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### Title

Synovitis does not mediate the relationship between body mass index and progression of radiographic knee osteoarthritis: data from the osteoarthritis initiative

### Permalink

<https://escholarship.org/uc/item/7w9597j0>

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### Publication Date

2021-04-01

### DOI

10.1016/j.joca.2021.02.362

Peer reviewed

factors that predict its onset and progression with the ultimate aim to mechanistically understand disease and develop targeted interventions. Traditionally, risk factors for knee osteoarthritis are considered 'local' to the joint or 'systemic' referring to whole-body systems. However, there are clear indications in the scientific literature that contextual factors such as socioeconomic position merit consideration. Further in depth scrutiny of socioeconomic factors is thus needed to justify a more biopsychosocial view on risk factors in knee osteoarthritis. The aims of this study were therefore to quantify the representation of socioeconomic factors in the knee osteoarthritis literature and to review the applied measurement instruments to assess socioeconomic factors and their impact on knee osteoarthritis outcomes.

**Methods:** The electronic bibliographic databases Medline (PubMed), Embase, CINAHL, Web of Science (psych articles) and Cochrane were screened independently by two reviewers to identify research articles dealing with the knee osteoarthritis population without arthroplasty and socioeconomic factors, with a third independent reader available to resolve conflicts. Included studies had to quantify the relationship between socioeconomic factors and at least one of the following target outcomes of interest: pain, function, physical activity, structural osteoarthritis status and progression, clinical examination outcomes and quality of life. Few additional exclusion criteria were set concerning the design (no qualitative studies) and language (only English or Dutch) and population age (above 16 years). Formal quality assessment was organized using the revised Cochrane Risk-Of-Bias-2 tool for randomized trials, Risk Of Bias In Non-randomized Studies of Interventions-1 and the Newcastle-Ottawa Scale for assessing the quality of non-randomised studies. Given the explorative nature of this scoping review, descriptive statistics (frequencies, percentages) were calculated as appropriate.

**Results:** After de-duplication, 7639 articles were available for screening for which 120 conflicts (1.6% of all studies) were resolved without the need for a third reader. The knee osteoarthritis population was confirmed in 4112 articles (1906, 25% excluded because of knee arthroplasty and 1621, 21% because of other issues related the population definition). Some studies were lost because hip and knee osteoarthritis were combined in the analysis. Socioeconomic factors could not be identified in 4058 (53%) papers and were only adjusted for in 211 (3%) articles. Socioeconomic factors seem thus to be underreported or understudied (14% of the knee osteoarthritis literature reported on these factors). A total of 231 (3%) papers was finally included for further scoping review. Pain (n=110, 48%), function (n=81, 36%), physical (in)activity (n=5%), structural osteoarthritis status and progression (n=7, 3%), osteoarthritis prevalence or risk (n=98, 43%), clinical examination outcomes (n=10, 12%) and quality of life (n=18, 8%) were the outcomes of interest in the 231 included studies. A total of 12 different socioeconomic factors were found in the literature in relationship with pain and function outcomes. Education was by far the most reported socioeconomic factor in the literature (51%), next to occupational status (28%), marital status (26%), income (19%), race/ethnicity (16%), family composition (13%), social status (10%), discrimination (3%), insurance (3%), combined scores (3%), job type (3%) and religion (3%). Although several studies assessed the same factor, the measurement instruments used differed dramatically, mainly in ordinal categories.

**Conclusions:** Few studies currently focus on contextual socioeconomic factors in knee osteoarthritis and their assessment is highly variable methodologically. Therefore, it appears that more attention should go to a standardised and feasible set of socioeconomic outcomes to include in clinical research on knee osteoarthritis. Given the available body of evidence found in this scoping review, the systematic analysis of the effect of socioeconomic factors on pain, function and prevalence of disease should be prioritised to enhance a biopsychosocial view on risk factors in knee osteoarthritis.

