity within the superolateral corner of the Hoffa's fat pad, as follows: grade 0, absent; grade 1, mild (<33% of total area); grade 2, moderate (33–66% of total area); grade 3, severe (>66% of total area) (Fig. 3). SHFP hyperintensity was considered present if the score was >0. Fifty knees were randomly chosen from the dataset and re-assessed by the primary reader (MJ) and secondary reader (AG). Intra-reader and inter-reader reliability (weighted Kappa) for presence of SHFP hyperintensity was 1.0 and 0.90 respectively. Inter-reader reliability for cartilage damage and for BMLs has been reported for the MOST cohort[23].

Statistical analysis

To investigate the relation of SHFP hyperintensity to structural damage in the PFJ and TFJ, we used separate logistic regression models using our three definitions of structural damage and two definitions of worsening structural damage. Each subregion was included as an independent observation and generalized estimating equations were used to account for the correlation between subregions within a knee. Analyses were performed separately the medial and lateral PFJ and TFJ compartments. Presence of SHFP hyperintensity and Hoffa's synovitis were included in the same model and adjusted for age, sex and body mass index (BMI). In addition we performed a dose–response analysis for SHFP hyperintensity and our outcomes using a three-level exposure: no SHFP hyperintensity, grade 1 and grades 2/3. Grades 2 and 3 were combined for this analysis due to the low number of knees exhibiting grade 3 lesions. Prevalence ratios (PRs) were reported for cross-sectional analyses and risk ratios (RRs) for longitudinal analyses.

Results

1,094 knees, one knee per participant, were included in the current analysis (Fig. 1). This left 2,188 subregions eligible in the medial and lateral PFJ and 5,470 subregions eligible in the medial and lateral TFJ. The mean (SD) age and BMI was 66.8 years ± 7.6 and 29.5 kg/m^2 ± 4.8, respectively; 65% were women (Table I). The prevalence of any SHFP (>0) hyperintensity was 13.3%. The prevalence of Hoffa-synovitis was 59%. Both SHFP hyperintensity and Hoffa-synovitis were concomitantly present in 9% of the knees.

Cross-sectional analysis

Compared to knees without SHFP hyperintensity, those with SHFP hyperintensity had 1.2 (95% Confidence Interval (CI), 1.1–1.4), 1.7 (CI, 1.3–2.3) and 1.6 (CI, 1.3–1.9) times the prevalence of lateral PFJ any cartilage damage, full-thickness cartilage damage and BMLs, respectively (Table II). SHFP hyperintensity was also related to any cartilage damage, full thickness cartilage damage and BMLs in the medial PFJ (PR = 1.1 (CI, 1.0–1.2), 1.3 (CI, 1.0–1.8), and 1.2 (CI, 1.0–1.4) respectively) (Table II). There was no relation between SHFP and structural damage in the medial TFJ (Table III). However a trend for protective effect of SHFP hyperintensity was seen in the lateral TFJ (PRs 0.9 (0.7–1.0) and 0.6 (0.4–1.0)) for any cartilage damage and full-thickness cartilage damage in the lateral TFJ respectively. In the dose–response analysis, in general we found similar associations for both groups, grade 1 and grade 2/3. For the PFJ, PRs varied between 1.1 (CI, 1.0–1.2) for the relation of grade 1 SHFP hyperintensity to any cartilage damage in the medial PFJ, and 1.8 (CI, 1.1–3.2) for the relation of grade 2/3 SHFP hyperintensity to full thickness cartilage damage in the lateral PFJ (Supplementary Table 1). No relation between SHFP and structural damage in both medial and lateral TFJ was found in the dose response analysis (Supplementary Table 2).

On the other hand, when Hoffa-synovitis was used as the exposure we found statistically significant associations between Hoffa-synovitis and structural damage in all compartments, regardless of the definition used for structural damage. PRs varied between 1.3 for any BML in the medial PFJ (CI, 1.2–1.6) and 3.0 for full-thickness cartilage damage in the medial TFJ (CI, 2.2–4.1) (Tables II and III).

