

Osteoarthritis and Cartilage



The relationship between foot and ankle symptoms and risk of developing knee osteoarthritis: data from the osteoarthritis initiative

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SUMMARY

Objective: To investigate whether foot and/or ankle symptoms increase the risk of developing (1) knee symptoms and (2) symptomatic radiographic knee osteoarthritis (OA).

Design: 1020 Osteoarthritis Initiative (OAI) participants who were at-risk of knee OA, but were without knee symptoms or radiographic knee OA, were investigated. Participants indicated the presence and laterality of foot/ankle symptoms at baseline. The main outcome was development of knee symptoms (pain, aching or stiffness in and around the knee on most days of the month for at least 1 month in the past year). A secondary outcome was development of symptomatic radiographic knee OA (symptoms plus Kellgren and Lawrence [KL] grade ≥ 2), over the subsequent 4 years. Associations between foot/ankle symptoms and study outcomes were assessed by logistic regression models.

Results: Foot/ankle symptoms in either or both feet significantly increased the odds of developing knee symptoms (adjusted odds ratio (OR) 1.55, 95% confidence interval (CI) 1.10 to 2.19), and developing symptomatic radiographic knee OA (adjusted OR 3.28, 95% CI 1.69 to 6.37). Based on laterality, contralateral foot/ankle symptoms were associated with developing both knee symptoms (adjusted OR 1.68, 95% CI 1.05 to 2.68) and symptomatic radiographic knee OA (adjusted OR 3.08, 95% CI 1.06 to 8.98), whilst bilateral foot/ankle symptoms were associated with developing symptomatic radiographic knee OA (adjusted OR 4.02, 95% CI 1.76 to 9.17).

Conclusion: In individuals at-risk of knee OA, the presence of contralateral foot/ankle symptoms in particular increases risk of developing both knee symptoms and symptomatic radiographic knee OA.

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Introduction

Knee osteoarthritis (OA) is a leading cause of joint pain¹ and disability² in middle- and older-aged individuals, and is one of the

most commonly managed conditions in primary care³. Recent incidence rates suggest around 6% of people aged over 45 years develop knee symptoms each year, whilst 2% develop symptomatic radiographic knee OA⁴. Knee OA symptoms and radiographic change that worsen over time can lead to costly surgical intervention. Thus understanding risk factors associated with the onset of knee symptoms alone or in combination with structural change is a major research focus.

Symptoms in the foot and/or ankle is a potential risk factor for knee pain and OA that has received limited attention to date. Like knee OA, foot/ankle symptoms are very common in middle- and older-aged adults. They affect approximately 24% of people aged

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over 45 years⁵, and account for a substantial number of primary care consultations in this population⁶. Foot pain is highly disabling, reduces quality of life⁷, adversely affects walking and other daily functional abilities⁷ and increases the risk of falls⁸. To date, the majority of studies investigating symptoms at the foot/ankle and knee have examined these problems in isolation. However, isolated joint pain is rare⁹, and concurrent symptoms at the foot/ankle and knee is the most common multi-joint presentation¹⁰, occurring far greater than expected by chance alone. In a recent cross-sectional study using data from the Osteoarthritis Initiative (OAI), we found that people with both symptomatic radiographic knee OA and foot/ankle symptoms reported significantly worse general and knee OA specific health outcomes, and poorer physical function, than those with knee OA but without foot/ankle symptoms¹¹. Despite the strong association between problems at these two sites, their temporal sequence has not yet been evaluated.

Investigating foot/ankle symptoms as a candidate risk factor for knee OA is attractive as it is simple to assess, and there is some evidence of potential modifiability using simple low-cost interventions such as off-the-shelf footwear¹². Furthermore, there are a number of plausible biological mechanisms linking foot/ankle symptoms to knee OA development. For example, there may be shared biomechanical risk factors for the two problems, such as a pronated foot type¹³ or inappropriate footwear¹⁴. Alternatively, people with foot/ankle symptoms may walk differently to offload their painful foot^{15–17}, altering knee function and increasing the risk of knee OA development. Finally, symptoms at these two sites may represent a widespread pain phenotype or an oligo- or poly-articular form of OA¹⁸.

