Incidence and Progression of Foot Osteoarthritis in a Longitudinal Cohort: the Johnston County Osteoarthritis Project

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Short title: Incidence and Progression of Foot Osteoarthritis

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Abstract

Introduction: To examine the incidence and progression of foot osteoarthritis (OA), as well as associated factors, in a community-based cohort.

Methods: Baseline (2013-2015) and follow-up (2016-2018) foot radiographs were available for 541 participants (71% women, mean age 69 years; 35% Black, 53% with obesity). The LaTrobe Foot Atlas was used to examine osteophytes (OP, score 0-3) and joint space narrowing (JSN, score 0-3) at 5 joint sites. Incident foot radiographic OA (rOA) was a baseline score <2 OP and JSN in all 5 joints with ≥2 OP or JSN at follow-up in any of the joints. Progression was a worsening OP or JSN score in a joint with baseline foot rOA. At baseline and follow-up, participants reported presence/absence of foot symptoms and completed the Foot and Ankle Outcome Score (FAOS) for each foot. Joint-based logistic regression models with generalized estimating equations were used to examine associations (adjusted odds ratio [aOR], 95% confidence interval [CI]) of foot rOA incidence and progression and with covariates.

Results: Among 928 feet without baseline rOA, 4% developed incident foot rOA (2% of those developed symptoms). Among 154 feet with baseline foot rOA, 55% had radiographic progression (16% of those had symptoms). Women and those with higher body mass index (BMI) were more likely to have incident foot rOA (aOR [95% CI] = 4.10 [1.22, 13.8] and 1.60 [1.31, 1.97], respectively); history of gout was associated with incidence or progression of foot rOA (2.75 [1.24, 6.07]. BMI was associated with worse scores on all FAOS subscale (aORs range 1.21-1.40).

Conclusion: Progression of foot rOA is common but not necessarily related to worsening symptoms. BMI may be a modifiable risk factor for foot OA.

Introduction

Osteoarthritis (OA) is the most common joint disease worldwide and is a major source of pain, disability, and healthcare expenditure [1]. OA affects about 15% of the population and commonly involves the hips, knees, and hands [2]. Foot OA has been described in the literature [3-9] but to a lesser extent than other joint sites. Foot involvement is of interest because foot pain has been identified as an independent risk factor for impaired balance, increased risk of falling, and locomotor disability [10]. Roughly one in six adults aged 50 years and older have symptomatic radiographic OA of the foot [11].

Previously, foot OA has been difficult to study due to a lack of a formal radiographic grading system as well as limited joint assessments [11, 12]. The Kellgren-Lawrence grading system [13] is one of the most widely used tools in OA classification, particularly for the knees [14], and has been used for classifying foot OA, although Menz et al. [15] state that it places too much importance on osteophyte formation. Therefore, to better classify foot OA by including specific grading of joint space narrowing, the La Trobe Atlas was created. In addition to scoring five joints within the foot and incorporating both osteophytes (OP) and joint space narrowing (JSN), it advocates for anteroposterior and lateral radiographic views of each joint since some features of OA, particularly at the midfoot, may be missed with only one view [11, 15].

In the literature, data regarding incidence and progression of foot OA are lacking, with two studies reporting on the incident first metatarsophalangeal joint (1st MTP) OA only [16, 17] and no known studies of incidence or progression of midfoot OA. Knowledge regarding this area is important given the significant consequences of OA at other joint sites. OA contributes to pain, decreased quality of life, and disability [18]. Understanding symptoms, risk factors, and how to objectively follow disease progression over time remains of high interest. Sociodemographic and clinical characteristics, particularly those that are easy to ascertain from medical records or questionnaires, may help with advancing the ability to identify individuals at high risk for incident or progressive foot OA. Based on prior studies of foot OA, potential factors include older age, female sex, higher body mass index (BMI), and history of foot injury [4, 11, 19]. Gout and OA are linked; the relationship may be bidirectional and influenced by shared risk factors of

age, sex, and obesity [20]. Among those who already have foot OA and pain, being on work disability or using medications for pain may be early signs of those who may have more severe disease or are at risk for progression. Understanding associated factors that are easy to assess could help guide treatment and preventive measures for foot OA. The objectives of this study were to describe the incidence and progression of foot radiographic OA, symptoms, and foot-related outcomes and associated factors in a large community-based cohort.