**PRESENTATION NUMBER: 331**  
**THE ASSOCIATION BETWEEN WORSENING OF SYNOVITIS AND RADIOGRAPHIC OSTEOARTHRITIS PROGRESSION IS MORE PRONOUNCED IN OBESE INDIVIDUALS: DATA FROM THE OSTEOARTHRITIS INITIATIVE**

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**Purpose:** Synovial inflammation in the knee is associated with knee osteoarthritis (KOA) progression. Yet, the relation of body mass index (BMI) to worsening of synovitis and OA progression remains unknown. This study investigated the association of synovitis progression during a 2-year period with radiographic KOA progression over 48 months in 3 groups of patients according to their BMI.

**Methods:** We analyzed 273 right knees from 243 participants of the Osteoarthritis Initiative (OAI). Subjects were randomly selected by matching for age, gender, race and baseline Kellgren-Lawrence (K-L). Three groups of 91 participants classified by their BMI were analyzed: normal weight (BMI < 24.9 kg/m<sup>2</sup>, average of 22.71 ± 1.69), overweight (BMI 25–29.9 kg/m<sup>2</sup>, average of 27.37 ± 1.40), and obese (BMI ≥ 30 kg/m<sup>2</sup>, average of 33.35 ± 2.80). MRI Osteoarthritis Knee Score (MOAKS) was used for a semi-quantitative evaluation (0–3) of effusion synovitis and Hoffa-synovitis at baseline and at 24 months of follow-up. OA radiographic progression was defined as a Kellgren-Lawrence scale increase of >=1 from baseline to 48 months of follow-up.

**Results:** In each group, mean age was 61.3 years, 80 % were women and 97% were Caucasian. Baseline knee KL was as follows: 44% grade 0, 32% grade 1, 17.6% grade 2 and 6.5% grade 3. Synovitis-effusion was detected in 53% of the knees (average score of 0.60 ± 0.62) and Hoffa-synovitis in 48% of the knees (average score of 0.56 ± 0.65). Of interest, patients with overweight had higher Hoffa-synovitis score than normal or obese patients. 83 patients from the normal weight group and 80 patients from the overweight and obese groups had MRI at both baseline and 24 months of follow up. At 2 years follow-up, 37% of the knees experienced a worsening of synovitis-effusion (average score of 0.93 ± 0.83), and 30% of the knees had a progression of Hoffa-synovitis (average of 0.77 ± 0.75). Worsening of synovitis was not associated with baseline BMI. KOA radiographic progression at 48 months of follow-up was observed in 30% of knees. Synovitis effusion progression at 2 years was associated with KOA radiographic progression at 48 months (83.1% of patients with synovitis-effusion progression at 2 years had KOA progression vs 30.5% of KOA progression in patients with no synovitis-effusion progression, p<0.01). This association was more pronounced in the obese group. 96.4% of the obese participants with synovitis had KOA radiographic progression, whereas 85.2% of the overweight subjects and 70.6% of the normal BMI groups had KOA progression (p<0.05). Hoffa synovitis progression at 2 years was also associated with radiographic progression at 48 months (89% of patients with Hoffa-synovitis progression at 2 years had KOA progression vs 33% of KOA progression in patients with no Hoffa-synovitis progression, p<0.01), but this association did not vary by BMI.

**Conclusions:** Synovitis effusion progression over 24 months was associated with OA radiographic progression at 48 months, and the progression was observed in nearly all of obese subjects. Treatments to reduce synovial effusions may slow the progression of knee OA in both obese and non-obese subjects.

**PRESENTATION NUMBER: 332**  
**SYNOVITIS DOES NOT MEDIATE THE RELATIONSHIP BETWEEN BODY MASS INDEX AND PROGRESSION OF RADIOGRAPHIC KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE**

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**Purpose:** Synovial inflammation is associated with knee osteoarthritis (KOA) progression. Body mass index (BMI) has also been associated with KOA progression. Yet, it is unclear whether synovial inflammation mediates the association of BMI with KOA progression. Here, we examined the mediating effect of synovitis in the association between BMI and progression of radiographic KOA in the Osteoarthritis Initiative (OAI) cohort.

**Methods:** We conducted a case-control study within the OAI. Cases (n = 315) were right knees with an increase of ≥ 1 Kellgren-Lawrence (K-L) from baseline to 48 months of follow-up. Controls (n = 315) were right knees that had no K-L change over 48 months. Cases and controls were matched by age, gender, race and baseline K-L. MRI Osteoarthritis Knee Score (MOAKS) was used for a semi-quantitative evaluation (0–3) of effusion synovitis and Hoffa-synovitis at baseline. The SPSS PROCESS macro was used to test the mediating effects.

