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Brief Report

Baseline meniscal extrusion associated with incident knee osteoarthritis after 30 months in overweight and obese women

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SUMMARY

Objective: To investigate the association between baseline meniscal extrusion and the incidence of knee osteoarthritis (KOA) after 30 months in a high-risk population of overweight and obese women, free of clinical and radiological KOA at baseline.

Methods: 407 middle-aged overweight women (body mass index – BMI $\geq$ 27 kg/m^2) were evaluated at baseline and after 30 months of follow-up. Meniscal extrusion was defined as grade $\geq$2 on MRI according to MRI Osteoarthritis Knee Score (MOAKS). The primary outcome measure was KOA after 30 months follow-up, defined using the following criteria: either incidence of radiographic KOA (Kellgren & Lawrence grade 2 or higher), or clinical osteoarthritis (OA) according to the American College of Radiology (ACR) criteria, or medial or lateral joint space narrowing (JSN) of $\geq$1.0 mm. Using generalized estimating equations (GEE), we determined the association between knees with and without meniscal extrusion and both outcomes, corrected for the baseline differences.

Results: 640 knees were available at baseline of which 24% (153) had meniscal extrusion. There was a significantly higher incidence of KOA according to the primary outcome measure in women with meniscal extrusion compared to those without extrusion (28.8%, odds ratio – OR 2.39, 95% CI 1.53, 3.73). A significantly higher incidence was found for the development of radiographic KOA (12.4%, OR 2.61, 95% CI 1.11, 6.13) and medial JSN (11.8%, OR 3.19, 95% CI 1.59, 6.41). Meniscal extrusion was not significantly associated with clinical KOA and lateral JSN.

Conclusion: Meniscal extrusion was associated with a significantly higher incidence of KOA, providing an interesting target for early detection of individuals at risk for developing KOA.

Introduction

Meniscal pathology, including tears, destruction and extrusion, is a common finding in knees with osteoarthritis (OA). Since knee osteoarthritis (KOA) is a largely irreversible condition, identifying risk factors before onset or in an early stage of the disease is of great importance. Meniscal extrusion might be such an interesting target for early detection. Extrusion is where the meniscus is partially or totally displaced from the tibial cartilage surface[1]. It can occur secondary to meniscal tears[2,3], but multiple other factors are related to extrusion, including higher age, obesity, history of knee trauma, malalignment and generalized OA[4,5]. The generally accepted idea is that a displaced meniscus affects the weight-bearing and load distribution capacities within the knee joint, which leads to loss of cartilage and increase in bone marrow lesions, ultimately resulting in KOA[6–8]. Multiple studies affirm this relationship between meniscal extrusion and the development of KOA or features thereof[6–10]. However, most of these studies were

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carried out in cohorts of subjects with established OA. In order to confirm that meniscal extrusion is largely independently related to incident KOA, evaluation should take place in a large high-risk population, free of KOA at baseline. Therefore, the objective of the present study was to evaluate the association between baseline meniscal extrusion and the incidence of KOA in a high-risk population, free of clinical and radiographic KOA at baseline.

Methods

Data collection/study population

Data were derived from the PROOF study, a large prospective intervention study in a high-risk population of 407 middle-aged overweight and obese women with a body mass index (BMI) of $\geq$27 kg/m^2, free of clinical and radiographic KOA at baseline. This study has been described in detail previously (ISRCTN 42823086)[11]. Aim of this study was to assess the preventative effect of a lifestyle intervention (diet and exercise) and of oral glucosamine sulphate (double-blind placebo controlled) on the development of KOA. At baseline, subjects filled in a questionnaire to assess physical activity and were asked for menopausal status and history of knee injury. Bodyweight, height, Heberden's nodes (as an indication for generalized OA), knee alignment and maximum strength of the quadriceps muscle were measured and, to assess the K&L grade, a standardized semi-flexed posteroanterior (PA) radiograph of both knees was taken according to the metatarsophalangeal (MTP) protocol[12]. The duration of follow-up was 30 months.

MRI technique and scoring

At baseline a multisequence 1.5 T Magnetic Resonance Imaging (MRI) of both knees was made, including a coronal and sagittal proton density (PD) weighted sequence with 3.0 mm slice thickness and a slice gap of 0.3 mm, which we used for our study. MRIs were scored by trained readers (JR, PvdP) as well as an experienced musculoskeletal radiologist (EO) using the MRI Osteoarthritis Knee Score (MOAKS)[13].

