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Changes in patellofemoral and tibiofemoral joint cartilage damage and bone marrow lesions over 7 years: the Multicenter Osteoarthritis Study

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SUMMARY

Objectives: To investigate changes in cartilage damage and bone marrow lesions (BMLs) on MRI in the patellofemoral and tibiofemoral joints (TFJs) over 7 years.
Methods: The Multicenter Osteoarthritis (MOST) Study is a cohort study of persons aged 50–79 years at baseline with or at high risk for knee osteoarthritis (OA). Knees were eligible for the current study if they had knee MRI (1.0T) assessed for cartilage damage and BMLs at the baseline and 84-month visits. Knees were categorized as having MRI-detected structural damage (cartilage and BMLs) isolated to the patellofemoral joint (PFJ), isolated to the TFJ, mixed or no damage at baseline and 84-months. We determined the changes in PFJ and TFJ structural damage over 7 years and used logistic regression to assess the relation of baseline compartment distribution to incident isolated PFJ, isolated TFJ and mixed damage.
Results: Among 339 knees that had full-thickness cartilage loss isolated to the PFJ or TFJ at baseline, only 68 (20.1%) developed full-thickness cartilage loss in the other compartment while 271 (79.9%) continued to only have the initial compartment affected. Compared to knees without full-thickness cartilage damage ($n = 582$), those with isolated TFJ and PFJ full-thickness cartilage damage had 2.7 (1.5, 4.9) and 5.8 (3.6, 9.6) times the odds of incident mixed full-thickness cartilage damage, respectively. Similar results were seen when using other definitions of MRI-defined structural damage.
Conclusions: Most knees with structural damage at baseline do not develop it in the other compartment. Knees that develop mixed structural damage are more likely to start with it isolated to the PFJ.

Introduction

Knee osteoarthritis (OA) can occur in either the patellofemoral joint (PFJ), the tibiofemoral joint (TFJ) or both. Little is known about the natural history of knee OA in regards to the compartment where disease begins and whether it tends to remain isolated to one compartment or subsequently develops in the other compartment. Knowledge about where OA starts and progresses to include both the PFJ and TFJ will provide information on targets for early intervention and prevention of disease burden. For example, recent studies have demonstrated that taping and bracing of the PFJ

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may improve knee pain and BMLS[1–3]. Future work is warranted to determine how these non-invasive treatment strategies affect PFJ and TFJ joint structures over time.

Duncan *et al.* reported on the incidence, progression and sequence of development of radiographic OA in the PFJ and TFJ in symptomatic adults[4]. They concluded that OA starts in the PFJ with the development of TFJ OA over time. They proposed that isolated symptomatic PFJ OA may be a marker for future development of TFJ OA and thus a target for the early management of knee OA. A limitation of this study was the use of radiographs, which could have missed early changes in the OA disease process. To date, there are no published studies examining the natural history of OA development in the PFJ and TFJ evaluated by MRI, which is more sensitive than radiographs for identifying structural damage, in both the TFJ and PFJ[5]. MRI affords direct assessment of cartilage damage and bone marrow lesions (BMLs), which are hallmark structural features of OA[6]. Additionally, it is unknown if changes in the distribution of cartilage damage and BMLs in the PFJ and TFJ are related to changes in knee pain. Because the experience of pain ultimately brings individuals to seek treatment, knowledge of how pain relates to structural changes in the PFJ and TFJ will ultimately help to prioritize how treatments are developed for knee OA to prevent disease burden.

The purpose of this study was to investigate patterns of change in cartilage damage and BMLs in the patellofemoral and TFJs over 7 years. Specifically, we describe which compartment tends to be involved first and whether disease that initially affects one compartment remains isolated or develops in the other compartment. A secondary aim was to investigate how changes in cartilage damage and BMLs among knee joint compartments relate to incident frequent knee pain (FKP).

