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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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Abstract

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 participants (62.2±9.0 years, , 61% females) with radiographic osteoarthritis (158 without JSN [noJSN], 175 with lateral JSN [latJSN], 589 with medial JSN [medJSN]) were analyzed using 3T MRI. One-year cartilage

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CONTRIBUTORS
WW and FE were involved in the conception and the analysis of the study. All authors were involved in the data interpretation, writing and critically revising the article.

COMPETING INTERESTS
Wolfgang Wirth has a part time appointment with and is co-owner of Chondrometrics GmbH, a company providing MR image analysis services to academic researchers and to industry. He has provided consulting services to MerckSerono. Marie-Pierre Hellio Le Graverand is a full-time employee of Pfizer. Susanne Maschek and Martin Hudelmaier have part time appointments with Chondrometrics GmbH and Susanne Maschek is also co-owner of Chondrometrics GmbH. Felix Eckstein is CEO and co-owner of Chondrometrics GmbH, he provides consulting services to MerckSerono, Sanofi Aventis, Abbot and Synarc, and has received speaker honoraria from Merck, GlaxoSmithKline, Genzyme, Medtronic, and Synthes. He has received research support from Pfizer, Eli Lilly, MerckSerono, Glaxo Smith Kline, Centocor R&D, Wyeth, Novartis, and Stryker. Michael Nevitt and John Lynch have no competing interests.

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≥0.35, magnitude: p=≥0.23). These results were confirmed by the location-independent ordered value 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.

Keywords

Magnetic resonance imaging; Knee osteoarthritis; lateral joint space narrowing; cartilage loss; cartilage thickness

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 (7); however whether lateral JSN is a predictor of lateral (or medial) femorotibial cartilage loss is currently 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 4796 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 3T 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 one year follow-up measurements were available from coronal FLASH acquisitions (3;9). In 565 knees, baseline, one year and two 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 one 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 9 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 one 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 2nd of the 0.7mm slices resulting in a slice thickness of 1.4mm, 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 femorotibal 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 5 in MT and LT and each 3 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 smallest increase) in cartilage thickness and OV 16 the subregion showing the largest increase (or smallest decrease) in subregional cartilage thickness within each knee.

Progressor classification

The smallest detectable change (SDC) methodology (20) was used to identify knees with significant cartilage thickness loss (progression) in the LFTC or MFTC. The SDC thresholds were computed using data from the OAI pilot study (13) and were −92 μm (FLASH) / −121 μm (DESS) for the LFTC and −102 μm (FLASH) / −111 μm (DESS) for the MFTC, respectively.

Statistical analysis

The annualized mean change (MC), the standard deviation of change (SD), and 95% confidence intervals (CI) of change in ThCtAB were determined between baseline and year one follow-up. The standardized response mean (SRM) was computed by relating the MC to the SD as a measure of the sensitivity to change. The effect sizes for the primary and the secondary comparisons were determined as the mean differences between the changes related to the pooled standard deviation of the changes.

In the current study, we determined the predictive value of unicompartimental lateral or medial JSN for both the frequency of structural progression (i.e. cartilage thickness loss exceeding the SDC threshold) and for the magnitude of change in cartilage thickness.

Because these two outcomes were considered complimentary to each other and not interpreted separately, we did not adjust the analyses for two outcome measures. The predictive value of unicompartimental lateral or medial JSN for the frequency of subsequent cartilage thickness loss in the narrowed compartment was reported as the probability of subsequent progression under the condition that JSN was present. The confidence intervals were calculated as described in (21). The predictive value of unicompartimental lateral or medial JSN for the magnitude of change in ThCtAB was assessed using non-parametric tests, because the distribution of the change in ThCtAB violated the assumptions of parametric statistical models. Non-parametric tests do not allow adjusting for potential confounding factors like age and BMI, but adjustment for these factors was not considered necessary given the weak association between change in ThCtAB and the factors age and BMI ($R^2 \leq 0.02$) in the current study.