Longitudinal analysis

Compared to knees without SHFP hyperintensity, knees with SHFP hyperintensity showed a trend for a longitudinal association with the two definitions of structural damage. For the PFJ, RRs varied between 1.1 (CI, 0.7–1.6) for worsening of cartilage damage in the lateral PFJ, and 1.4 (CI, 1.0–1.9) for worsening of BMLs in the medial PFJ. However statistical significance was reached only in the latter case. For the TFJ, we found no association between SHFP hyperintensity and the two definitions of worsening of structural damage.

In the dose–response analysis, we found a similar trend for a longitudinal association between grade 1 SHFP hyperintensity and the definitions of worsening of structural damage in the PFJ, not reaching statistical significance. RRs varied between 1.1 (0.7–1.8) for worsening of cartilage damage in the lateral PFJ and 1.2 (0.8–1.9) for worsening of cartilage damage in the medial PFJ. Interpretation of grade 2/3 results was greatly limited due to the small number of knees in this category along with a small number of cases (Supplementary Table 1). No similar trend was found for the TFJ (Supplementary Table 2).

On the other hand, when Hoffa-synovitis was used as the exposure we found a statistically significant association between both definitions of worsening of structural damage and presence of Hoffa-synovitis at baseline in all compartments. RRs varied between 1.3 (CI, 1.0–1.7) for worsening of BML in the medial PFJ and 1.9 (CI 1.2–2.9) for worsening of BML in the lateral TFJ (Tables II and III).

Discussion

Our results suggest that SHFP hyperintensity is associated cross-sectionally with local structural damage in the PFJ and is not related to structural damage in the TFJ. We noted a trend for a protective effect of SHFP hyperintensity in the lateral TFJ, which is consistent with our hypothesis that SHFP hyperintensity is a local disease of the PFJ and not the whole joint. Longitudinally, there was a trend for an association between SHFP hyperintensity at baseline and worsening of cartilage damage and BMLs in the medial PFJ over 2 years. However statistical significance was only reached for BML worsening in the medial PFJ. On the other hand, we found statistically significant associations between Hoffa-synovitis and widespread structural damage both cross-sectionally and longitudinally, which is in line with previous publications[9–12]. To the best of our knowledge this is the first large scale epidemiologic study to report the prevalence of SHFP hyperintensity and its relation to the presence of site-specific structural damage in the knee.

While the primary goal of this study was to report on the association between SHFP hyperintensity and structural damage in the different compartments of the knee, we also included Hoffa-synovitis as the exposure to make the distinction between these two entities. In fact, Hoffa-synovitis has been extensively studied in the field of knee OA and has been shown to be associated with radiographic and MR-based structural damage both cross-sectionally[11,12] and longitudinally[10,24]. Specifically, MR-based studies showed that Hoffa-synovitis is associated with widespread cartilage damage in different knee compartments[11]. In our study, when Hoffa-synovitis was used as the exposure, we found consistent results with prior publications, in that PRs and RRs for structural damage were increased in all knee

compartments, regardless of the definition used for structural damage, both cross-sectionally and longitudinally. In contrast, when SHFP hyperintensity was used as the exposure in cross-sectional analyses, PRs of structural damage showed a statistically significant increase in both the lateral and medial PFJ for all definitions of structural damage. When assessing the dose response relationship using a three-level exposure of SHFP hyperintensity, in general the cross-sectional results are similar to our main analyses. The longitudinal results of the dose–response relationship should be interpreted with caution as these findings are likely due to the low prevalence of grades 2/3 SHFP hyperintensity and the low frequency of longitudinal changes in this group.

While the mechanical origin of SHFP hyperintensity has already been reported[1,2,4–6,25–27], and has been recently supported by a study based on the same cohort[28], our study adds to the understanding of SHFP hyperintensity as a possible marker of local knee structural damage. Our findings are relevant insofar as PFJ OA has been increasingly seen as a separate yet important subgroup of knee OA[29]. There is accumulation of cross-sectional and longitudinal data suggesting that PFJ OA may be an early event of widespread knee OA[30–32]. For instance, we recently reported in a longitudinal study that knees that develop both PFJ and TFJ structural damage after 7 years of follow-up often start with isolated PFJ involvement at baseline[32]. In a similar fashion to Hoffa-synovitis, which is a recognized surrogate of widespread cartilage damage[9,11,12], SHFP hyperintensity may potentially represent a site-specific surrogate of cartilage damage earlier in the disease process.

