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Lateral and medial joint space narrowing predict subsequent cartilage loss in the narrowed, but not in the non-narrowed femorotibial compartment – data from the Osteoarthritis Initiative

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SUMMARY

Objective: To determine the predictive value of unicompartimental joint space narrowing (JSN) for MRI-based cartilage thickness loss in the narrowed and the non-narrowed femorotibial compartment.
Methods: 922 knees from 922 Osteoarthritis Initiative (OAI) participants (62.2 ± 9.0 years, 61% females) with radiographic OA (158 without JSN [noJSN], 175 with lateral JSN [latJSN], 589 with medial JSN [medJSN]) were analyzed using 3 T MRI. One-year cartilage thickness change was determined in the lateral (LFTC) and medial femorotibial compartment (MFTC), and in femorotibial subregions. The probability of subsequent cartilage loss was calculated using predefined thresholds. The predictive value of JSN for the probability and magnitude of cartilage loss was compared between latJSN, medJSN and noJSN knees using Fisher's exact and Mann–Whitney-*U* tests.
Results: The probability of cartilage loss was greater in the narrowed compartment of latJSN/medJSN knees (34.9%/32.4%) than in noJSN knees (13.3%/12.7%, $P \leq 6.4 \times 10^{-6}$) and so was the magnitude of cartilage thickness change ($P \leq 8.2 \times 10^{-6}$). No significant differences were observed between the narrowed compartments of latJSN vs medJSN knees (probability: $P = 0.58$, magnitude: $P = 0.19$) or between the non-narrowed compartment of latJSN/medJSN vs noJSN knees (probability: $P \geq 0.35$, magnitude: $P = \geq 0.23$). These results were confirmed by the location-independent ordered value (OV) analyses of femorotibial subregions.
Conclusion: The predictive value of latJSN for lateral compartment cartilage loss was comparable to that of medJSN for medial compartment cartilage loss, whereas cartilage loss in the non-narrowed compartment was similar to that in noJSN knees. These findings provide important clues to predicting progression of knee OA, and in tailoring inclusion criteria for clinical trials.

Introduction

Knee osteoarthritis (OA) is a slowly progressing disease with a high prevalence in elderly people[1]. Predicting who will (and who will not) progress symptomatically and/or on a structural level therefore is important from a clinical management perspective. Cartilage thickness change is a hallmark of OA and change in the femorotibial joint was reported to be indistinguishable from healthy reference subjects in the early stages of radiographic OA (ROA; i.e., Kellgren & Lawrence grade [KLG] 2)[2,3], potentially because cartilage thinning and thickening occur simultaneously at this stage[4,5]. Greater and more uniform cartilage loss was observed in knees with advanced ROA (KLG 3 or 4)[3,6], in which joint space narrowing (JSN) was evident on baseline radiographs. Previous studies have reported that medial JSN was a strong predictor of subsequent structural progression in the medial femorotibial compartment (MFTC) [7]; however whether lateral JSN is a predictor of lateral (or medial) femorotibial cartilage loss is currently

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unknown. Also, the association between unicompartimental lateral or medial JSN with cartilage loss in the non-narrowed femorotibial compartment has not been previously reported.

The objective of this study therefore was to determine the predictive value of unicompartimental lateral or medial JSN for subsequent cartilage thickness loss in both the narrowed and the non-narrowed femorotibial compartment when compared to knees without JSN.

Methods

The study was performed using data from the Osteoarthritis Initiative (OAI, clinicaltrials.gov identifier: NCT00080171, http://oai.ucsf.edu/), an on-going multi-center study targeted at identifying and validating biomarkers for knee OA. At baseline, the OAI cohort included 4,796 participants aged 45–79 years. General exclusion criteria were presence of rheumatoid or other inflammatory arthritis, bilateral end-stage knee OA, inability to walk without aids, and MRI contraindications[8]. At each of the annual visits, the OAI collected clinical data and acquired both 3 T MRI of the knees[9] and bilateral fixed-flexion radiographs (8). Semi-quantitative readings of medial and lateral JSN and osteophyte grades were based on the OARSI atlas[10] and were performed centrally by experienced readers from Boston University, using the bilateral fixed-flexion radiographs. Baseline and follow-up radiographs of each knee were independently assessed by two readers with the baseline radiograph identified to the readers and the follow-up radiographs randomly ordered. Discrepancies between readings were adjudicated with a third reader present.

Subject selection

Longitudinal cartilage thickness measurements were available for two subsamples of the OAI[8]: In 906 knees, baseline and 1 year follow-up measurements were available from coronal FLASH acquisitions[3,9]. In 565 knees, baseline, 1 year and 2-year follow-up measurements were available from sagittal DESS acquisitions[9,11]. The selection process of both subcohorts has been published previously[3,8,11] and both MR protocols have been validated and compared directly with respect to quantitative assessments of cartilage loss[12,13].