Methods

Study Population

This cohort study is reported as per Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines. Data were obtained from the Johnston County OA Project (JoCoOA), a prospective community-based cohort of residents of Johnston County, North Carolina who identified as Black or White and were at least 45 years old at enrollment (Original Cohort 1991-1997, Enrichment Cohort 2003-2004). Details of the JoCoOA are described elsewhere [21-24]. All participants completed written informed consent, and the Institutional Review Board at the University of North Carolina, Chapel Hill has continuously approved the JoCoOA (IRB #92–0583). For the present analysis, we utilized data from two study visits that included collection of foot radiographs: 2013-2015 (referred to as baseline for the present analysis) and 2016-2018 (follow-up).

Incident and Progressive Foot Radiographic OA

Weight-bearing radiographs of the feet were obtained in dorsoplantar and lateral views. Radiographs were assessed by an expert musculoskeletal radiologist (JBR). The La Trobe Foot Atlas was used to examine osteophytes (OP, score 0-3) and joint space narrowing (JSN, score 0-3) in five specified joints: 1st MTP, 1st & 2nd cuneo-metatarsal, navicular-1st cuneiform, and talo-navicular joints. Because there is no standard approach for using the La Trobe Atlas to define changes in foot OA over time, our research team, led by experts in foot radiography (JBR), foot OA research (YMG, LG, CB), and longitudinal analyses of OA cohorts (YMG, AEN, CA, LG, CB) developed an algorithm for determining clinically relevant definitions for incident and

progressive foot OA. Baseline foot OA was defined as score of ≥2 in OP or JSN in at least one joint. Incident foot radiographic OA (rOA) was defined as baseline score <2 OP and JSN in all 5 joints with ≥2 OP or JSN at follow-up in any of the five joints. Progression was defined as a worsening score of OP or JSN by follow-up in any of the 5 foot joints for a foot that already had rOA in at least one foot joint (e.g., new ≥2 OP or JSN in a foot joint that did not have rOA at baseline but another foot joint in that foot had rOA at baseline; worsening OP or JSN score in a foot joint that had ≥2 OP or JSN baseline).

Foot Symptoms

Using a standard question from the Behavioral Risk Factor Surveillance System to assess chronic joint symptoms, participants were asked at baseline and follow-up to rate their foot symptoms (i.e., pain, aching, or stiffness) in each foot as 0-10 (none to extreme) on most days of any month in the past 12 months. Foot symptoms worsening was defined as an increase in the foot symptoms rating from baseline to follow-up.

Foot and Ankle Outcome Score

The Foot and Ankle Outcome Score (FAOS), a 42-item questionnaire assessing patient relevant outcomes in five subscales (pain, other symptoms, activities of daily living [ADL], sport and recreation function, foot and ankle-related quality of life [QOL]), was obtained and scored by subscale (0-100 = extreme problems to no problems). Worsening of each FAOS subscale was defined as any decrease in the score from baseline to follow-up. A previous study demonstrated sufficient reliability and validity of the FAOS in the JoCoOA, with high internal consistency for all subscales; high test-retest reliability for pain, ADL, and QOL subscales; and moderate convergent validity [25].

Demographic and Clinical Characteristics

The following demographic and clinical characteristics were included in analyses because of their potential associations with foot OA and symptoms. Participants reported their age (continuous), sex (men/women), and race (Black/White). For these analyses, age was a

continuous variable. Height was measured using a calibrated stadiometer, and weight was measured using a balance-beam scale. BMI was calculated as body weight in kilograms divided by the square of height in meters. Work disability was defined as self-report of currently receiving work disability payments from either government or disability insurance. Non-steroidal anti-inflammatory drug (NSAID) use was defined as current use excluding low-dose aspirin (81 mg daily). History of gout in the left or right foot was defined as self-report of being told by a physician of having gout. Prior foot injury in the left or right foot was defined as a history of an injury to the foot that limited the participant's ability to walk for at least two days.