Definitions

Meniscal extrusion was defined as grade 2 or grade 3 extrusion according to the MOAKS criteria, which corresponds to an extrusion of 3 mm or more. Grade 0 or 1 extrusion (<2 mm, 2–2.9 mm) was considered as no extrusion. The primary outcome measure was the incidence of KOA, defined using the following criteria: either radiographic KOA (Kellgren & Lawrence (K&L) grade 2 or higher), clinical OA according to the ACR criteria, or medial or lateral joint space narrowing (JSN) of $\geq$1.0 mm. Subsequently we evaluated the exact location of extrusion by subdividing both the medial and lateral meniscus into the body and anterior horn (resulting in four subregions).

Statistical analysis

Knees with and without meniscal extrusion were compared for the primary outcome measure and its separate items using generalized estimating equations (GEE), with which we corrected for both the correlation between two knees within subjects as well as the baseline differences between the two groups. To correct for the potential effects of the interventions of the original trial, their mutual interactions and their interactions with baseline meniscal extrusion on the outcomes, a sensitivity analysis in which all these factors were added to the analyses was performed. Furthermore, the effect of additional adjustment for baseline K&L grade was evaluated. The outcomes are being presented in percentages, odds ratios (ORs) and confidence intervals. A two-sided *P*-value of <0.05 was considered statistically significant. All analyses were performed with the SPSS-software, version 22.0.0.0 (2013, IBM, NY, USA).

Results

Patient characteristics

Initially, 407 women were enrolled in the study, of which 330 women and 640 knees were eligible for statistical analysis; 77 women and 174 knees did not have an MRI at baseline, or had incomplete data regarding the primary outcome measure, or had K&L $\geq$ 2 at baseline and were therefore excluded from the analysis. Of these 640 knees, 153 showed meniscal extrusion on MRI (23.7%). The majority of the extrusions were located in the medial meniscus; primarily in the body (71%), followed by anterior extrusion (35%). Only a few knees had extrusion in the lateral meniscus. The subjects had a mean age of 56.2 ± 3.0 years and a mean BMI of 32.5 ± 4.26 kg/m2. More than one-third (69%) of the women were postmenopausal (n = 102). At baseline, there were significant differences between knees with and without meniscal extrusion regarding age, history of knee injury, varus alignment, Heberden's nodes, maximum strength of the quadriceps muscle, osteophytes in the tibiofemoral joint, bone marrow lesions in the tibiofemoral joint and meniscal pathologies (of which the latter three were scored on MRI). Consequently, the main model was adjusted for all these variables.

Association meniscal extrusion and primary and secondary outcome measures

Associations between baseline meniscal extrusion, the primary outcome measure and its separate criteria are shown in Table I. 28.8% of the 153 knees with meniscal extrusion at baseline had

Table I
Associations between meniscal extrusion and incident KOA after 30 months (n total = 640 knees, n meniscal extrusion = 153, n no meniscal extrusion = 487)

	Knee OA*		Radiographic knee OA		Clinical knee OA		Medial JSN		Lateral JSN	
	Incidence, %	OR (95% CI)	Incidence, %	OR (95% CI)	Incidence, %	OR (95% CI)	Incidence, %	OR (95% CI)	Incidence, %	OR (95% CI)
Total	17.8 (113/640)		5.5 (35/640)		5.2 (33/640)		5.5 (35/640)		6.4 (41/640)	
Meniscal extrusion	28.8 (44/153)	2.39 (1.53, 3.73)	12.4 (19/153)	2.61 (1.11, 6.13)	6.5 (10/153)	1.62 (0.7, 3.74)	11.8 (18/153)	3.19 (1.59, 6.41)	8.5 (13/153)	1.5 (0.84, 2.66)
No meniscal extrusion	14.2 (69/487)	1 (reference)	3.3 (16/487)	1 (reference)	4.7 (23/487)	1 (reference)	3.5 (17/487)	1 (reference)	5.7 (28/487)	1 (reference)

* Defined as the incidence of radiographic KOA (K&L grade $\geq$ 2), clinical KOA (ACR criteria) or medial or lateral JSN ($\geq$1.0 mm) at follow-up. All analyses were adjusted for age, history of knee injury, varus alignment, Heberden's nodes, maximum strength of the quadriceps muscle, osteophytes in the tibiofemoral joint, bone marrow lesions in the tibiofemoral joint and meniscal pathologies.