Only knees with definite ROA according to the central readings[8] were included in the current analysis, with definite ROA being defined as definite osteophytes with or without (medial or lateral) JSN. For this analysis, cartilage thickness measurements at baseline and 1 year follow-up were included. We studied only one knee per participant to avoid the need to take correlation between individuals' knees into account[14,15]. From the 544 (of 906) radiographically eligible knees of the FLASH subsample and 541 (of 565) eligible knees of the DESS subsample, 27 knees (12 FLASH, 15 DESS) were excluded because of bicompartimental (medial and lateral) JSN, and nine knees (all DESS) in subjects with data from both knees. From the remaining 532/517 FLASH/DESS knees, 127 were overlapping between both subsamples and were excluded from the larger FLASH subsample. The remaining 405 FLASH and 517 DESS knee image pairs (baseline and 1 year follow-up) from 922 participants were pooled for the analyses[16].

MRI-based measurement of cartilage thickness

Cartilage thickness measurements were based on manual segmentations as described previously[3,16]. After quality control of each MR data set by one expert (M.H.), segmentation of the weight-bearing femorotibial cartilages in paired images was performed by 12 trained readers (Chondrometrics GmbH), with blinding to acquisition order (baseline vs follow-up) and radiographic status. All segmentations were quality controlled by one of two experts (S.M. and F.E.) and were subsequently corrected by the readers, if necessary.

Segmentation of the total subchondral bone area (tAB) and the articular cartilage surface area (AC) was performed in the medial and the lateral tibia (MT/LT), and in the central, weight-bearing medial and the lateral femoral condyle (cMF/cLF)[17]. Osteophytes were excluded from the segmentation. Because the coronal orientation of the FLASH datasets precludes the segmentation of the posterior parts of the femoral condyle, the weight-bearing parts of the femoral condyles were defined as the 60% between the anterior border of the intercondylar notch and the posterior aspects of the femoral condyles for both the FLASH and the DESS acquisitions[16]. In the DESS subsample, segmentation was performed for every second of the 0.7 mm slices resulting in a slice thickness of 1.4 mm, as this was shown to provide a comparable sensitivity to change as the segmentation of every slice[16].

The mean cartilage thickness (ThCtAB) over the tAB was computed for each of the four femorotibial cartilage plates, including denuded areas as 0 mm thickness[18]. Lateral compartment (LFTC) cartilage thickness was computed as the sum of LT and cLF, and medial compartment (MFTC) cartilage thickness as the sum of MT and cMF. Subregional changes were computed in central external, internal, anterior, and posterior subregions of LT and MT, and in central external, and internal subregions of cLF and cMF[18]. Ordered values (OV) of subregional changes represent a location-independent measure of change in cartilage thickness. OVs are computed by ordering the change observed in the 16 femorotibial subregions (each five in MT and LT and each three in cMF and cLF) within each knee in ascending order[6,19]. Ordered value 1 (OV1) therefore represents the subregion with the largest decrease (or the smallest increase) in cartilage thickness and OV 16 the subregion

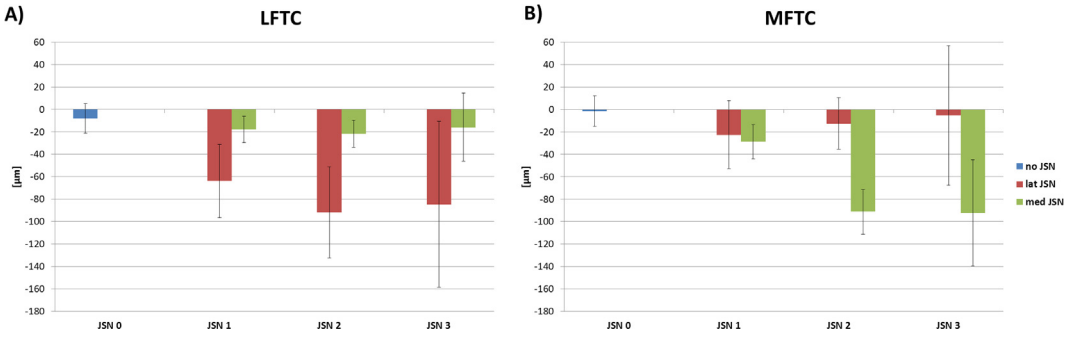

Fig. 1. MC and 95% CIs of the change in cartilage thickness in knees without JSN (noJSN), with lateral JSN 1–3 (latJSN), and with medial JSN 1–3 (medJSN) in A) the LFTC and B) the MFTC.