

Englund M, Guermazi A, et al. Meniscal tear in knees without surgery and the development of radiographic osteoarthritis among middle-aged and elderly persons: The Multicenter Osteoarthritis Study. *Arthritis Rheum* 2009;60(3):831-839.

Design: Nested case-control study

Purpose of study: to evaluate the association between meniscal damage in non-operated knees and the later development of radiographic tibiofemoral OA

Population/sample size/setting:

- 3026 subjects recruited through media and community outreach campaigns for a prospective epidemiologic cohort study from Birmingham, Alabama and Iowa City, Iowa
- Study subjects wither had symptomatic knee OA at baseline or were considered to be at risk of developing the disease
 - o Risk factors for knee OA were overweight, frequent knee pain, aching, or stiffness in the previous month, a history of major knee injury, or a history of knee surgery
- Exclusion criteria were screening positive for rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, chronic reactive arthritis, bilateral knee replacement surgery, inability to walk without aid, or a condition which made continued participation in the study unlikely

Assessment of exposure:

- The “exposure” of interest was any degree of meniscal damage
- Baseline MRI images were obtained and were repeated 30 months later, with meniscal damage considered to be meniscal tear, maceration, or damage of either the anterior horn, posterior horn, or body segment of the medial and lateral menisci, initially graded into five degrees of severity:
 - o 0=intact
 - o 1=minor tear or parrot-beak tear
 - o 2=nondisplaced tear breaking 2 or more surfaces
 - o 3=displaced tear or partial maceration or destruction
 - o 4=complete maceration or destruction
 - For purposes of later analysis, these 5 grades were collapsed into 3 categories: 0 (no damage), 1 (minor tear), and 2-4 (nondisplaced tears, displaced tears, and complete maceration)
- An increased intrameniscal signal was regarded as a tear if it communicated with the inferior or superior margins of the meniscus on at least 2 slices

- Meniscal extrusion was also graded using the tibial plateau osteochondral junction as the reference point, and defined as 0 (absent), grade 1 ($\leq 50\%$) and 2 ($> 50\%$ from the midposterior coronal slice where the medial tibial spine was of maximal volume)

Assessment of outcome:

- OA was graded according to the Kellgren-Lawrence (KL) criteria using posteroanterior and lateral radiography with a fixed-flexion protocol, both at baseline and at 30 months
 - o KL grade 1=doubtful joint space narrowing and possible osteophytic lipping
 - o KL grade 2=definite osteophytes, definite joint space narrowing
 - o KL grade 3=multiple moderate osteophytes, definite joint space narrowing, some sclerosis, and possible joint contour deformity
 - o KL grade 4=large osteophytes, marked joint space narrowing, severe sclerosis, and definite joint contour deformity
- The population at risk at baseline consisted of those in whom radiographic tibiofemoral OA or patellofemoral OA was absent
 - o Absence of tibiofemoral OA meant having KL grade 0 or grade 1 knee OA
 - o Absence of patellofemoral OA (defined as a grade 2 osteophyte or grade 1 joint space narrowing) was determined from the lateral films
- An incident case of OA was defined by the 30 month film, where tibiofemoral OA of KL grade 2 or more, or patellofemoral OA was present
 - o To satisfy the definition of incident OA, the authors required both (1) osteophyte development or enlargement and the (2) visual presence of joint space narrowing, but did not measure this quantitatively
 - o If the only change from baseline to 30 months was enlargement of an incipient osteophyte, the subject was not classified as a case of OA

Assessment of association between exposure and outcome:

- The authors identified 212 knees with newly developed OA of KL grade 2 or higher in 200 subjects at 30 months, of whom 149 subjects had a readable baseline MRI
 - o Of these 149 subjects, 121 were finally included as cases after excluding those with patellofemoral OA only or because of having had previous knee surgery
- From the same study centers in which the cases were identified, 294 controls were randomly selected for purposes of comparison, in whom no evidence of OA was present on the 30 months films
- In the cases, the frequency of KL grade 1 x-rays at baseline was more common (70%) than in the control cases with no OA at 30 months (21%)
- In the cases, meniscal damage grade 1 or higher at baseline (54%) was more frequent than in control knees (18%) , but no cases had grade 4 meniscal damage

- The effect size for meniscal damage was computed as an odds ratio (OR), which was adjusted for other factors which could be associated with both meniscal damage and with knee OA, such as age, sex, physical activity, BMI, and mechanical knee alignment
 - o The OR for a minor meniscal tear versus no meniscal damage was 3.0 with a 95% Confidence interval (CI) from 1.4 to 6.4
 - o For more severe meniscal damage, the OR was 7.9 with a 95% CI from 4.4 to 14.0
- An additional analysis was done which excluded any knee with KL grade 1 changes at baseline, since these were considered to possibly represent early knee OA; when this analysis was done, the OR was 7.4 with 95% CI from 3.2 to 17.0
- Gender of the subject did not influence the ORs, which were the same in men and women
- Although this was not part of the initial plan of analysis, the authors noted that newly occurring meniscal damage developed sometime between baseline and followup in 29 case knees and in only 6 control knees

Authors' conclusions:

- A meniscal tear is a potent structural risk factor for later development of tibiofemoral OA
- This association is present in knees which have never been operated on, and means that the association is not explained by damage from a meniscectomy
- The subjects in the study were drawn from a general population of people with risk factors for OA, such as overweight, frequent knee pain, and stiffness
- The association is therefore likely to be valid in the general population of middle-aged and older people without other known risk factors for OA
- A degenerative meniscal tear should be viewed as a signal of early OA disease and patients with meniscal damage should be treated accordingly

Comments:

- The nested case-control design presents many advantages in terms of study design
 - o The exposure data is collected prospectively, avoiding many potential biases which arise when this is collected retrospectively
 - o The exposure does not depend on patient self-report, but was based on radiographs which were assessed by readers who were unaware of the case/control status of the subjects they were reviewing
 - o Similarly, the outcome was defined radiographically and was read by radiologists unaware of the case/control status of the subjects

- Because both cases and controls are nested within a defined cohort, potential biases are avoided which can occur if cases and controls are selected from different source populations
- The 30 month followup time frame was adequate to detect an elevated odds ratio for meniscal damage and knee OA, but the confidence intervals were fairly wide, leaving some imprecision in the estimate of the effect of meniscal damage
- The outcome was radiographic OA, and correlation with symptomatic knee OA is less clearly defined
- Knee alignment did not influence the estimate of the odds ratios and appears not to be a factor in the association between OA and meniscal damage
- There appears to be a mistake in the statement of the definition of the mechanical axis, which was defined by a line from the center of the head of the femur to the center of the tibial spine, and another line from the center of the talus to the center of the tibial spine
 - The usual method of defining this angle actually draws the first line from the center of the femoral head to the intercondylar notch rather than the tibial spine; this is what is done with other studies being conducted on this population, and is probably how the mechanical axis was measured in this study as well

Assessment: high quality nested case-control study providing good evidence that meniscal damage, even in the absence of knee surgery, is associated with a significantly increased risk of development of radiographic tibiofemoral OA within 30 months of its detection on MRI