As primary analysis, we compared the probability of progression and the magnitude of change between the narrowed compartment of knees with lateral or medial JSN to that observed in the respective compartment of knees without JSN using Fisher's exact tests (probability of progression) and Mann-Whitney-U tests (magnitude of change). The type I error rate was set to $p=0.05/2=0.025$ to account for 2 parallel tests (medial / lateral JSN). The non-parametric Kruskal-Wallis test was used to explore differences in change between knees with different grades of lateral or medial JSN, and Mann-Whitney-U tests were used as post-hoc tests in case the Kruskal-Wallis test identified significant differences between groups.

As secondary analyses, we compared the predictive value of lateral or medial JSN for the probability of progression and magnitude of change between a) the narrowed compartment of knees with lateral JSN (LFTC) and the narrowed compartment of knees with medial JSN (MFTC) and b) between the non-narrowed compartment of JSN knees with the respective compartment of no-JSN knees. Fisher's exact (probability) and the Mann-Whitney-U test (magnitude) were used for these comparisons. The type I error rate was set to $p=0.05/2=0.025$ to account for 2 parallel comparisons in the second analysis (medial/lateral JSN). The comparison between the narrowed compartment of knees with medial and lateral JSN was repeated with stratification by (medial and lateral) JSN grades, to explore the impact of JSN grades on the magnitude of change.

To explore the impact of unicompartimental lateral and medial JSN on the nonlocation-specific magnitude of subregional cartilage thickness loss, the above tests were also applied to OV 1 and OV 16 without adjustment for parallel comparisons. Analyses were performed using SPSS 20 (IBM Corporation, NY, US).

Results

The sample comprised 264 left and 658 right knees from 922 OAI participants. The central radiographic readings classified 175 (19%) knees as having unicompartimental lateral JSN, 589 (64%) knees as having unicompartimental medial JSN, and 158 (17%) knees as having definite ROA (i.e. definite osteophytes), but no JSN (Table 1). Lower JSN grades (1 and 2) were more frequent than higher grades, both in the lateral and medial compartment (Table

1). Participants with lateral JSN (63.2±8.9y) and medial JSN (62.5±9.0y) of the analyzed knee were somewhat older than participants without JSN of the analyzed knee (59.9±8.6, p=0.001, Table 1). The BMI of participants with lateral JSN of the analyzed knee (29.1±5.0kg/m^2) was lower than that of participants without JSN of the analyzed knee (30.0±4.6kg/m^2, p=0.003), but the BMI did not differ between participants with medial JSN (30.3±4.8kg/m^2) and without JSN of the analyzed knee (p=0.52, Table 1). The interval between the baseline and the one-year follow-up MRI acquisition was on average 393±47 days in the FLASH and 380±39 days in the DESS sample.

Narrowed compartment of knees with lateral and medial JSN

The probability of subsequent progression (i.e. cartilage thinning exceeding the SDC threshold) was greater in the narrowed compartment of knees with lateral JSN or medial JSN than in the respective compartment of knees without JSN (LFTC lateral JSN vs. no-JSN: 34.9 % 95%CI: [27.8, 41.9] vs. 13.3% [8.0, 18.6], $p=6.4\times10^{-6}$; MFTC medial JSN vs. no-JSN: 32.4% [28.6, 36.2] vs. 12.7% [7.5, 17.8], $p=3.0\times10^{-7}$).

The mean cartilage thinning was significantly greater in the LFTC of lateral JSN knees (−81μm, 95%CI: [−106, −55]) than in the LFTC of knees without any JSN (−8μm [−21, −5], $p= 8.2\times10^{-6}$, Table 2). Similarly, MFTC cartilage thinning was significantly greater in knees with medial JSN (−63μm [−75, −50]) than in knees without JSN (−2μm [−15, 12], $p=6.0\times10^{-6}$, Table 2). The greater cartilage thinning in JSN knees also resulted in a greater SRM in the narrowed compartment of JSN knees (Table 2). The effect sizes for these primary analyses are reported in Table 4.

LFTC cartilage thinning tended to be greater in knees with lateral JSN grades 2/3 than in those with grade 1, but the differences between groups were not significant (p=0.59, Table 3). In comparison, MFTC cartilage thinning differed significantly between knees with different grades of medial JSN ($p=3.0\times10^{-6}$, Table 3) with cartilage thinning being significantly greater in knees with medial JSN 2 and 3 than in knees with medial JSN 1 (medial JSN 2/3: $p=2.0\times10^{-6}$ / 0.004, Table 3). The cartilage thinning observed in knees with medial JSN 2 did not differ significantly from that observed in medial JSN 3 knees (p=0.89, Table 3).

