BASELINE MENISCAL EXTRUSION ASSOCIATED WITH INCIDENT KNEE OSTEOARTHRITIS AFTER 30 MONTHS IN OVERWEIGHT AND OBESE WOMEN

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ABSTRACT

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 knee OA at baseline.

Methods

407 middle-aged overweight women (BMI ≥ 27 kg/m^2) were evaluated at baseline and after 30 months of follow-up. Meniscal extrusion was defined as grade ≥ 2 on MRI according to MOAKS. The primary outcome measure was KOA after 30 months follow-up, defined using the following criteria: either incidence of radiographic knee OA (Kellgren & Lawrence grade 2 or higher), or clinical OA according to the ACR criteria, or medial or lateral joint space narrowing (JSN) of ≥ 1.0 mm. Using generalized estimating equations, 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%, OR 2.39, 95% CI 1.53, 3.73). A significantly higher incidence was found for the development of radiographic knee OA (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 knee OA 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.

KEYWORDS

Meniscus, extrusion, knee, osteoarthritis, overweight, obesity.

INTRODUCTION

Meniscal pathology, including tears, destruction and extrusion, is a common finding in knees with osteoarthritis (OA). Since knee OA 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 osteoarthritis (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 knee OA[6-8]. Multiple studies affirm this relationship between meniscal extrusion and the development of knee OA or features thereof [6-10]. However, most of these studies were carried out in cohorts of subjects with established OA. In order to confirm that meniscal extrusion is largely independently related to incident knee OA, evaluation should take place in a large high-risk population, free of knee OA at baseline. Therefore, the objective of the present study was to evaluate the association between baseline meniscal extrusion and the incidence of knee OA in a high-risk population, free of clinical and radiographic knee OA 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 ≥ 27kg/m2, free of clinical and radiographic knee OA 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 knee OA. 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 MTP protocol[12]. The duration of follow-up was 30 months.

MRI technique and scoring

At baseline a multisequence 1.5 Tesla 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 knee OA, defined using the following criteria: either radiographic knee OA (Kellgren & Lawrence (K&L) grade 2 or higher), clinical OA according to the ACR criteria, or medial or lateral joint space narrowing (JSN) of ≥ 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 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 ≥ 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 3 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 1. 28.8% of the 153 knees with meniscal extrusion at baseline had developed knee OA (adjusted OR 2.39, 95% CI 1.53, 3.73), which is significantly more compared to the group without extrusion (14.2%). Incidence of radiographic knee OA was seen in 12.4% of the knees with extrusion, which is also significantly higher compared to the control knees (adjusted OR 2.61, 95% CI 1.11, 6.13). Furthermore, medial JSN was seen significantly more often in knees with meniscal extrusion (11.8%, adjusted OR 3.19, 95% CI 1.59, 6.41). The incidence rates of both clinical knee OA and lateral JSN were also higher for patients with extrusion, but these differences did not reach statistical significance. Of the four separate locations, only extrusion of the medial meniscus body was significantly associated with the incidence of knee OA (Table 2). Since the numbers of lateral extrusion were too low for reliable statistical analysis, only the percentages and OR’s of medial extrusion are shown in the table. The sensitivity analyses showed a non-significant interaction between either of the original interventions and baseline meniscal extrusion. The interaction between the original interventions was statistically significant, but did not influence the outcomes significantly (data not shown). Additional adjustment for baseline K&L grade did not essentially affect the results from the main model (data not shown).

DISCUSSION

We assessed the association between baseline meniscal extrusion with the incidence of knee OA in a high-risk population, free of clinical and radiographic knee OA at baseline. We found that almost 30% of our population developed knee OA, which is a remarkably high percentage considered the relatively short follow-up time of 30 months. Since this study was performed in a large high-risk population without OA at baseline, this result provides strong evidence that extrusion is related to incident knee OA.

The results further indicate a discrepancy between radiographic and clinical signs of knee OA, since knees with meniscal extrusion did not show a statistically significant association with clinical knee OA, despite a higher incidence of almost 40% compared to those without. Particularly for mild knee OA, the most likely cause for this phenomenon is the variability in pain perception between individuals.