We acknowledge several limitations in our study. The first limitation was the lack of histologic or pathologic confirmation of the SHFP abnormalities seen on MR images. However, this is inherent to the nature of any epidemiological study, where there was no surgical intervention during the study to obtain a sample in order to confirm imaging findings. It is well established in the literature that PFJ alignment and morphology is related to SHFP hyperintensity[1,4–6,27,28] and we have not investigated that question in this study. The focus of our study was to determine if, similar to the known relation of Hoffa-synovitis to TFJ OA, SHFP hyperintensity may be a local marker of PFJ OA, regardless of the cause (one of which could be malalignment and abnormal morphology). A more sophisticated study using marginal structural modeling could better answer the questions of the exact causal pathway and mediating affects among the aforementioned variables but is beyond the scope of the current study. Also the clinical implication of SHFP hyperintensity cannot be determined on the basis of our results. It is unknown if therapeutic interventions, such as bracing, taping, physical therapy, or surgery, may alter the evolution of this MR finding. To the best of our knowledge there are no publications on the histologic nature of SHFP hyperintensity. While our results suggest SHFP hyperintensity is associated with PFJ structural damage we cannot infer causation. SHFP hyperintensity may be an early structural correlate of PFJ OA, as Hoffa-synovitis is an early marker for TFJ OA, but this needs to be confirmed by larger longitudinal studies. Also the finding of a potentially protective effect of the presence of SHFP hyperintensity with structural damage in the lateral TFJ needs to be further explored to understand if this finding can be confirmed. Explanations based on the current study remain speculative other that it supports the hypothesis of SHFP hyperintensity being a local phenomenon. In summary, SHFP hyperintensity is associated with structural findings consistent with PFJ OA. While more studies are needed to determine the clinical

implications of such MR findings, our results suggest that SHFP hyperintensity should potentially be included in MR-based semi-quantitative whole joint assessment of knee OA, as a possible surrogate of early PFJ OA.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Competing interests

Dr. Guermazi is President, shareholder Boston Imaging Core Lab (BICL), LLC; and Consultant to MerckSerono, TissueGene, Ortho-Trophix and Genzyme. Dr. Roemer is CMO, shareholder Boston Imaging Core Lab (BICL), LLC.