Lateral vs. medial JSN

The probability of subsequent progression did not differ significantly between the LFTC in knees with lateral JSN and the MFTC in knees with medial JSN (p=0.58). Similarly, the mean change in the narrowed compartment (MFTC or LFTC) did not differ significantly between knees with medial and lateral JSN (p=0.19) and the sensitivity to change was comparable in the narrowed compartment of knees with lateral and medial JSN, respectively (−0.48 vs. −0.41, Table 2). Explorative analyses of mean change stratified by JSN grade did also not differ significantly between knees with lateral and medial JSN (medial vs. lateral JSN1/2/3: p=0.06/0.83/0.76, Table 3). The effect sizes for this secondary analysis are reported in Table 4.

Non-narrowed compartment of knees with lateral and medial JSN

The probability of subsequent progression did not differ significantly between the non-narrowed compartment of JSN knees and the respective compartment of knees without JSN (MFTC progression in lateral JSN knees: 16.6% [11.1, 22.1], p=0.35; LFTC progression in medial JSN knees: 14.9% [12.1, 17.8], p=0.70). The mean change in the non-narrowed compartment (MFTC or LFTC) of knees with unicompartimental lateral or medial JSN did also not differ significantly from the mean change observed in knees without JSN (MFTC: lateral vs. no JSN: p=0.23; LFTC: medial JSN vs. no JSN: p=0.60; Table 2). The effect sizes for this secondary analysis are reported in Table 4.

Ordered values

The change in OV 1 was significantly greater in knees with unicompartimental lateral and medial JSN than in knees without JSN (lateral/medial JSN: $p=1.1\times10^{-9}/8.7\times10^{-7}$, Table 2). Change in OV 1 did not differ significantly between knees with lateral JSN 1, 2, or 3 (p=0.62), but differed significantly between knees with medial JSN 1, 2, or 3 ($p=9.9\times10^{-9}$, Table 3). Post-hoc test showed that OV 1 was significantly smaller in medial JSN 1 than in medial JSN 2 knees ($p=1.5\times10^{-9}$) and showed a borderline significant difference when comparing OV 1 between knees with medial JSN 1 and 3 (p=0.046, Table 3). No significant difference was observed for OV1 between knees with medial JSN 2 and 3 (p=0.27, Table 3).

OV 16 was not significantly different between knees with lateral or medial JSN when compared to those without JSN (lateral/medial JSN: p=0.25/0.56, Table 2), but differed significantly between knees with different grades of lateral JSN (p=0.02, Table 3). Post-hoc tests showed that OV 16 was significantly greater in knees with lateral JSN 2 than in knees with lateral JSN 3 (p=0.01, Table 3). No significant difference was observed for change in OV 16 between knees with medial JSN 1, 2, or 3 (p=0.39). Results for ordered values 2 – 16 are shown in Online Tables 1 & 2.

When comparing knees with unicompartimental lateral and medial JSN, OV 1 was significantly greater in knees with lateral JSN 1 than in knees with medial JSN 1 (p=0.004, Table 3), However, OV 1 did not differ significantly between knees with higher grades of medial and lateral JSN (JSN 2: p=0.72, JSN 3: p=0.47, Table 3). OV 16 did not differ significantly between knees with medial and lateral JSN 1 to 3 ($p\geq0.06$, Table 3).

Stratification by MRI sequence (FLASH or DESS) did not change the principal observations made above (data not shown).

Discussion

The aim of this study was to evaluate the predictive value of unicompartimental lateral and medial JSN for subsequent structural change (i.e. cartilage thickness loss) in the narrowed femorotibial compartment of knees with JSN. The results show a significantly greater probability of subsequent progression and a significantly increased magnitude of cartilage thinning in the narrowed (lateral or medial) compartment of JSN knees, when compared with knees without JSN. Unicompartimental lateral and medial JSN were found to have a comparable predictive value for structural progression in the narrowed compartment, but

were not associated with an increased magnitude of cartilage thinning in the opposite (no JSN) compartment.