Analyses

Descriptive statistics of counts and percentages for categorical variables and means and standard deviation (SD) for continuous variables were produced. For variables at the person-level, these were provided out of the total number of participants. For variables at the foot-level, these were provided out of the total number of feet [left and right]. Foot-level logistic regression models with generalized estimating equations (GEE) were used to examine associations of foot rOA incidence and progression and covariates of age, sex, race, BMI, work disability, NSAID use, gout, and foot injury. Laterality was accounted for in models for the foot-level variables of gout and injury (e.g., left foot injury corresponded to left foot OA outcomes). For adjusted models, we selected a consistent set of covariates to control for based on prior knowledge of their associations with the independent and dependent variables, as well as statistical assessment that supported them as likely confounders across models. For each model, two-way interactions between covariates and baseline foot rOA status were assessed at a 0.10 alpha level, and adjusted odds ratios and 95% confidence intervals (aOR [95% CI]) were shown by baseline status if significant. Otherwise, overall associations were shown. Assumptions under logistic regression were met with 1) dependency among feet addressed by use of GEE methods in the models, 2) a binary response for each outcome following a binomial distribution, 3) for continuous predictors linearity assessed by testing non-linear polynomials, and 4) assessment of none or minimal multicollinearity by verifying that the largest condition

index be less than 30 [26]. Analyses were conducted using the statistical software package SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

Of the 864 participants with foot data at baseline, 323 (37%) did not attend the follow-up visit. Compared to those who attended the follow-up visit, those who did not attend were more likely to be older, receiving work disability, men, or have lower FAOS scores, but were not notably different based on other measured factors (Supplementary Table). Out of a total of 582 participants who attended both research clinic visits, 41 participants were excluded due to missing foot radiograph data at baseline or follow up, leaving 541 participants (1082 feet) with data available for analysis (Figure 1). Compared to the 541 participants with foot radiograph data, the 41 participants without these data tended to be older (73 vs 69 years) with a higher BMI (35 vs 31 kg/m^2) and more foot pain (39% vs 19% with foot pain at baseline). There were no notable differences by sex, race, or education. The mean time between study visits was 3.5 years (standard deviation ± 0.7 years, range 2-5 years).

Over 22% of participants had foot rOA at baseline. The mean age of participants was 69 years and 71% were women, 35% were Black, and 53% had obesity (mean BMI 31 kg/m^2, Table 1). Approximately 60% of participants had used NSAIDs within the last two weeks and 22% reported work disability. Compared to those without foot rOA at baseline, participants with foot rOA were more likely to be women, identify as Black, and have a higher BMI. History of gout and prior foot injury were observed in about 6% and 2% of feet, respectively. Of the 1082 feet in this study, 154 (14%) met the definition for rOA at baseline. Among feet with rOA at baseline, the most affected joint was the 1st MTP (42%) followed by the talo-navicular (31%). Foot symptoms were reported among 20% of individuals with foot rOA (24/120); similarly, foot symptoms occurred in 20% of feet with rOA (31/154).

Among the 928 feet with no rOA at baseline, roughly 4% of feet developed incident foot rOA and 1.5% had incident rOA with symptoms at follow up (Table 2). Of the 154 feet with rOA at baseline, over half (55%) had rOA worsening and 16% had rOA worsening with symptoms at

follow up. Compared to feet without baseline rOA, feet with baseline rOA had higher proportions of worsening foot symptoms (19.5% vs. 13.8%) and FAOS subscale scores (ranges 33.1-43.5% vs. 26.3-34.4%).

Women and those with higher BMI were more likely to develop incident foot rOA (aOR [95%CI] = 4.10 [1.22, 13.8] and 1.60 [1.31, 1.97], respectively; Table 3). Self-reported history of gout was associated with increased odds of incidence or progression of foot rOA (aOR [95%CI] = 2.75 [1.25, 6.07]). Black race, compared to White, was less likely to be associated with incidence or progression foot rOA with new foot symptoms at follow up (aOR [95%CI] = 0.37 [0.15, 0.90]). Among those without baseline foot rOA, having a higher BMI was associated with significantly increased odds of incident foot rOA with foot symptoms at follow up (aOR [95%CI] = 1.81 [1.39, 2.36]). A history of foot injury was strongly associated with incidence or progression of foot rOA with symptoms at follow-up (aOR [95%CI] =4.99 [1.57, 15.9]).