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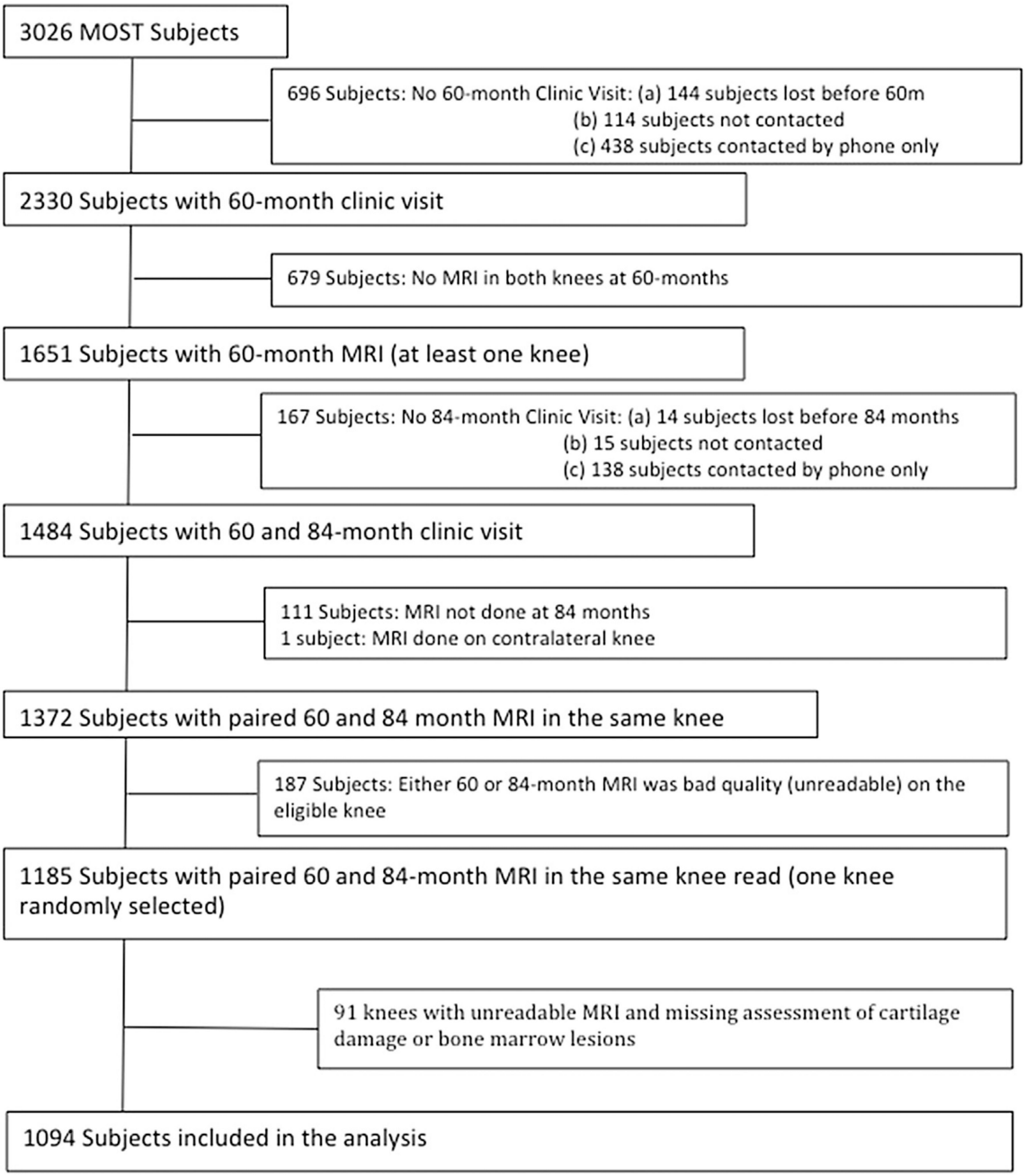

Fig. 1.
Flow chart of subjects/subregions included in analysis.