It has been previously reported that medial JSN was associated with greater subsequent structural progression in the medial femorotibial compartment (7;22), but no previous study has comprehensively examined the predictive value of lateral JSN for progression in in the entire LFTC. The focus of the current study was therefore set on knees with lateral JSN. However, we also included knees with medial JSN in the analysis, in order to compare the predictive value of lateral and medial JSN with subsequent cartilage thinning in the narrowed and non-narrowed compartment.

Two studies explored the relationship of lateral JSN with tibial cartilage volume: In a cross-sectional study, Ciccutini et al. reported a significant negative association between lateral JSN and cartilage volume in the lateral tibia (23). Saunders et al. reported an association between lateral JSN and both medial and lateral cartilage volume loss in the tibia (24), whereas we did not find lateral JSN to be associated with greater medial femorotibial cartilage thickness loss compared with knees without JSN. A possible explanation is that the study by Saunders et al. did not control for the ROA status in the medial compartment of these knees, and that in the lateral JSN group knees with medial (bicompartimental) JSN were not eliminated. In addition, only a minority of the knees was found to have osteophytes (<10%) in this study and these were reported to be more predictive for cartilage volume loss than JSN (>50% had medial JSN and ~20% had lateral JSN).

Although the radiographic acquisition protocol of the OAI focused on reproducible delineation of the medial (and not necessarily the lateral) tibial plateau, we find that lateral JSN is of similar predictive value for subsequent cartilage thickness loss in the LFTC as medial JSN for progression in the MFTC. The strong relationship of JSN with structural progression in the same, but not in the opposite (no JSN) compartment indicates that relying exclusively on Kellgren & Lawrence grades during the enrollment of participants to clinical trials is suboptimal, if compartment-specific (medial or lateral) structural measures are defined as outcomes. Because of the higher prevalence of medial JSN (25), participants enrolled by having KLG3 or 4 in the target knee are more likely to show medial than lateral progression. However, the notable amount of knees with lateral JSN is not likely to contribute to medial progression. Excluding knees with predominantly lateral disease (26;27), in turn, limits the generalizability of the findings. To circumvent this issue, it is possible to select individually, in each knee, the predominantly affected compartment as a structural outcome, based on compartment-specific JSN and osteophyte scores (28). This approach is supported by the similar frequency and magnitude of change in knees with lateral vs. medial JSN in the current analysis. An alternative, and potentially more efficient, approach may be the use of non-region specific measures as outcomes, such as ordered values (19). These were previously shown to provide a greater sensitivity to differences in change between KLG2 and KLG3 knees (6) and also a greater sensitivity in identifying risk factors of progression than location-specific measures (29). Given the high sensitivity to differences in change between knees with lateral JSN and knees without JSN shown in the current study, and the high sensitivity to differences in change between knees with and

without medial OA demonstrated previously (19), studies including knees with both medial and lateral OA might benefit greatly from selecting ordered values as outcomes.

Unicompartimental radiographic JSN was found to be a significant predictor of subsequent cartilage thickness loss in this study, and it should be kept in mind that the radiographic joint space width is not maintained by cartilage only. Meniscus extrusion was also reported to be associated with change in radiographic JSW (30), and a decreased JSW could therefore be caused by any combination of cartilage loss and meniscus extrusion. However, previous studies have shown that not only preexisting cartilage damages (31) but also meniscus extrusion (31;32) is predictive for subsequent cartilage thickness loss. In a recent cross-sectional study, Bloecker et al. found a significantly lesser coverage of the cartilage by the medial meniscus in knees with medial JSN than in those without medial JSN (33). Given the important role of the meniscus in load distribution, a reduced mechanical protection of the cartilage by the meniscus is likely to accelerate the structural damage, and a recent study has reported a significant association between meniscus lesions and cartilage thickness loss in adjacent cartilage subregions (34).The same may apply to lateral extrusion of the meniscus in knees with latJSN, exposure of the LFTC cartilage, and subsequent cartilage loss, but future work must confirm lateral meniscus position in latJSN knees to confirm this hypothesis.