**Results:** The mean age of participants was 61 years, 70.8% were women, and 87% were white. Baseline knee KL was as follows: 36.8% grade 0, 30.2% grade 1, 25.1% grade 2 and 7.9% grade 3. 24.9% were normal weight (BMI < 24.9 kg/m<sup>2</sup>), 37.1% were overweight (BMI 25–29.9 kg/m<sup>2</sup>) and 37.0% were obese (BMI ≥ 30 kg/m<sup>2</sup>). Average BMI was 28.63 ± 4.8. 49.8% had synovitis effusion with a score of 0.56 ± 0.6, and 51.9% had Hoffa synovitis with a score of 0.61 ± 0.66. Compared with controls, cases had higher BMI (29.1 ± 4.7 vs 28.2 ± 4.9, p<0.05), and were more likely to be obese (41.5% vs. 34.3%) than controls (p <0.05). At baseline, cases had higher prevalence of both synovitis effusion and Hoffa-synovitis than controls (59.6% vs 40.1%, p<0.01 for synovitis-effusion and 61.9% vs 42%, p<0.01, for Hoffa synovitis respectively). Yet, in the mediation analysis, neither synovitis effusion nor Hoffa synovitis mediated the relationship between BMI and KOA progression.

**Conclusions:** Preliminary findings from mediation analysis showed that neither synovitis effusion nor Hoffa synovitis mediated the relationship between BMI and progression of radiographic KOA over a 4-year period. A longer duration of follow-up may be required to determine if synovitis mediates the association between BMI and progression of KOA.

#### PRESENTATION NUMBER: 333

#### THE CLINICAL RADIOGRAPHIC INCIDENCE OF POST-TRAUMATIC OSTEOARTHRITIS 10 YEARS AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION: DATA FROM THE MOON NESTED COHORT

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**Purpose:** The incidence of post-traumatic osteoarthritis (PTOA) using clinical radiographic grading criteria at 10 years after anterior cruciate

**Table 1.** Demographics at time of ACL reconstruction, intraoperative findings, and repeat non-ACL surgery<sup>a</sup>

Variable	Level	Median (interquartile range) or Number (percentage)
Age, years		21 (19, 25)
Sex	Male	65 (49%)
	Female	68 (51%)
Body Mass Index (BMI), kilograms/meters <sup>2</sup>		22.9 (21.0, 25.1)
Smoking status	Current	4 (3%)
	Quit	8 (6%)
	Never smoked	121 (91%)
ACL graft type	BTB autograft	82 (62%)
	Hamstring autograft	47 (35%)
	Allograft	4 (3%)
Marx activity score		16 (12, 16)
Medial meniscus status	Normal	84 (63%)
	Stable untreated tear	12 (9%)
	Stable tear, trephination	2 (1.5%)
	Repaired tear	22 (16.5%)
	Partial meniscectomy	13 (10%)
Lateral meniscus status	Normal	58 (44%)
	Stable untreated tear	24 (18%)
	Stable tear, trephination	2 (1.5%)
	Repaired tear	10 (7.5%)
	Partial meniscectomy	39 (29%)
Medial compartment articular cartilage status	Grade 0-1	121 (91%)
	Grade 2+	12 (9%)
Lateral compartment articular cartilage status	Grade 0-1	111 (83%)
	Grade 2+	22 (17%)
Patellofemoral compartment articular cartilage status	Grade 0-1	124 (93%)
	Grade 2+	9 (7%)
Additional ipsilateral surgery (non-ACL surgery)	No	108 (81%)
	Yes	25 (19%)
	Surgery for arthrofibrosis <sup>b</sup>	14/25 (56%) <sup>c</sup>
	Partial meniscectomy	11/25 (44%) <sup>c</sup>
	Removal tibial hardware	2/25 (8%) <sup>c</sup>
	Chondroplasty	2/25 (8%) <sup>c</sup>
	Microfracture	1/25 (4%) <sup>c</sup>
	Removal loose body	1/25 (4%) <sup>c</sup>
Additional contralateral surgery (non-ACL surgery)	No	133 (100%)
	Yes	0 (0%)

**Key:** ACL= anterior cruciate ligament; BTB=bone-patellar tendon-bone; Grade = modified Outerbridge articular cartilage grade

<sup>a</sup> Reported values are for the 133/146 subjects with bilateral radiographs at 10 years follow-up who did not undergo revision ipsilateral ACL surgery or contralateral primary ACL surgery.

