A Cross-sectional Analysis of Radiographic Ankle Osteoarthritis Frequency and Associated Factors: The Johnston County Osteoarthritis Project

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ABSTRACT. ***Objective.*** Because there are no epidemiologic data regarding the frequency of ankle osteoarthritis (OA) in a general population, we sought to analyze this disabling condition in a large, well-characterized, community-based cohort of older individuals.

Methods. Cross-sectional data, including ankle radiographs, were from the most recent data collection (2013–2015) of the Johnston County OA Project. Radiographic ankle OA (rAOA) was defined as a Kellgren-Lawrence arthritis grading scale of ≥ 2 on weight-bearing lateral and mortise radiographs. The presence of pain, aching, or stiffness in the ankles as well as history of ankle injury (limiting ability to walk for at least 2 days) were assessed. Chi-square statistics (categorical variables) and Student t tests (continuous variables) were used to compare all participant characteristics by rAOA status. Joint-based logistic regression models with generalized estimating equations were used to examine associations of rAOA and covariates of interest [age, body mass index (BMI), sex, race, ankle symptoms, and injury history].

Results. Of 864 participants with available data, 68% were women, 34% were African American, with a mean age of 72 years and BMI of 31 kg/m^2. Nearly 7% of this sample had rAOA. Increasing age, high BMI, history of ankle injury, and presence of ankle symptoms were all independently associated with greater odds of having rAOA; no significant differences were seen by sex or race.

Conclusion. The frequency of rAOA was higher than estimates generally quoted in the literature. While injury was an important contributor, other factors such as age, BMI, and symptoms were also significantly associated with rAOA. (First Release February 15 2017; J Rheumatol 2017;44:499–504; doi:10.3899/jrheum.161076)

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Osteoarthritis (OA) is the most common form of arthritis and is a leading cause of disability[1]. Although ankle OA is less commonly seen clinically than hip and knee OA[2,3], there are no community-based studies of the epidemiology of ankle OA to substantiate the widely quoted 1% frequency of this condition[4,5,6]. Most studies in ankle OA are of endstage clinical populations[5,6,7], which have also suggested that the etiology of ankle OA is almost always posttraumatic[4,8,9,10]. This is in contrast to hip and knee OA, which are more often considered primary (although injury is an important risk factor); 1 study estimated that while 1.6% of hip and 9.8% of knee OA were posttraumatic, 79.5% of ankle OA was secondary to trauma[11]. The difference may be attributable at least in part to the unique anatomical and biomechanical characteristics of the ankle compared with hip and knee (e.g., smaller contact area, higher proteoglycan density, lower shear

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forces)[4,12]. Kraus, *et al* identified radiographic ankle OA in 15% of individuals with symptomatic knee OA, yet fewer than 5% reported any prior injury or surgery[13], suggesting that there may be a greater burden of ankle OA than currently appreciated, and that other risk factors typically associated with OA, such as obesity, may be contributing.

Regardless of cause, ankle OA can be a source of significant morbidity because patients with endstage ankle OA have a reduced quality of life and substantial functional limitations, equivalent to those reported by patients with endstage hip OA, congestive heart failure, and endstage kidney disease[5,9]. Additionally, treatments for ankle OA are more limited than those for hip and knee given the poorer outcomes of surgical interventions for endstage disease[14].

In addition to the surprising lack of community-based epidemiologic studies of ankle OA, there has been minimal investigation into other potential contributors to this disabling condition. Therefore, to better understand characteristics associated with ankle OA, we examined its associations with factors [i.e., body mass index (BMI), sex, race, presence of ankle symptoms, and history of ankle injury] that may identify groups with a higher frequency of ankle OA in a large community-based cohort of older African American and white individuals.

MATERIALS AND METHODS

We used cross-sectional data from the Johnston County OA Project (JoCo OA), an ongoing community-based study of OA and its risk factors in Johnston County, North Carolina, USA, which has been previously described in detail[15]. The JoCo OA Project is a prospective, longitudinal cohort study in African American and white men and women aged at least 45 years, who were residents of 1 of 6 Johnston County townships for at least 1 year and capable of completing the study protocol. The JoCo OA Project has been continuously approved by the Institutional Review Boards of the University of North Carolina at Chapel Hill (92-0583) and the Centers for Disease Control and Prevention (Protocol #1820.0).