Among those with foot rOA at baseline, worsening of foot symptoms was less likely with older age (aOR [95%CI] = 0.70 [0.50, 0.99], Table 3). Regardless of foot rOA status at baseline, work disability was associated with worsening of foot symptoms (aOR [95%CI] = 1.81 [1.07, 3.04], Table 3) and FAOS worsening, particularly for pain, ADL, and sports and recreation subscales (aOR [95%CI] = 2.08 [1.26, 3.43], 2.09 [1.33, 3.27], and 2.19 [1.35, 3.55], respectively, Table 4). A higher BMI was associated with increased odds for worsening of all FAOS subscales (aORs range 1.21-1.40 with 95%CIs between 1.04 and 1.66). Older age was not associated with worsening of FAOS symptoms or QOL. In fact, among those with baseline foot rOA, older age was associated with lower odds of worsening in FAOS pain and ADL subscales (aOR [95%CI]= 0.74 [0.58, 0.96] and 0.77 [0.60, 0.98], respectively). History of gout was associated with increased odds of worsening for FAOS ADL and sports and recreation subscales (aOR [95%CI]= 1.59 [1.09, 2.31] and 1.47 [1.10, 1.96], respectively), and history of foot injury was associated with increased odds of worsening on the FAOS ADL subscale (aOR [95%CI]= 2.57 [1.18, 5.61]).

Discussion

In this large community-based cohort, we aimed to estimate the incidence and progression of foot rOA, foot symptoms, and foot-related outcomes, as well as examine associations with factors that may help identify those at risk for the occurrence or progression of these conditions. In this study, the incidence of foot rOA over 3.5 years was low (<5%) with few (<2%) having foot symptoms at follow-up. Progression of foot rOA was observed in the majority of those with foot rOA (55%) but was not necessarily associated with worsening symptoms (16%). Worsening foot symptoms and FAOS subscale scores were higher among feet with baseline rOA compared to those without rOA. Compared to those without foot rOA, those with foot rOA at baseline were more likely to be women, have a higher BMI, and identify as Black. Women and individuals with a higher BMI had higher odds of incident foot rOA, while self-reported history of gout was associated with higher odds of both incidence and progression of foot rOA. Foot injury was linked to higher odds of incidence and progression of foot rOA with symptoms at follow up. Higher BMI was associated with increased odds for worsening of foot symptoms and of all FAOS subscales.

Nearly 1 in 7 feet had rOA at baseline, and of the joints affected, foot rOA was most commonly seen in the 1st MTP, followed by talo-navicular and navicular-1st cuneiform joints; this observation is somewhat consistent with other cohorts [27]. Other studies have shown the 1st MTP to be the most common foot joint site for OA using the Kellgren-Lawrence grading system with a focus on forefoot involvement as opposed to the La Trobe Atlas [11], which focuses on the medial column of the foot based on the developers' identification of the joints most commonly affected by OA. Our results differ from prior reports that found the 2nd cuneometatarsal joint to be the second most commonly affected foot joint [7, 15]. Variation in results may be due to differences in the study samples; prior studies appeared to recruit those with foot pain or clinical samples whereas JoCoOA enrolled from a general, bi-racial, rural population without regard to pain or disease status [21] . A cross-sectional study from the United Kingdom (UK) highlighted the importance of identifying midfoot OA [28]. In that study, midfoot OA was divided into central midfoot (2nd cuneo-metatarsal) and medial midfoot (1st

cuneo-metatarsal, navicular-1st cuneiform, and talo-navicular). Having both central and medial involvement was associated with increased pain scores, dorsally located midfoot pain, hallux valgus, flatter foot posture and loss of medial arch height. Likewise, another UK study identified that participants with a polyarticular phenotype with midfoot OA involvement tended to have more severe pain and disability compared to isolated 1st MTP OA [29]. Although the 1st MTP is commonly involved, this information highlights that midfoot OA may be underrecognized in the literature.

Incidence of foot OA has not been widely reported. For 1st MTP OA, the Clearwater OA Study [17] reported incidence of 25-27% over a seven-year period (N=1592), and the Chingford Study [16] reported incidence of 13.5% and 8.3% among women over a 19-year period in the right and left 1st MTP, respectively (N=193). The incidence of foot rOA in our study may be lower due to a shorter follow-up time and differences in population (i.e., Clearwater OA Study enrolled volunteers and was not population-based; Chingford Study included only women). Those with greater risk for health problems may be more likely to volunteer for a project like the Clearwater OA Study, thus limiting generalizability of results. Radiographic progression of foot OA has not been widely reported either. One prospective analysis of a community cohort examined foot symptoms over an 18-month period and found that symptoms improved across all foot OA subtypes [30]. Together with our findings, this may suggest that progression of foot rOA does not always correspond to pain.