A limitation of the current study is the lack of alignment measures, which are not yet available for the OAI. Several studies have established a strong association between malalignment and cartilage loss (35;36). However, from a clinical perspective, JSN grades are far more simple to obtain (and more frequently available in studies than alignment measures on long limb radiographs). The progressor definition used in the current study was based on the smallest detectable change approach (20), providing a threshold beyond which change is likely to be greater than measurement error. However, no threshold has yet been identified that relates structural progression directly to a clinical outcome (e.g. worsening in symptoms) and this should be addressed in future studies. The results have not been adjusted for potential confounding factors (e.g. BMI or age). However, BMI and age were quite balanced across JSN categories and were only weakly associated with change in cartilage thickness when stratifying for radiographic disease stage (JSN, $R^2 \leq 0.02$). Therefore, adjustments would not have changed any of the conclusions. Advanced statistical modeling might allow to further improve the estimation of the effect of baseline JSN for cartilage loss.

In conclusion, unicompartimental lateral and medial JSN were found to be strong predictors for structural progression (i.e. cartilage thickness loss) in the narrowed femorotibial compartment. The probability of subsequent lateral cartilage thickness loss in knees with lateral JSN was comparable to that of medial cartilage thickness loss in knees with medial JSN and was significantly greater than that in knees without JSN. However, lateral or medial JSN did not increase the probability or magnitude of subsequent cartilage thickness loss in the non-narrowed compartment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Marie-Pierre Hellio Le Graverand, Michael Nevitt, and John Lynch were involved in the discussion and interpretation of the data and in the editing of this manuscript. However, the funders were not involved in setting up the study concept or the statistical analysis.

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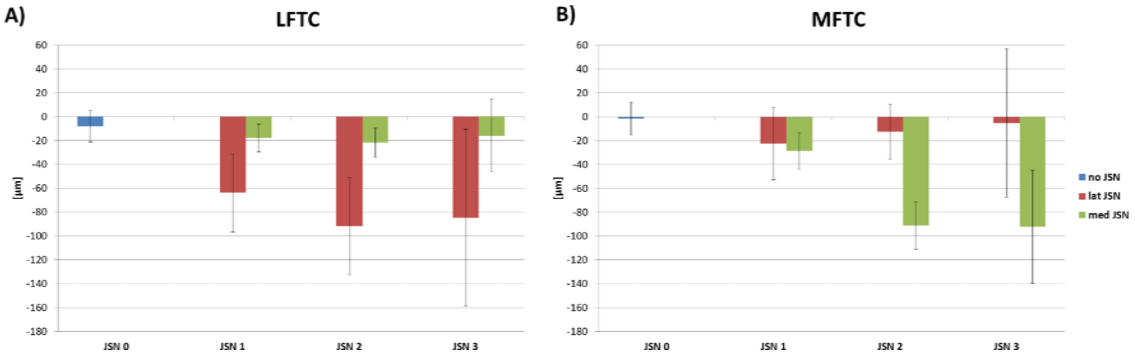

Figure 1.

Mean change and 95% confidence intervals 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 lateral femorotibial compartment (LFTC) and B) the medial femorotibial compartment (MFTC).