Standardized lateral and mortise views of the ankle were obtained in weight-bearing at the most recent data collection of the JoCo OA (2013–2015) as described in a recent atlas[16]; the tibiotalar joints were graded by an expert musculoskeletal radiologist (JBR) with excellent intrarater reliability ($\kappa = 0.91$)[16]. The Kellgren-Lawrence arthritis grading scale (KL) was modified for this purpose, such that grade 0 indicated no radiographic findings of OA, grade 1 indicated "minute osteophytes of doubtful clinical significance," grade 2 included definite osteophytes and mild joint space narrowing (JSN), grade 3 reflected the presence of definite osteophytes and moderate JSN, and grade 4 was the combination of definite osteophytes and severe JSN[16]. For these analyses, the presence of radiographic ankle OA (specifically tibiotalar OA) was defined as a KL ≥ 2. We analyzed associations based on a KL of 1 or more, as well as osteophyte and JSN grades. Ankle symptoms were considered present based on an affirmative response to the question, "On most days of any 1 month in the last 12 months, did you have pain, aching, or stiffness in your left/right ankle?" History of ankle injury was self-reported based on an affirmative response to the question, "Have you ever injured your (right/left) ankle badly enough that it limited your ability to walk for at least 2 days?"

Two sets of analyses were conducted: (1) at the person-level to examine the associations of ankle OA and independent variables within participants, and (2) at the joint-level (left ankle, right ankle) for examination of these associations within the same joint. At the person-level, chi-square statistics for categorical variables and Student t tests for continuous variables were used to compare all participant characteristics by the presence or absence of ankle OA. At the joint-based level, complete case analyses were conducted using logistic regression models with generalized estimating equations (GEE) to account for intraperson correlations. Separate logistic regression models with GEE were performed to examine the discrete associations of ankle OA with age, BMI, sex, race, ankle symptoms, and history of ankle injury ("unadjusted OR"). Next, a multiple logistic regression model with GEE was conducted adjusting for all other factors ("adjusted OR"). All models were run separately for each ankle OA definition (KL 2 vs < 2 and KL 1 vs < 1).

RESULTS

Data for these analyses were from the third followup (T3) of the JoCo OA Project (2013–2015). Over 2000 individuals were eligible for participation and were contacted. The main reasons for nonparticipation in this data collection were the following: moved away from the study area (n = 295), became physically or mentally unable to participate (n = 415), or inability to locate or contact (n = 267), with other reasons as noted (Figure 1). A total of 908 individuals attended the study clinic visit at T3. Compared with the full cohort's baseline characteristics, those who participated in T3 were younger at baseline (56 vs 62 yrs) and had higher education levels (85% completed high school vs 58%), as expected. The proportions by sex, race, and BMI category were similar for participants and nonparticipants, with about one-third men, one-third African American, and two-thirds overweight or obese.

Data for radiographic OA, symptoms, and injuries of the ankle, as well as demographic and clinical characteristics, were available for 864 individuals, of whom 68% were women and about a third were African American, with a mean age of 72 years, and mean BMI of 31.0 kg/m^2 (Table 1). The 44 individuals without ankle radiographs were somewhat older and heavier, and were more likely to be men, African American, and symptomatic. Fifty-six of the 864 included participants had radiographic ankle OA defined as a KL of 2 or more in at least 1 ankle, for a frequency of 6.5% in this sample. Those with radiographic ankle OA were on average slightly older, heavier, and less often African American compared with those without ankle OA (Table 1). Those with ankle OA were also more likely to report prior injury and ankle symptoms, particularly involving both ankles.

The distribution of radiographic grades in the sample is shown in Table 2. More than half of the participants had a KL of 1 in either the left or right ankle. More than 3% of the cohort had a KL equal to 2 in either the left or right ankle, while less than 1% of the participants had a KL of either 3 or 4 on their ankle radiographs. About 60% of ankle radiographs had an osteophyte grade of 1 or greater, while only 4% had JSN graded 1 or more.

Associations between radiographic ankle OA and covariates are shown in Table 3. In models adjusted only for intraperson correlation (between the 2 ankles of 1 participant), the odds of ankle OA were increased for older participants (although not statistically significantly), those who