In the present study, the major factors associated with foot rOA with symptoms, or symptomatic foot OA, included BMI and prior foot injury. Increases in BMI by 5 kg/m^2 were associated with nearly twice the odds of symptomatic foot OA. A study from the UK showed that risk factors for symptomatic foot OA included age above 75 years, female sex, manual occupation, and obesity [6]. Although we did not see an association between age and worsening foot rOA, this may be due to a lack of JoCoOA participants at this study time point who were younger than 55 years of age. Studies of OA affecting other joint sites have reported similar associated factors. Reyes et al.[31] showed that both knee and hip OA were associated with increased BMI. The knee was more strongly associated with obesity than the hip, and

263 depending upon the BMI category, knee OA incidence increased up to 4.7 times. These results
264 emphasize the importance of a healthy weight and weight loss for those with obesity to
265 manage OA and extend this to management of foot OA.

266 History of foot injury was not statistically significantly associated with incidence or progression
267 of foot rOA in this study, but the odds were 2.75 times higher compared to no injury. Although
268 the foot injury was uncommon (2.4% at baseline), it was strongly associated with symptomatic
269 foot OA incidence and progression, with nearly five times higher odds than no injury. Prior foot
270 injury also was linked to worsening physical function (FAOS ADL). Little has been published on
271 the relationship between injury and symptomatic OA of the foot in large cohort studies[4, 19].
272 In the Clinical Assessment Study of the Foot, a history of foot or ankle injury was related to
273 symptomatic midfoot OA (aOR 1.60, 95% CI 0.98, 2.60), although this result was not statistically
274 significant [19]. The current study provided estimates of the longitudinal association between
275 foot injury and OA in a general population of middle age to older adults who were not selected
276 based on foot pain. Although the period between study visits was somewhat short (~3.5 years),
277 the results suggest a strong link between injury and symptomatic OA outcomes at the foot,
278 similar to associations seen between injury and OA at the knee and ankle [32].

279 Self-report of history of gout was significantly associated with incidence or progression of foot
280 rOA, which adds to our understanding of the complex relationship between gout and OA at the
281 foot. Prior studies have suggested that the presence of OA may predispose a joint to gout [33],
282 with monosodium urate crystals from hyperuricemia more often being deposited in OA
283 affected joints than healthy joints. For example, in a study of 164 individuals with acute gout
284 flares, the odds of OA at the 1st MTP and midfoot were 2-3 times higher compared those
285 without gout flares [34]. In a cross-sectional study of individuals with foot pain, the odds of
286 having at least three foot joints affected by rOA was four times higher among those with than
287 without gout (aOR [95%CI] = 4.00 [0.99, 16.10]) [35]. Alternatively, OA may occur more often
288 among joints damaged by gout flares. Based on evidence from the literature, a bidirectional
289 relationship is highly likely [20, 36].

A higher BMI also was a risk factor for poorer scores on the FAOS. This observation held true for all patient-related aspects, including symptoms, pain, ADL, sports and recreation, and quality of life. Prior foot injury and self-reported history of gout also were linked to worse FAOS subscales related to function (activities of daily living, sports and recreation). The FAOS has not been broadly utilized in foot OA. Historically, FAOS has been used to characterize outcomes in those with lateral ligament reconstruction, hallux valgus, and adult acquired flatfoot deformity [37]. Mani et al. [37] looked at FAOS in patients with ankle OA and compared this to another widely used questionnaire, the Short-Form 12 version 2 (SF-12). They concluded that the FAOS was not highly reliable across all five domains but may be helpful when assessing pain, activities of daily living and quality of life. A previous study of the JoCoOA showed satisfactory reliability and validity of the FAOS in this cohort. [25]

Older age was less likely to be associated with worsening of foot symptoms (pain, aching, and stiffness), pain (FAOS pain), and physical function (FAOS ADL) among feet with baseline rOA. Although we cannot be certain based on our available data, potential loss of pain sensitivity for lower intensity pain and elevated pain tolerance thresholds that can occur with aging [38] could be playing a role in our results. Among adults with foot rOA, those who are older may be less likely to detect pain changes over time or may be able to better tolerate those changes than younger adults. Those who were younger in our cohort were at least 55 years of age at baseline and were in a period of life where they were likely more mobile and active than older adults. Thus, increasing pain and declines in physical function could be more detectable for these adults than for older adults. Future studies examining pain perception may elucidate associations between aging and foot pain and impaired foot-related function.