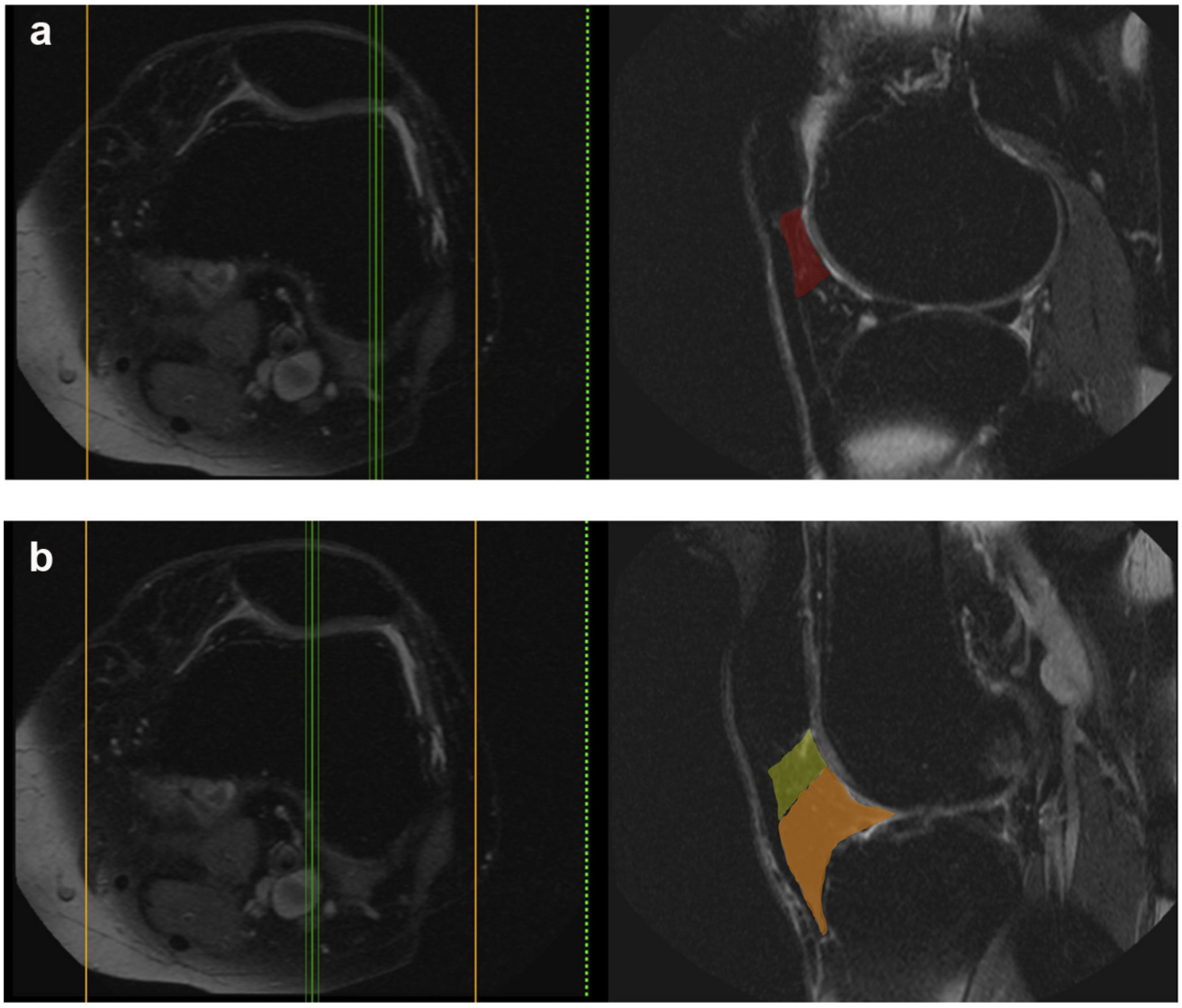

Fig. 2.

MR images showing areas of (a) 'SHFP hyperintensity, and (b) Hoffa's fat pad synovitis. (a) SHFP hyperintensity is scored on the lateral-most sagittal image, between the lateral femoral condyle and the patellar tendon (red). (b) Hoffa-synovitis is scored on the several sagittal images around midline, and is divided into infraptellar (yellow), and intercondylar (orange) synovitis.