<sup>b</sup> Surgery for arthrofibrosis included arthroscopic anterior debridement, synovectomy, and/or manipulation under anesthesia.

<sup>c</sup> Percentages equal greater than 100% as one or more procedures couple be performed at time of

repeated time of repeat non-ACL surgery

**Table 2.** Incidence of radiographic osteoarthritis

OA definition	ACL reconstructed knee	Contralateral knee	Present in ACL reconstructed knee and absent in contralateral knee
Definite osteophytes*	43% (57/133)	10% (13/133)	37% (44/120)
Joint space narrowing**	27% (35/133)	5% (7/133)	23% (29/126)

\*Definite osteophytes defined as KL grade 2 or higher, IKDC grade B or higher, and OARSI osteophyte grade 1 or higher (any compartment)

\*\*Joint space narrowing defined as OARSI grade 1 narrowing or higher in any compartment.

**Table 3.** Radiographic osteoarthritis severity

	ACL reconstructed knee	Contralateral knee
IKDC grade		
A	76 (57%)	120 (90%)
B	47 (35%)	11 (8%)
C	8 (6%)	2 (2%)
D	2 (2%)	0 (0%)
Modified KL grade		
0	47 (36%)	102 (77%)
1	29 (21%)	18 (14%)
2	47 (35%)	11 (8%)
3	8 (6%)	2 (2%)
4	2 (2%)	0 (0%)
OARSI maximum JSN grade, medial and lateral compartments		
0	98 (73%)	126 (94%)
1	29 (22%)	6 (5%)
2	4 (3%)	1 (1%)
3	2 (2%)	0 (0%)
OARSI maximum osteophyte grade (tibial + femoral osteophyte grade), medial and lateral compartments		
0	76 (57%)	120 (90%)
1	34 (26%)	5 (4%)
2	17 (13%)	6 (5%)
3+	6 (4%)	2 (1%)

Key: Reported as number (percentage)

ligament reconstruction (ACLR) has not been well-defined in a prospective cohort of young athletic patients. Among young athletic patients, there is a high incidence of clinical radiographic PTOA at 10 years after ACLR. Additionally, there is a significant difference in clinical radiographic osteoarthritis changes (joint space narrowing [JSN] and osteophyte formation) between the ACL reconstructed and contralateral knees at 10 years.

**Methods:** The first 146 patients in an ongoing nested cohort study within a prospective cohort presented for minimum 10-year follow-up. Included patients had a sports-related ACL injury, were age <33 years at time of ACLR, no prior history of ipsilateral or contralateral knee surgery, and no revision ACLR before follow-up. Bilateral knee metatarsophalangeal (MTP) view radiographs were obtained and graded by International Knee Documentation Committee (IKDC), Osteoarthritis Research Society International (OARSI), and modified Kellgren-Lawrence (KL) criteria by two blinded reviewers. The incidence and severity of ipsilateral and contralateral radiographic osteoarthritis were determined among patients without a contralateral ACL injury before 10-year follow-up (n=133). Baseline characteristics are presented in Table 1.

**Results:** Inter-rater reliability was substantial for IKDC (Gwet's AC1 = 0.71), moderate for KL (0.48), and almost perfect for OARSI (0.84) grading systems. Among patients with a contralateral radiographically normal knee, the 10-year incidence of clinical radiographic PTOA after ACLR is 37% as defined by osteophytes and 23% as defined by JSN. The maximum side-to-side difference in medial or lateral compartment OARSI osteophyte grade was 0 in 65% of patients, 1 in 20%, and 2+ in 15%. The maximum difference in OARSI JSN grade was 0 in 77% of patients, 1 in 19%, and 2+ in 4%. The incidence of radiographic OA is presented in Table 2, and the severity of OA is presented in Table 3.