Strengths of this study include the use of data from a large community-based cohort that did not select for individuals with foot joint concerns or any clinical diagnoses. By following participants longitudinally over an average of 3.5 years, we were able to calculate incidence and progression of foot rOA. For consistency, our radiographs were obtained by a single expert technologist and read in a standardized manner, with one musculoskeletal radiologist (JBR) with decades of experience interpreting the films for the JoCoOA. Having a single reader also

may be a limitation, but our radiologist has a long record in the JoCoOA of excellent intra- and inter-rater reliability for radiographic reads (weighted kappas ≥0.90) [39, 40]. A limitation to our study was the inclusion of mostly older adults (mean age 69) and therefore less generalizability to younger populations. Additionally, there was study attrition, which occurs in most longitudinal studies and may contribute to bias since those with poorer health are less likely to return for follow-up visits. Some items of our study were self-reported, such as gout or foot injury, and our data on gout did not specify the joints affected by gout. Also, few participants had a history of gout or foot injury, and accordingly, it was not feasible to sufficiently determine their associations with OA of specific regions of the foot (e.g., 1st MTP, midfoot). We utilized an approach to defining incidence and progression of foot rOA based on established strategies for defining rOA, and future studies should examine these definitions and explore variations of these definitions across diverse samples. Considering that not all injuries are medically attended and thus not available in the medical record, self-report would lessen misclassification of foot injury. Given the paucity of information regarding foot OA, this study provides important insights into associated risk factors for foot OA and strategies for future research.

In summary, progression of foot rOA is relatively common, although it is not necessarily related to worsening symptoms. The factors that may be important for foot OA development include sex, BMI, and history of gout. Given the strong association of foot rOA and FAOS with higher BMI, BMI may be a modifiable risk factor for the development of foot rOA, similar to other weight-bearing joints such as the knee. Strategies for prevention of foot injuries are likely important for symptomatic foot rOA. Further studies should determine if interventions, such as weight loss, could lead to better symptom control in foot OA and should examine the association of foot OA with OA at other joint sites.

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Statement of ethics

This study used an existing data from the JoCoOA. All participants completed written informed consent. The JoCoOA has been continuously approved by the University of North Carolina at Chapel Hill Institutional Review Board #92-0583.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conception and design: RE, AEN, CA, JBR, CB, LSG, YMG; Acquisition of data: JBR, YMG; Analysis and interpretation of data: RE, AEN, CA, JBR, CB, LSG, YMG. Drafting the manuscript: RE, AEN, CA, YMG; Critical revisions for important intellectual content: RE, AEN, CA, JBR, CB, LSG, YMG. Final approval of the version to be published: all. YMG is accountable for all aspects of the work.

Data Availability Statement

The datasets that were used and analyzed during the current study are not publicly available because they contain identifying information that could compromise the privacy of research participants. The data are available upon reasonable request from the co-Principal Investigators of the JoCoOA, Dr. Amanda E. Nelson (amanda_nelson@med.unc.edu) and Dr. Yvonne M. Golightly (corresponding author, ygolightly@unmc.edu).

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Figure legends

Fig. 1. Flow diagram of participants.

Table 1. Characteristics of the study sample by foot radiographic osteoarthritis (rOA) status at baseline and frequency of outcomes.