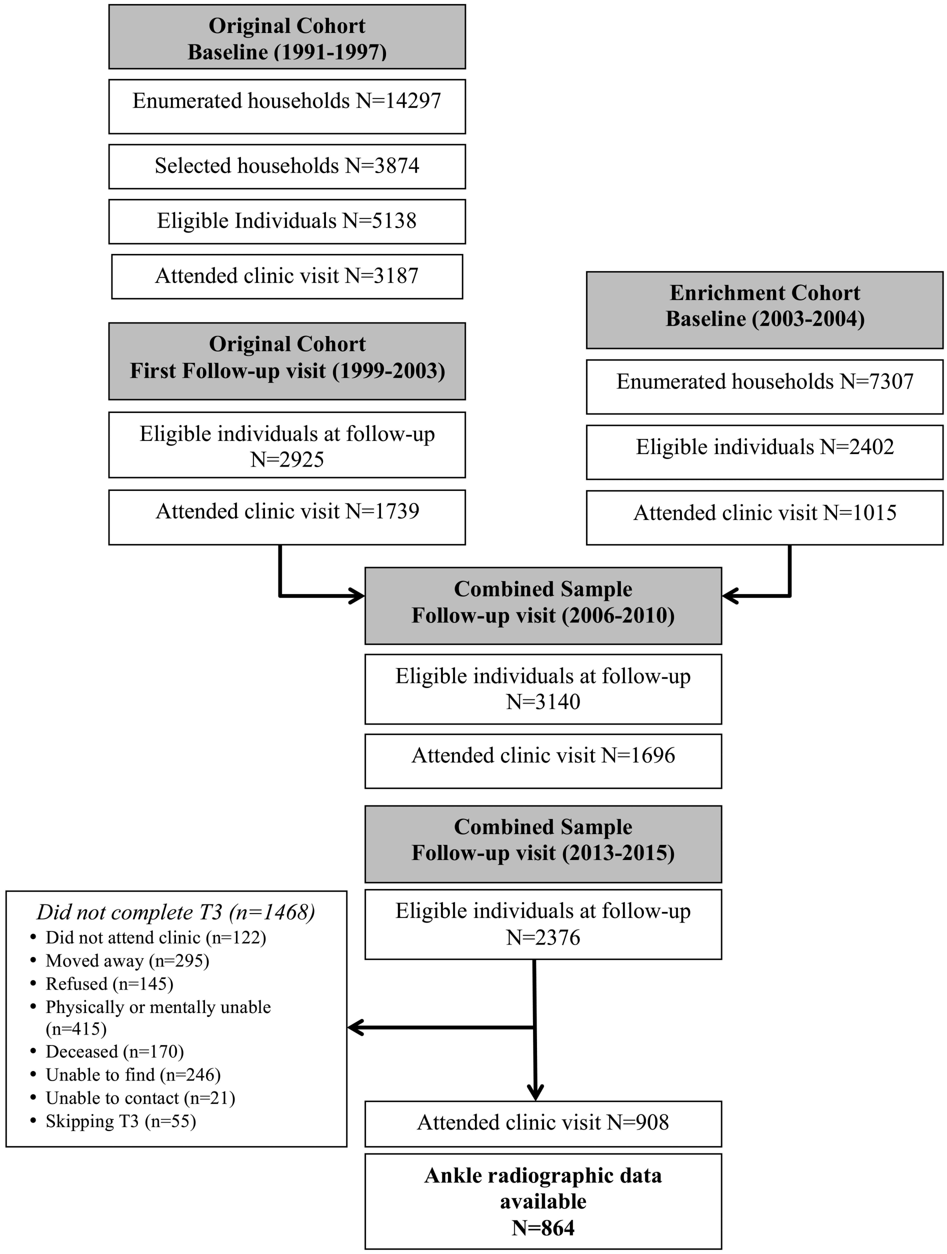

Figure 1. Flow diagram of included participants.

were obese, and those reporting ankle symptoms or a history of ankle injury. When included in a model simultaneously, all covariates were found to be independently and statistically significantly associated with radiographic ankle OA. Individuals aged 70 years or over had twice the odds of ankle OA compared with younger individuals. Obese participants had twice the odds of ankle OA compared with nonobese individuals. A history of ankle injury conferred 2× higher odds of ankle OA, while self-reported ankle symptoms were associated with a 3-fold increase in the odds of ankle OA. No significant differences were seen by sex or race in either model (Table 3).

In an analytical fashion, we also considered an outcome a KL of 1 or more, which affected three-quarters (644/864) of participants. Compared with those who had KL = 0 in both ankles, those with KL of 1 or more were slightly heavier and less often African American or women, and were more likely to report prior ankle injury (12.7% vs 7.3%) and ankle symptoms (19.3% vs 10.0%). In adjusted models (Table 4), the association with obesity was similar to the radiographic OA (KL 2 or more) outcome. However, in contrast with the main analysis, there was no association with age, and significant differences were noted for both sex (women had about half the odds of having KL 1 or more compared with men)

Table 1. Characteristics of participants overall and by KL groupings. Values are n/N (%) unless otherwise specified.