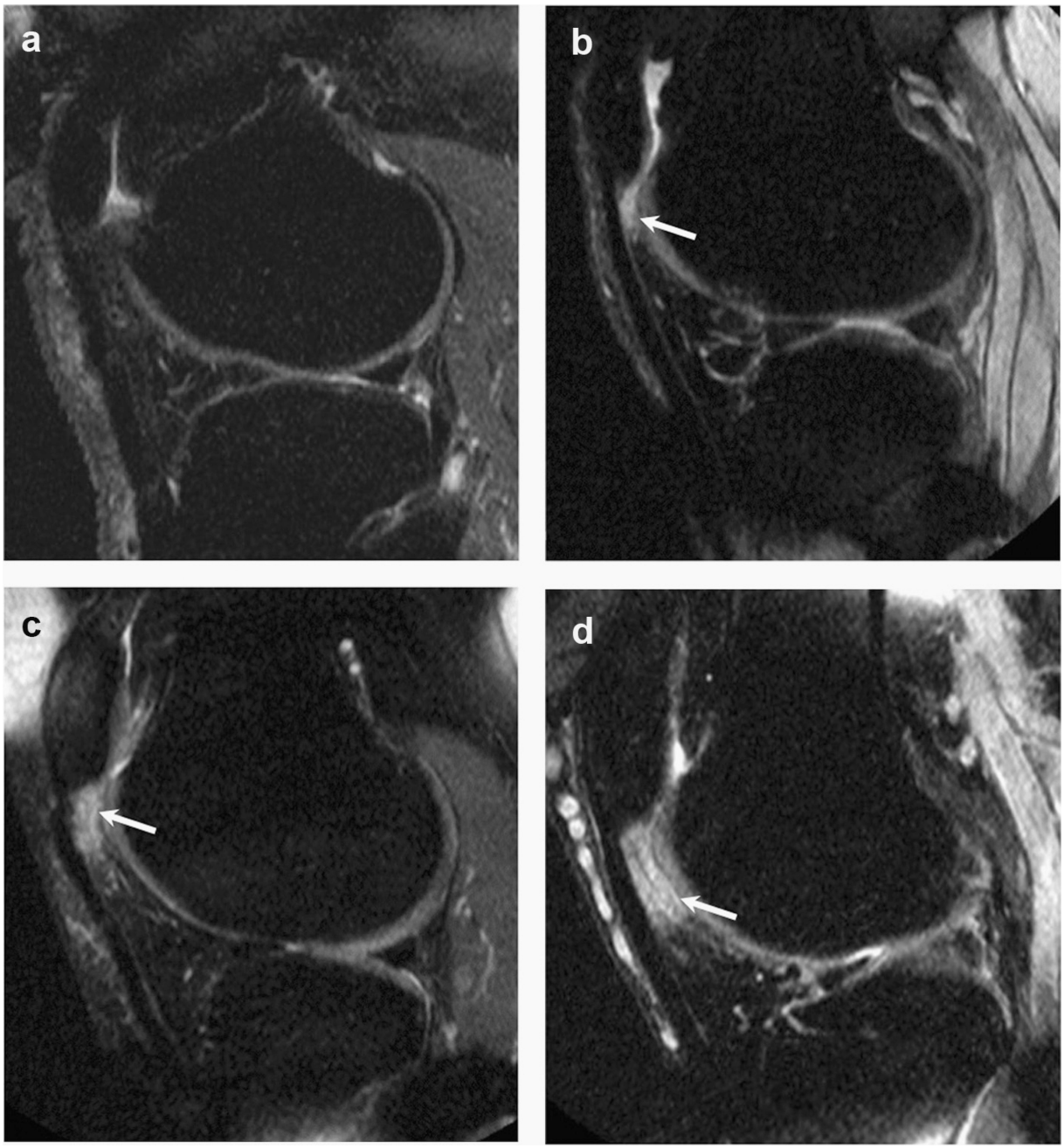

Fig. 3.

Sagittal short tau inversion-recovery images showing grades of SHFP hyperintensity. (a) Grade 0, normal; (b) grade 1, mild; (c) grade 2, moderate; (d) grade 3, severe.

Table I

Characteristics of the study sample

Characteristics*	(*n* = 1,094 knees – 1,094 participants)	Knees with SHFP hyperintensity (*n* = 145)	Knees without SHFP hyperintensity (*n* = 949)	Knees with Hoffa's synovitis (*n* = 650)	Knees without Hoffa's synovitis (*n* = 444)
Age (years)	66.8 (7.6)	65.9 (7.5)	67.0 (7.6)	67.2 (7.7)	66.3 (7.4)
Sex (% female)	65.1%	71.7%	64.1%	66.3%	66.3%
BMI (kg/m^2)	29.5 (4.8)	28.8 (4.5)	29.7 (4.8)	29.6 (4.7)	29.4 (4.9)
SHFP hyperintensity ((*n* (%))					
Grade 0	949 (86.8%)				
Grade 1	114 (10.4%)				
Grade 2	28 (2.6%)				
Grade 3	3 (0.3%)				

*Data are means ± standard deviation unless otherwise noted.