The primary aim of this study was to use longitudinal data from the OAI to examine whether foot/ankle symptoms predict the development of knee symptoms over 4 years in people without knee symptoms or radiographic knee OA, but at-risk of knee OA, at baseline. A secondary aim was to examine whether foot/ankle symptoms also predict the development of symptomatic radiographic knee OA over 4 years. It was hypothesized that foot/ankle symptoms would increase the odds of developing knee symptoms and symptomatic radiographic knee OA in people at risk of knee OA.

Methods

Study population

The OAI is an ongoing prospective multicentre cohort study designed to evaluate and identify biomarkers for the onset and/or progression of knee OA in people aged between 45 and 79 years. The study enrolled 4796 men and women from four sites in the United States, including Baltimore, Maryland; Columbus, Ohio; Pittsburgh, Pennsylvania; and Pawtucket, Rhode Island. All protocols and procedures were approved by the institutional review board at each site¹⁹ and all participants provided informed consent. Details regarding general exclusion criteria and the wider study protocols are available online for public access (<http://www.oai.ucsf.edu/>). In the current study, we analysed OAI participants who were at risk of knee OA, defined as the presence of two or more established characteristics including: overweight, identified using age- and sex-specific criteria; a history of knee injury causing walking difficulties; any knee surgery; an immediate family history of a total knee replacement for OA; Heberden's nodes; repetitive knee bending during occupational or recreation activities; or aged between 70 and 79 years. From this subcohort, we only included people who did not have frequent knee symptoms (defined as pain, aching or stiffness in and around the knee on most days of the month for at least 1 month in the past year) or radiographic evidence of knee OA (Kellgren and Lawrence [KL] grade ≥ 2) in either knee at

baseline. We excluded people (rather than knees) with these outcomes because the presence of symptomatic knee OA in one knee greatly increases the risk of developing contralateral knee OA which may confound results^{20–22}. Demographic, clinical and radiographic characteristics of both knees for all participants were evaluated at baseline and at 12, 24, 36 and 48-month follow-up visits.

Demographic characteristics and covariates

Demographic data collected included age, sex and race (White, Black/African American or Asian/other non-white). Covariates included body mass index (BMI), comorbidities and depression. As well as recording BMI values, we also classified participants as obese ($>30 \text{ kg/m}^2$), overweight (≥ 25 and $\leq 30 \text{ kg/m}^2$) or normal weight ($<25 \text{ kg/m}^2$). Comorbidities were assessed using the questionnaire version of the Charlson comorbidity index (CCI)²³, and we dichotomized the cohort into those with 'no comorbidities' and those with 'one or more comorbidities'. Depression was measured using the Centre for Epidemiological Studies Depression Scale (CES-D). Scores were summed and a score of ≥ 16 was used to indicate significant depressive symptoms²⁴.

Risk factor

The primary risk factor was self-reported foot/ankle symptoms at baseline, defined as pain, aching or stiffness in the foot and/or ankle on more than half of the days during the past 30 days, consistent with definitions used in previous studies^{5,10}. In addition to classifying participants based on the presence or absence of symptoms in either foot/ankle, we further stratified foot/ankle symptoms as ipsilateral, contralateral or bilateral relative to each knee.

Incidence outcomes

Knee symptoms

Participants were asked about the presence of knee symptoms at baseline, and at the 12, 24, 36 and 48 month follow-up visits for each knee. Incident knee symptoms was defined as development of pain, aching or stiffness in and around the knee on most days of the month for at least 1 month in the previous year, reported at any of the follow up visits, consistent with the OAI definition and based on American College of Rheumatology criteria for clinical knee OA²⁵.

Symptomatic radiographic knee OA

Weightbearing fixed-flexion posteroanterior radiographs of both knees were taken at baseline and at the 12, 24, 36 and 48 month follow-up visits. Radiographs were evaluated using the KL grading system (grades range 0–4) by two central OAI senior musculoskeletal experts blinded to all other participant data and to each other's readings. Incident symptomatic radiographic knee OA was defined as knee symptoms (as per definition above) and the presence of KL grade ≥ 2 based on the central OAI reading, at any of the follow up visits.

Statistical analysis

Baseline characteristics of participants with and without foot/ankle symptoms were summarised as number (%) for categorical variables and as mean (standard deviation (SD)) or median (interquartile range (IQR)) for continuous variables, as appropriate. Groups were compared using χ^2 -squared tests, analysis of variance, Wilcoxon rank-sum or Kruskal–Wallis rank tests respectively.

To investigate the primary aim (development of knee symptoms), we analysed the association between any foot/ankle

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