Methods

Study sample

Knees for the current study were from participants in the Multicenter OA (MOST) Study. 3,026 participants were recruited from Iowa City, Iowa and Birmingham, Alabama. The MOST cohort consists of older adults that have or are at risk of developing knee OA. Some subjects had knee pain and radiographic OA (52% with Kellgren Lawrence grade $\geq$2) at baseline where others were at high risk for developing knee pain and OA based on being overweight, or having a history of knee injury or surgery. Subjects were ineligible if they had bilateral knee replacements or rheumatoid/other inflammatory arthritis[7].

MRI acquisition

Knee MRIs were acquired at the baseline and 84-month visits. A 1.0 Tesla extremity MRI system (OrthOne™, ONI Medical Systems Wilmington, MA) was used with a phased array knee coil to obtain the following sequences[8,9]: Fat-suppressed fast spin echo intermediate 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 proton-density-weighted (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).

Semi-quantitative MRI assessment

In MOST, one randomly selected knee per individual was selected to be read for MRI features. Two musculoskeletal radiologists (FWR, AG) used the Whole-Organ Magnetic Resonance Imaging Score (WORMS)[10] to assess cartilage morphology and BMLs[8,9] in fourteen regions in the PFJ and TFJ. Inter-reader weighted kappa values for WORMS scores ranged from 0.62–0.78[9]. Any cartilage damage was defined as a WORMS score $\geq$2, full-thickness cartilage damage was defined by WORMS scores of 2.5, 5, or 6, which denotes focal full-thickness defects, different degrees of diffuse full-thickness damage, respectively. Any size BML was defined as WORMS scores of $\geq$1. At baseline and 7-year follow up, knees were categorized as having structural damage isolated to the PFJ, isolated to the TFJ, mixed (both PFJ and TFJ) or no damage in either compartment. We used three different definitions of structural damage: 1. Full-thickness cartilage damage (primary outcome), 2. Any cartilage damage, and 3. Any BML (Figs. 1 and 2).

We then created the following categories of change in the compartmental distribution of structural damage: no damage, isolated PFJ, isolated TFJ and mixed at both time points (no change); incident isolated TFJ, incident isolated PFJ and incident mixed damage. We further divided the incident mixed group into knees that had no damage, isolated PFJ and isolated TFJ damage at baseline.

FKP assessment

At the baseline and 84-month visits FKP was assessed in each knee by asking participants: “Do you have pain, aching or stiffness on most days of the month?”

Statistical analysis

We first described the change in compartmental distribution of structural damage over 7 years using the definitions described above and used logistic regression to assess the relation of baseline compartment distribution to incident isolated PFJ, isolated TFJ and mixed damage, adjusting for age, sex and BMI. We then determined the relation of change of compartment distribution of structural damage over 7 years to incident FKP (knees were eligible if FKP was not present at baseline and present at 84-months) using logistic regression adjusting for age, sex and BMI. In sensitivity analyses we used a structural damage definition that required the presence of both cartilage damage and BMLs for a compartment to be considered to have structural damage. Results of this analysis were similar to the main analyses presented below and are not presented here.

Results

We restricted our analysis to knees that had knee MRI assessed for cartilage damage and BMLs at the baseline and 84-month study visits. In MOST one randomly selected knee from each subject who attended both the 60 and 84-month visits had their MRI read for cartilage damage and BMLs (n = 1185 knees). Of these knees, 1012 and 762 knees had complete MRI readings at the baseline and 84-month visits for cartilage morphology and BMLs, respectively (Fig. 3). Due to resource restrictions there were less knees that had BMLs assessed. Age, sex and BMI distribution for the entire MOST cohort and those included in the current study are presented in Table I. Since our focus was on the development of new disease findings in compartments initially unaffected or isolated to one compartment, we excluded knees that at baseline already had involvement of both the PFJ and TFJ (mixed damage). 592, 91 and 130 knees were removed with mixed any cartilage damage, full-

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