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Table II

Relation of SHFP hyperintensity to PFJ cartilage damage and BMLs

	SHFP Hyperintensity Absent (*n* = 949 knees; 1,898 subregions†)	SHFP Hyperintensity Present (*n* = 145 knees; 290 subregions†)	Synovitis Absent (*n* = 444 knees; 888 subregions†)	Synovitis Present (*n* = 650 knees; 1,300 subregions†)
Lateral PFJ				
Any Cartilage Damage				
WORMS ≥ 2 *n* (%)	739/1,895 (39.0)	142/290 (49.0)	252/888 (28.4)	629/1,297 (48.5)
Adjusted PR* (95% CI)	Ref	**1.2 (1.1–1.4)**	Ref	**1.7 (1.5–1.9)**
Full Thickness Cartilage Damage				
WORMS 2.5, 5–6 *n* (%)	244/1,895 (12.9)	63/290 (21.7)	61/888 (6.9)	246/1,297 (19.0)
Adjusted PR* (95% CI)	Ref	**1.7 (1.3–2.3)**	Ref	**2.6 (1.9–3.6)**
Worsening of Cartilage Damage				
Any increase in WORMS score from 60 to 84 months *n* (%)	146/1,798 (8.1)	23/266 (8.7)	55/863 (6.4)	114/1,201 (9.5)
Adjusted RR* (95% CI)	Ref	1.1 (0.7–1.6)	Ref	**1.5 (1.1–2.0)**
Any BML				
WORMS ≥ 1 *n* (%)	442/1,894 (23.3)	107/290 (36.9)	150/888 (16.9)	399/1,296 (30.8)
Adjusted PR* (95% CI)	Ref	**1.6 (1.3–1.9)**	Ref	**1.8 (1.5–2.1)**
Worsening of BMLs				
Any increase in WORMS score from 60 to 84 months *n* (%)	181/1,878 (9.6)	33/289 (11.4)	59/882 (6.7)	155/1,285 (12.1)
Adjusted RR* (95% CI)	Ref	1.2 (0.8–1.7)	Ref	**1.8 (1.3–2.4)**
Medial PFJ				
Any Cartilage Damage				
WORMS ≥ 2 *n* (%)	1,044/1,895 (55.1)	178/290 (61.4)	401/888 (45.2)	821/1,297 (63.3)
Adjusted PR* (95% CI)	Ref	**1.1 (1.0–1.2)**	Ref	**1.4 (1.3–1.5)**
Full Thickness Cartilage Damage				
WORMS 2.5, 5–6 *n* (%)	273/1,895 (14.4)	56/290 (19.3)	80/888 (9.0)	249/1,297 (19.2)
Adjusted PR* (95% CI)	Ref	**1.3 (1.0–1.8)**	Ref	**2.0 (1.6–2.6)**
Worsening of Cartilage Damage				
Any increase in WORMS score from 60 to 84 months *n* (%)	128/1,859 (6.9)	26/275 (9.5)	50/877 (5.7)	104/1,257 (8.3)
Adjusted RR* (95% CI)	Ref	1.3 (0.9–2.0)	Ref	**1.4 (1.0–2.0)**
Any BML				
WORMS ≥ 1 *n* (%)	534/1,895 (28.2)	99/290 (34.1)	210/888 (23.7)	423/1,297 (32.6)
Adjusted PR* (95% CI)	Ref	**1.2 (1.0–1.4)**	Ref	**1.3 (1.2–1.6)**
Worsening of BMLs				
Any increase in WORMS score from 60 to 84 months *n* (%)	180/1,878 (9.6)	40/289 (13.8)	75/880 (8.5)	145/1,287 (11.3)
Adjusted RR* (95% CI)	Ref	**1.4 (1.0–1.9)**	Ref	**1.3 (1.0–1.7)**

*All models included both SHFP hyperintensity and synovitis and were further adjusted for age, sex and BMI.

[†]Eligible subregions for each analysis. PR: prevalence ratio. RR: risk ratio. BML: Bone marrow lesion. PFJ: Patellofemoral joint. Ref: 1.0 (reference). **Bold:** statistical significance.

