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Quantitative measures of meniscus extrusion predict incident radiographic knee osteoarthritis – data from the Osteoarthritis Initiative

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SUMMARY

Objective: To test the hypothesis that quantitative measures of meniscus extrusion predict incident radiographic knee osteoarthritis (KOA), prior to the advent of radiographic disease.
Methods: 206 knees with incident radiographic KOA (Kellgren Lawrence Grade (KLG) 0 or 1 at baseline, developing KLG 2 or greater with a definite osteophyte and joint space narrowing (JSN) grade ≥1 by year 4) were matched to 232 control knees not developing incident KOA. Manual segmentation of the central five slices of the medial and lateral meniscus was performed on coronal 3T DESS MRI and quantitative meniscus position was determined. Cases and controls were compared using conditional logistic regression adjusting for age, sex, BMI, race and clinical site. Sensitivity analyses of early (year [Y] 1/2) and late (Y3/4) incidence was performed.
Results: Mean medial extrusion distance was significantly greater for incident compared to non-incident knees (1.56 mean ± 1.12 mm SD vs 1.29 ± 0.99 mm; +21%, $P < 0.01$), so was the percent extrusion area of the medial meniscus (25.8 ± 15.8% vs 22.0 ± 13.5%; +17%, $P < 0.05$). This finding was consistent for knees restricted to medial incidence. No significant differences were observed for the lateral meniscus in incident medial KOA, or for the tibial plateau coverage between incident and non-incident knees. Restricting the analysis to medial incident KOA at Y1/2 differences were attenuated, but reached significance for extrusion distance, whereas no significant differences were observed at incident KOA in Y3/4.
Conclusion: Greater medial meniscus extrusion predicts incident radiographic KOA. Early onset KOA showed greater differences for meniscus position between incident and non-incident knees than late onset KOA.

Introduction

The menisci are critical for the mechanical protection of the knee cartilage by enabling consistent force transmission[1–3], and thereby keeping the mechanical stress on cartilage and subchondral bone within reasonable limits[2–5]. Meniscal tears are highly prevalent in the general population[6] and represent a risk factor for the onset and progression of knee osteoarthritis (KOA)[7,8]. Meniscus extrusion (subluxation) is a common consequence of meniscal tears[9,10] and has been frequently observed in patients with KOA[11]. Semi-quantitative magnetic resonance imaging (MRI) measures of extrusion using the Whole Organ Magnetic Resonance Imaging Score (WORMS), Boston Leeds Osteoarthritis Knee Score

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(BLOKS) or the MRI Osteoarthritis Knee Score (MOAKS) have been identified as important predictors of structural progression over time (i.e., cartilage loss)[12–15]. There also have been studies that attempted to determine predictors of incident KOA using semi-quantitative scoring systems of the meniscus. In a study from Badlani *et al.*, focusing on persons with radiographic OA in one knee, semi-quantitative measures of medial meniscus extrusion were associated with greater risk of incident KOA in the contra-lateral, previously healthy knee[16]. In contrast, Sharma *et al.* who investigated pre-radiographic MRI lesions in persons with increased risk of KOA but with Kellgren Lawrence Grade (KLG) 0 knees at the time of examination, reported that meniscal extrusion assessed using semi-quantitative approaches was modestly (Odds Ratio 1.72, 95% CI [0.63, 4.71]) but not significantly associated with incident cartilage damage, but meniscal extrusion was present in only 14% of knees studied[17].

We recently developed three dimensional quantitative measurement technology using MRI to determine meniscus size, shape, and position relative to the tibial plateau cartilage[18–20]. Using this technique we showed previously that measures of medial meniscus extrusion were increased and tibial coverage was decreased in knees with medial radiographic joint space narrowing (JSN)[11], compared with contra-lateral knees without JSN[11], and compared with healthy reference knees[19].

The objective of the present study was to test the hypothesis that quantitative measures of meniscus position such as meniscus extrusion and percent (%) tibial plateau cartilage coverage prior to the advent of radiographic evidence of disease predict incident radiographic KOA. Specifically, we aimed to identify which quantitative measure of meniscus position predicts early or late onset of incident radiographic KOA most strongly.