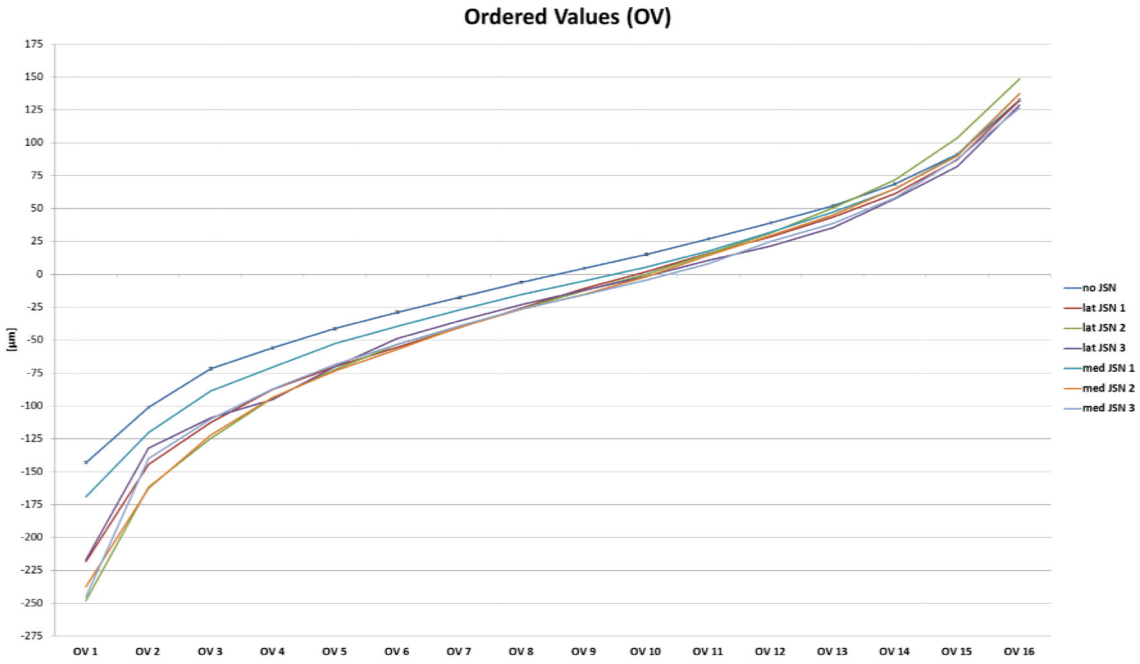

Figure 2.

Mean change in ordered values 1 – 16 (OV 1 – OV 16) in knees without JSN (noJSN), with lateral JSN 1 – 3 (lat JSN 1-3), and with medial JSN 1 – 3 (med JSN 1-3).

Table 1

Demographics and joint space narrowing (JSN) scores in knees without JSN (noJSN), with lateral JSN (latJSN) and medial JSN (medJSN)

	no JSN (N=158)	lat JSN (N=175)	med JSN (N=589)
Age (SD)	59.9 ± 8.6	63.2 ± 8.9	62.5 ± 9.0
BMI (SD)	30.0 ± 4.6	29.1 ± 5.0	30.3 ± 4.8
Sex (m/f)	40 / 118	56 / 119	265 / 324
MRI (DESS/FLASH)	79 / 79	105 / 70	333 / 256
lat/med JSN 0 (%)	158 (100.0)	0 (0)	0 (0)
lat/med JSN 1 (%)	0 (0)	65 (37.1)	270 (45.8)
lat/med JSN 2 (%)	0 (0)	90 (51.4)	280 (47.5)
lat/med JSN 3 (%)	0 (0)	20 (11.4)	39 (6.6)

Age: years; BMI: kg/m^2; Sex: Number of male (m) and female (f) subjects; MRI: Number of knees analyzed using the sagittal DESS and the coronal FLASH sequence; lat/med JSN 0-3: Number and percentage of knees scored as having unicompartimental (lateral or medial JSN)

Table 2

Change in cartilage thickness in knees without joint space narrowing (noJSN), with lateral JSN (latJSN), and medial JSN (medJSN)

	no JSN					lat JSN					med JSN				
	MC	**SD**	**CI**		**SRM**	**MC**	**SD**	**CI**		**SRM**	**MC**	**SD**	**CI**		**SRM**
LFTC	−8	84	−21	5	−0.09	−81	168	−106	−55	−0.48	−20	100	−28	−11	−0.20
LT	−8	52	−16	0	−0.15	−46	75	−57	−34	−0.61	−16	55	−20	−11	−0.29
cLF	0	65	−10	10	0.00	−35	119	−53	−17	−0.29	−4	74	−10	2	−0.05
MFTC	−2	87	−15	12	−0.02	−15	117	−33	2	−0.13	−63	154	−75	−50	−0.41
MT	5	45	−2	12	0.11	−8	52	−15	0	−0.15	−20	70	−26	−14	−0.29
cMF	−6	63	−16	4	−0.10	−8	94	−22	6	−0.08	−43	111	−51	−34	−0.38
OV 1	−143	74	−155	−132		−233	169	−259	−208		−207	160	−220	−194	
OV 16	132	79	120	145		140	79	128	152		137	80	130	143	

Mean change (MC), standard deviation of the change (SD), and 95% confidence intervals of the change (CI) in cartilage thickness in the lateral/medial femorotibial compartment (LFTC/MFTC), the lateral/medial tibia (LT/MT), the central, weight-bearing part of the lateral/medial femur (cLF/cMF), the subregion showing the highest negative change within each knee (OV1), and the subregion showing the highest positive change within each knee (OV16). The standardized response mean (SRM) was reported for compartment measures and cartilage plates but not for ordered values. All changes in μm.