Person-Level Characteristics	All participants (n=541)	No Foot rOA at baseline (n=421)	Foot rOA at baseline (n=120)
Age, mean±SD (years)	69.4±6.9	69.2±6.8	70.2±7.3
Women, n, %	382, 70.6%	290, 68.9%	92, 76.7%
Black, n, %	190, 35.1%	139, 33.0%	51, 42.5%
BMI, mean±SD (kg/m^2)	31.2±6.4	30.6±6.0	33.2±7.5
NSAID use past 2 weeks, n, %	325, 60.1%	248, 58.9%	77, 64.2%
Work disability, n, %	119, 22.0%	89, 21.1%	30, 25.0%
Foot-Level Characteristics	**All feet (n=1082)**	**No Foot rOA at baseline (n=928)**	**Foot rOA at baseline (n=154)**
History of gout, n, %	67, 6.2%	59, 6.4%	8, 5.2%
Prior foot injury, n, %	26, 2.4%	20, 2.2%	6, 3.9%
Foot joints with rOA:			
1st metatarsophalangeal, n, %	64, 5.9%	n/a	64, 41.6%
1st cuneometatarsal, n, %	13, 1.2%	n/a	13, 8.4%
2nd cuneometatarsal, n, %	34, 3.1%	n/a	34, 22.1%
navicular-1st cuneiform, n, %	38, 3.5%	n/a	38, 24.7%
talonavicular, n, %	48, 4.4%	n/a	48, 31.2%

SD=standard deviation; BMI=body mass index; NSAID=nonsteroidal anti-inflammatory drug

Table 2. Incidence and progression (%) of foot radiographic OA (rOA) and other outcomes at follow up by baseline foot OA status.

Outcome at follow-up	No baseline foot rOA (n=928)	Baseline foot rOA (n=154)
Foot rOA worsening	41, 4.4%	84, 54.5%
Foot rOA worsening with symptoms	14, 1.5%	25, 16.2%
Foot symptoms worsening	128, 13.8%	30, 19.5%
FAOS* Symptoms worsening	319, 34.4%	67, 43.5%
FAOS Pain worsening	265, 28.6%	53, 34.4%
FAOS ADL worsening	244, 26.3%	61, 39.6%
FAOS Sports and Recreation worsening	268, 28.9%	51, 33.1%
FAOS QOL worsening	293, 31.6%	63, 40.9%

FAOS = Foot and Ankle Outcome Score

Table 3. Association (aOR [95% CI]) between covariates and foot rOA and symptoms outcomes, stratified by radiographic osteoarthritis (rOA) status where interactions were significant (n=1082).

Risk Factors	Incidence or progression of foot rOA	Incidence or progression of foot rOA with symptoms at follow-up	Foot symptoms worsening*
Age: 5 years older	1.14 (0.97, 1.34)	1.01 (0.76, 1.35)	n/a
No rOA at baseline	n/a	n/a	1.02 (0.85, 1.23)
rOA at baseline	n/a	n/a	0.70 (0.50, 0.99)
Women vs. Men	n/a	2.35 (0.77, 7.22)	1.58 (0.93, 2.71)
No rOA at baseline	4.10 (1.22, 13.8)	n/a	n/a
rOA at baseline	0.46 (0.19, 1.08)	n/a	n/a
Black vs. White	1.04 (0.64, 1.69)	0.37 (0.15, 0.90)	0.59 (0.35, 1.00)
BMI: 5 kg/m^2 increase	n/a	n/a	1.16 (0.97, 1.38)
No rOA at baseline	1.60 (1.31, 1.97)	1.81 (1.39, 2.36)	n/a
rOA at baseline	1.11 (0.90, 1.36)	1.07 (0.78, 1.47)	n/a
Work disability	0.74 (0.39, 1.42)	1.24 (0.43, 3.63)	1.81 (1.07, 3.04)
NSAID use	1.38 (0.82, 2.31)	1.95 (0.74, 5.14)	1.29 (0.79, 2.10)
History of gout	2.75 (1.25, 6.07)	2.01 (0.68, 5.92)	1.42 (0.81, 2.49)
Foot injury	2.75 (0.73, 10.4)	4.99 (1.57, 15.9)	1.59 (0.61, 4.13)

BMI = body mass index, NSAID = nonsteroidal anti-inflammatory drug

Models adjusted for race, work disability, NSAID use, any foot symptoms at baseline.

*n=1080

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Table 4. Association (aOR [95% CI]) for covariates and worsening for each Foot and Ankle Outcome Scale (FAOS) subscale outcomes, stratified by radiographic osteoarthritis (rOA) where interactions were significant (n=1080).