Table III

Relation of SHFP hyperintensity to TFJ cartilage damage and BMLs

	SHFP Hyperintensity Absent (*n* = 949 knees; 4,745 subregions†)	SHFP Hyperintensity Present (*n* = 145; 725 subregions†)	Synovitis Absent (*n* = 444; 2,220 subregions†)	Synovitis Present (*n* = 650; 3,250 subregions†)
Lateral TFJ				
Any Cartilage Damage				
WORMS ≥ 2 *n* (%)	1,048/4,745 (22.1)	137/725 (18.9)	340/2,220 (15.3)	845/3,250 (26.0)
Adjusted PR* (95% CI)	Ref	0.9 (0.7–1.0)	Ref	**1.7 (1.4–1.9)**
Full Thickness Cartilage Damage				
WORMS 2.5, 5–6 *n* (%)	272/4,745 (5.7)	24/725 (3.3)	80/2,220 (3.6)	216/3,250 (6.7)
Adjusted PR* (95% CI)	Ref	0.6 (0.4–1.0)	Ref	**1.8 (1.2–2.6)**
Worsening of Cartilage Damage				
Any increase in WORMS score from 60 to 84 months *n* (%)	280/4,716 (5.9)	41/725 (5.6)	102/2,214 (4.6)	219/3,227 (6.8)
Adjusted RR* (95% CI)	Ref	0.9 (0.6–1.5)	Ref	**1.4 (1.0–2.0)**
Any BML				
WORMS ≥ 1 *n* (%)	264/4,745 (5.6)	34/725 (4.7)	63/2,220	235/3,250 (7.2)
Adjusted PR* (95% CI)	Ref	0.8 (0.5–1.2)	(2.8)Ref	**2.5 (1.8–3.6)**
Worsening of BMLs				
Any increase in WORMS score from 60 to 84 months *n* (%)	152/4,740 (3.2)	17/725 (2.3)	45/2,220 (2.0)	124/3,245 (3.8)
Adjusted RR* (95% CI)	Ref	0.7 (0.4–1.4)	Ref	**1.9 (1.2–2.9)**
Medial TFJ				
Any Cartilage Damage				
WORMS ≥ 2 n *(%)*	1,531/4,745 (32.3)	210/725 (29.0)	492/2,220 (22.2)	1,249/3,250 (38.4)
Adjusted PR* (95% CI)	Ref	0.9 (0.8–1.1)	Ref	**1.7 (1.5–1.9)**
Full Thickness Cartilage Damage				
WORMS 2.5, 5–6 *n* (%)	452/4,745 (9.5)	58/725 (8.0)	92/2,220 (4.1)	418/3,250 (12.9)
Adjusted PR* (95% CI)	Ref	0.8 (0.6–1.2)	Ref	**3.0 (2.2–4.1)**
Worsening of Cartilage Damage				
Any increase in WORMS score from 60 to 84 months *n* (%)	363/4,652 (7.8)	58/718 (8.1)	137/2,208 (6.2)	284/3,162 (9.0)
Adjusted RR* (95% CI)	Ref	1.1 (0.7–1.6)	Ref	**1.4 (1.1–1.8)**
Any BML				
WORMS ≥ 1 *n* (%)	617/4,745 (13.0)	72/723 (10.0)	174/2,220	515/3,248 (15.9)
Adjusted PR* (95% CI)	Ref	0.8 (0.6–1.0)	(7.8)Ref	**2.0 (1.6–2.5)**
Worsening of BMLs				
Any increase in WORMS score from 60 to 84 months *n* (%)	346/4,745 (7.3)	41/721 (5.7)	110/2,220 (5.0)	277/3,246 (8.5)
Adjusted RR* (95% CI)	Ref	0.8 (0.5–1.2)	Ref	**1.7 (1.3–2.2)**

*All models included both SHFP hyperintensity and synovitis and were further adjusted for age, sex and BMI.

[†]Eligible subregions for each analysis. PR: prevalence ratio. RR: risk ratio. BML: Bone marrow lesion. TFJ: Tibiofemoral joint. Ref: 1.0 (reference). **Bold:** statistical significance.