One of the strengths of our study is that we evaluated four meniscal subregions, while most studies in the field focused on medial body extrusion only. Still, our data confirm that medial body extrusion is more strongly associated with incident knee OA than any other location, which, to save time and costs, supports the choice for one sole measurement location in previous and future studies. The vast majority of the meniscal extrusions were located in the medial meniscus, especially in the body (71%), which corresponds to previous findings[6,9]. The difference seen in our study however is slightly more pronounced, with only 12 knees (8%) showing lateral extrusion.

Since we demonstrated that meniscal extrusion is largely independently related to the development of knee OA, it is important to know what causes meniscal extrusion. Crema *et al.* performed a large observational study among 1527 patients and 2131 knees and described several extrusion related factors[2]. Independent of the type and location (e.g. radial, longitudinal, vertical, complex, root and non-root), tears of the meniscus are associated with extrusion in both compartments, which was confirmed by Zhang *et al.* in a recent study using longitudinal data[3]. Crema *et al.* further demonstrated an independent association of tibiofemoral cartilage damage with meniscal extrusion, most likely due to the altered weight bearing and load distribution capacities in knees with a displaced meniscus[6-10]. Their hypothesis is that the cascade begins with loss of cartilage, narrowing the tibiofemoral space, squeezing the meniscus and leading to extrusion. Still, there is limited evidence which supports this theory that cartilage damage is predictive for meniscal extrusion.

Meniscal tears and cartilage damage however are both largely non-modifiable risk factors. To prevent development or progression of meniscal extrusion and thus knee OA, knowledge about modifiable factors is important. Malalignment might be an interesting modifiable factor related to both meniscal extrusion and knee OA, where varus alignment is associated with medial extrusion and valgus alignment with lateral extrusion[14]. Nevertheless, it is not clear whether malalignment on its own precedes extrusion, or is just secondary to progressive meniscal extrusion and knee OA. Englund *et al.* showed that a higher BMI is related to meniscal extrusion, although this was not confirmed in another study sample[3,4]. Since obesity is modifiable, one can hypothesize that losing weight might reduce or reverse extrusion, thus preventing development or progression of knee OA. The results of the study of Landsmeer *et al.* could be interpreted as an extension of these findings[15]. They found that the diet and exercise program resulted in significantly less progression of meniscal extrusion in the same population used in the present study.

The definition for meniscal extrusion used for the present study was grade 2 or grade 3 according to the MOAKS criteria, which corresponds to an extrusion of 3 mm or more. MOAKS is an evolution of older methods such as KOSS, WORMS and BLOKS and has proven itself as a valid tool for the evaluation of MRI OA features[13]. However, a semi-quantitative scoring method for the meniscus does not take into account the proportion of the tibial cartilage surface covered by the meniscus. It does not consider the absolute sizes of both meniscus and tibial plateau which obviously varies between individuals. Several recent studies described a new approach for quantitative MRI analysis of meniscal extrusion using 3D imaging techniques[9,10], which might be a more reliable way to assess volumetric morphometry and extrusion of the meniscus and a more truthful representation of the in vivo situation.

CONCLUSION AND IMPLICATIONS

With this prospective study among middle-aged overweight and obese women without knee OA at baseline we provided solid evidence that meniscal extrusion is a largely independent predictor for the development of knee OA, which gives further insight in the pathogenesis of the disease. Meniscal extrusion might be used for early detection of patients at risk for developing knee OA and could potentially be used for future preventative therapies, especially in the young to middle-aged patient, which the field currently lacks. However, what this preventative therapies should look like, is still unknown.

CONTRIBUTIONS

JvdV contributed to the analysis and interpretation of data, writing of the manuscript and final approval of the article. JR contributed to the conception and design of the study, including collection and assembly of data, semi-quantitative scoring of the MRIs, analysis and interpretation of data and critical revision of the article for important intellectual content. SBZ contributed to conception and design of the study including obtaining of funding, analyses and interpretation of data and critical revision of the article for important intellectual content. DV and EO contributed to the conception and design of the study and to the critical revision of the article for important intellectual content. PvdP contributed to the semi-quantitative scoring of the MRIs and to the critical revision of the article for important intellectual content. All authors approved the final version of the manuscript.

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COMPETING INTERESTS

All authors declare no conflicts of interest.

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