Risk Factors	FAOS Symptoms	FAOS Pain	FAOS-Activities of Daily Living	FAOS Sports and Recreation	FAOS Quality of Life
Age: 5 years older	1.13 (0.99, 1.31)	n/a	n/a	n/a	1.01 (0.89, 1.15)
No rOA at baseline	n/a	1.01 (0.88, 1.16)	1.09 (0.94, 1.26)	1.12 (0.97, 1.29)	n/a
rOA at baseline	n/a	0.74 (0.58, 0.96)	0.77 (0.60, 0.98)	0.89 (0.71, 1.13)	n/a
Women vs. Men	n/a	1.41 (0.93, 2.13)	1.58 (1.04, 2.42)	1.57 (1.01, 2.43)	1.31 (0.89, 1.94)
No rOA at baseline	1.47 (0.95, 2.27)	n/a	n/a	n/a	n/a
rOA at baseline	0.60 (0.26, 1.37)	n/a	n/a	n/a	n/a
Black vs. White	0.95 (0.63, 1.45)	0.87 (0.58, 1.30)	0.82 (0.55, 1.24)	0.72 (0.47, 1.11)	0.69 (0.47, 1.02)
BMI: 5 kg/m^2 increase	1.40 (1.19, 1.66)	1.22 (1.05, 1.41)	1.21 (1.04, 1.41)	1.31 (1.11, 1.54)	1.24 (1.06, 1.44)
Work disability	1.39 (0.85, 2.27)	2.08 (1.26, 3.43)	2.09 (1.33, 3.27)	2.19 (1.35, 3.55)	1.60 (1.02, 2.50)
NSAID use	1.16 (0.78, 1.72)	1.10 (0.76, 1.59)	1.15 (0.79, 1.69)	1.17 (0.78, 1.74)	1.19 (0.84, 1.70)
Gout	0.98 (0.65, 1.47)	0.87 (0.54, 1.40)	1.59 (1.09, 2.31)	1.47 (1.10, 1.96)	1.56 (0.93, 2.62)
Foot injury	n/a	1.52 (0.56, 4.13)	2.57 (1.18, 5.61)	1.17 (0.43, 3.19)	1.21 (0.55, 2.68)
No rOA at baseline	0.57 (0.21, 1.56)	n/a	n/a	n/a	n/a
rOA at baseline	1.60 (0.90, 2.84)	n/a	n/a	n/a	n/a

BMI = body mass index, NSAID = nonsteroidal anti-inflammatory drug, n/a = not applicable

Models adjusted for: race, work disability, NSAID use, any foot symptoms at baseline, and FAOS subscale at baseline.

Supplementary Table. Characteristics of participants with follow-up data (included in analysis) compared to those who did not return to the follow-up visit.

Characteristics	Returned to Follow-Up Visit	
	Yes (n=541)	No (n=323)
Baseline Age, mean±SD (years)	69.4±6.9	74.0±7.7
Women, n, %	382, 70.6%	207, 64.1%
Black, n, %	190, 35.1%	99, 30.7%
Baseline BMI, mean±SD (kg/m^2)	31.2±6.4	30.2±6.2
NSAID use past 2 weeks, n, %	325, 60.1%	195, 60.4%
Work disability, n, %	119, 22.0%	87, 26.9%
History of gout, n, %	49, 9.1%	44, 13.6%
Prior foot injury, n, %	22, 4.1%	11, 3.4%
Foot joints with rOA:		
1st metatarsophalangeal, n, %	55, 10.2%	33, 10.2%
1st cuneometatarsal, n, %	11, 2.0%	10, 3.1%
2nd cuneometatarsal, n, %	28, 5.2%	15, 4.6%
navicular-1st cuneiform, n, %	33, 6.1%	17, 5.3%
talonavicular, n, %	36, 6.7%	24, 7.4%
Any foot symptoms	100, 18.5%	76, 23.5%
FAOS Symptoms, mean±SD	91.1±11.7	89.1±13.2
FAOS Pain, mean±SD	91.3±15.0	88.6±16.9
FAOS ADL, mean±SD	93.0±15.1	89.9±17.8
FAOS Sports and Recreation, mean±SD	83.9±27.6	75.4±35.0
FAOS QOL, mean±SD	86.6±20.8	82.7±22.9

SD=standard deviation; BMI=body mass index; NSAID=nonsteroidal anti-inflammatory drug; FAOS=Foot and Ankle Outcome Score