Methods

Study participants

The subsample analyzed was drawn from the Osteoarthritis Initiative (OAI). The OAI is a multi-center, population-based longitudinal cohort study, targeted at identifying risk factors associated with the onset and progression of KOA, and at characterizing biomarkers of the disease. Participants of the OAI were between 45 and 79 years old at baseline and included a diversity of ethnic backgrounds. Participants with rheumatoid or other inflammatory arthritis, bilateral end stage KOA, inability to walk without aids, or MRI contraindications were excluded. Informed consent was obtained from all participants and the study was approved by local ethics committees.

In the current study we analyzed those knees that exhibited incident radiographic KOA on central readings of fixed flexion radiographs. These were defined as knees with KLG 0 or 1 at baseline that, by the year 4 follow-up, developed Kellgren and Lawrence grade 2 or greater using a recommended definition[21] that requires both a definite osteophyte and OARSI JSN grade $\geq$1. About 30% of these knees were KLG0, and about 70% were KLG1 at baseline. After the 4-year follow-up period, 125 (29%) of knees had KLG 2, 69 (16%) of the knees had KLG 3 and 12 (3%) had KLG 4. These knees were matched to a control group of knees according to their KL grade at baseline drawn from the same cohort that did not develop incident KOA up to the 4 year follow-up, (69 (16%) knees had KLG 0 and 163 (37%) knees had KLG 1) so that a total of 438 case and control knees were studied (Table I).

We further performed sensitivity analyses in which we separated incidence of medial and lateral radiographic KOA and compared a subcohort of 166 incident knees with medial KOA to the control group of 232 non-incident knees, as well as 59 incident knees with lateral KOA to 232 non-incident knees, respectively. For the group with incident medial KOA, another sensitivity analysis was done, studying knees with medial incidence early ((either at year 1 or 2 follow-up; $n = 107$), or late (either at year 3 or 4 follow-up; $n = 59$).

Quantitative analysis of meniscus position

Sagittal double echo at steady state MR images with water excitation (DESSwe) were acquired of each knee using 3 Tesla Magnetom Trio magnets (Siemens Erlangen, Germany) and quadrature transmit-receive knee coils (USA Instruments, Aurora, OH)[22,23]. The coronal multi-planar reconstruction (MPR) of the sagittal DESSwe was used for the quantitative analysis of the meniscus position. The coronal MPR DESSwe was interpolated from the near-isotropic sagittal DESSwe (resolution: 0.365 × 0.465 × 0.7 mm) with an in-plane resolution of 0.37 mm × 0.7 mm and a slice-thickness of 1.5 mm[24,25,22]. Meniscus segmentation and morphometry from the DESS was previously shown to yield acceptable inter-observer reliability and good agreement with measurements made from a coronal intermediate-weighted turbo spin echo (IW-TSE) sequence[26] as well as high intra-observer reliability[18–20]. The advantage of the DESS is that it provides better resolution with thinner slices (1.5 vs 3 mm) than the coronal IW TSE sequence, and a better delineation of the tibial plateau cartilage surface area than the coronal IW TSE and also that it has been validated for accurately depicting tibial cartilage[24].

All images underwent initial quality control. Manual segmentation of the medial and lateral tibial plateau area (i.e., the area of cartilage surface, including denuded areas of subchondral bone = ACdAB[18,20]), and the surfaces of the medial and lateral meniscus (tibial, femoral and external) was performed by a single experienced operator (K.E.). Segmentation and quantitative analysis was performed using dedicated image analysis software

Table I
Demographics of participants with incident radiographic KOA ($n = 206$) vs those without incident radiographic KOA ($n = 232$) participants

		Incident KOA	No incident KOA	*P*-value
Age	Mean (SD)	61.5 (8.7)	61.0 (9.0)	0.564
Gender	Male	72 (35%)	91 (39%)	0.36
	Female	134 (65%)	141 (61%)	
Race/Ethnicity	White	171 (83%)	216 (93%)	0.001
	Non-White	35 (17%)	16 (7%)	
BMI	Mean (SD)	29.1 (4.2)	27.6 (0.3)	<0.001
Kellgren & Lawrence Grade	0	55 (27%)	70 (30%)	0.42
	1	151 (73%)	162 (70%)	
History of knee injury	No	109 (54%)	138 (60%)	0.2
	Yes	94 (46%)	93 (40%)	

SD = standard deviation.

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