Table 3

Change in cartilage thickness in knees with lateral and medial JSN stratified by JSN score (1-3)

	JSN 1					JSN 2					JSN 3				
	MC	SD	CI		SRM	MC	SD	CI		SRM	MC	SD	CI		SRM
Lateral JSN:															
LFTC:	−64	132	−96	−31	−0.48	−92	193	−132	−51	−0.48	−85	158	−159	−11	−0.53
LT	−46	76	−64	−27	−0.60	−45	77	−61	−29	−0.58	−49	62	−78	−20	−0.79
cLF	−18	84	−39	3	−0.22	−47	140	−76	−17	−0.33	−36	114	−89	18	−0.31
MFTC:	−23	123	−53	8	−0.18	−13	110	−36	10	−0.11	−5	133	−68	57	−0.04
MT	−13	56	−27	0	−0.24	−1	52	−12	10	−0.03	−17	40	−36	1	−0.44
cMF	−9	97	−33	15	−0.09	−11	86	−29	7	−0.13	12	120	−44	68	0.10
OV 1	−218	150	−255	−181		−248	190	−288	−208		−217	119	−272	−162	
OV 16	132	65	116	148		149	76	133	164		129	126	70	188	
Medial JSN:															
LFTC:	−18	97	−29	−6	−0.18	−22	104	−34	−10	−0.21	−16	93	−46	14	−0.17
LT	−14	54	−21	−8	−0.27	−19	58	−25	−12	−0.32	−10	51	−26	7	−0.18
cLF	−3	69	−12	5	−0.05	−3	75	−12	6	−0.04	−6	94	−37	24	−0.07
MFTC:	−29	129	−44	−13	−0.22	−91	171	−111	−71	−0.53	−92	146	−140	−45	−0.63
MT	−7	56	−14	−1	−0.13	−31	81	−40	−21	−0.38	−34	62	−54	−14	−0.55
cMF	−22	97	−33	−10	−0.22	−61	121	−75	−46	−0.50	−59	102	−92	−26	−0.58
OV 1	−169	124	−184	−154		−238	157	−256	−219		−245	296	−341	−149	
OV 16	137	72	129	146		137	86	127	147		127	87	98	155	

Mean change (MC), standard deviation of the change (SD), and 95% confidence intervals of the change (CI) in cartilage thickness in the lateral/medial femorotibial compartment (LFTC/MFTC), the lateral/medial tibia (LT/MT), the central, weight-bearing part of the lateral/medial femur (cLF/cMF), the subregion showing the highest negative change within each knee (OV1), and the subregion showing the highest positive change within each knee (OV16). The standardized response mean (SRM) was reported for compartment measures and cartilage plates but not for ordered values. All changes in μm.

Table 4

Absolute effect size for differences in change in cartilage thickness between knees with lateral JSN, medial JSN, and knees without JSN

	Lateral JSN vs. no JSN	Medial JSN vs. no JSN	Lateral JSN vs. medial JSN
Narrowed compartment:			
LFTC/MFTC	0.54	0.43	0.11
LT/MT	0.58	0.38	0.36
cLF/cMF	0.36	0.35	0.07
Non-narrowed compartment:			
LFTC/MFTC	0.13	0.12	0.04
LT/MT	0.25	0.15	0.15
cLF/cMF	0.02	0.05	0.05
Ordered values:			
OV 1	0.68	0.43	0.16
OV 16	0.10	0.05	−0.04

Lateral/medial femorotibial compartment: LFTC/MFTC; lateral/medial tibia: LT/MT; central, weight-bearing part of the lateral/medial femur: cLF/cMF; ordered values 1/16: OV1/OV16. The effect size was determined as the difference in change related to the pooled standard deviation of the respective changes for the narrowed compartment (LFTC change in knees with lateral JSN vs. knees without JSN or LFTC change in knees with lateral JSN vs. MFTC change in knees with medial JSN), in the non-narrowed compartment and for compartment-independent ordered values.