Participant Characteristics	Total Sample, n = 864	KL ≥ 2 in at Least 1 Ankle, n = 56	KL < 2 Both Ankles, n = 808
Age, yrs, mean (SD)	71.6 (7.6)	72.6 (7.3)	71.1 (7.6)
BMI, kg/m^2, mean (SD)	30.8 (6.4)	33.6 (6.69)	30.6 (6.3)
Women	589/864 (68.2)	38/56 (66.1)	551/808 (68.2)
African American	289/864 (33.5)	17/56 (30.4)	272/808 (33.7)
History of ankle injury	97/854 (11.4)	11/56 (19.6)	86/798 (10.8)
Right ankle injury	51/854 (6.0)	7/56 (12.5)	44/798 (5.5)
Left ankle injury	33/854 (3.9)	1/56 (1.8)	32/798 (4.0)
Bilateral ankle injury	13/854 (1.5)	3/56 (5.4)	10/798 (1.3)
Any ankle symptoms	146/863 (16.9)	19/56 (33.9)	127/807 (15.7)
Right ankle symptoms	31/863 (3.6)	2/56 (3.6)	29/807 (3.6)
Left ankle symptoms	24/863 (2.8)	6/56 (10.7)	18/807 (2.2)
Bilateral ankle symptoms	91/863 (10.5)	11/56 (19.6)	80/807 (9.9)

KL: Kellgren-Lawrence arthritis grading scale; BMI: body mass index.

Table 2. Breakdown of sample by specific KL, osteophyte, and JSN grade. Values are n/N (%) unless otherwise specified.

Radiographic Measure*	Grade	Left Ankle	Right Ankle
KL	0	349/861 (40.5)	326/863 (37.8)
	1	479/861 (55.6)	508/863 (58.9)
	2	28/861 (3.3)	27/863 (3.1)
	3	3/861 (0.4)	2/863 (0.2)
	4	2/861 (0.2)	0/863 (0.0)
Osteophytes	0	348/864 (40.3)	323/863 (37.4)
	≥ 1	516/864 (59.7)	540/863 (62.6)
JSN	0	828/864 (95.8)	825/863 (95.6)
	≥ 1	36/864 (4.2)	38/863 (4.4)

* 864 participants with ankle radiographs, 1 missing right KL read, and 3 missing left KL read. KL: Kellgren-Lawrence arthritis grading scale; JSN: joint space narrowing.

Table 3. Adjusted OR and 95% CI (n = 1702 ankles*) for associations between covariates and radiographic ankle OA (KL 2 or more).

Characteristic	OR[1] (95% CI)	Adjusted OR[2] (95% CI)
Age ≥ 70 yrs	1.74 (0.98–3.08)	2.01 (1.11–3.48)†
Age < 70 yrs	Referent	Referent
BMI ≥ 30 kg/m^2	1.96 (1.10–3.49)†	1.97 (1.12–3.48)†
BMI < 30 kg/m^2	Referent	Referent
Women	1.06 (0.59–1.88)	0.99 (0.55–1.79)
Men	Referent	Referent
African American	0.88 (0.48–1.59)	0.89 (0.48–1.65)
White	Referent	Referent
Ankle injury	2.54 (1.24–5.22)†	2.33 (1.11–4.92)†
No injury	Referent	Referent
Ankle symptoms	3.30 (1.84–5.92)†	2.99 (1.65–5.42)†
No ankle symptoms	Referent	Referent

* n = 864 individuals/1728 ankles; missing data on injury (10 individuals/20 ankles), symptoms (1 individual/2 ankles), or KL (4 ankles) results in 1702 ankles available for complete case analysis. † Statistically significant. [1] Adjusted only for intraperson correlation using generalized estimating equations. [2] Adjusted for intraperson correlation and all other listed covariates. OA: osteoarthritis; BMI: body mass index; KL: Kellgren-Lawrence arthritis grading scale.

and race (African Americans were 25% less likely to have KL 1 or more). Again noted, while not as strong as for radiographic OA defined by a KL of 2 or more, were statistically significant associations for ankle injury and ankle symptoms; comparisons are shown graphically in Figure 2.

DISCUSSION

We report a nearly 7% frequency of radiographic ankle OA (defined as a KL ≥ 2) in this first (to our knowledge) community-based cohort study of older African American and white men and women. In this cross-sectional study, radiographic ankle OA was associated with older age, obesity, prior injury, and ankle symptoms. The frequency of a KL ≥ 1 was very high in this sample and showed similar associations, although additional differences were seen by sex and race. There was a very low frequency of more severe changes in this cohort, with only 7 ankles having a KL ≥ 3.

The risk of OA increases with age, but individuals with posttraumatic OA are often younger than those with primary OA. The association between age and radiographic ankle OA in our present study is consistent with what little information is available in the literature. In a cohort of patients with endstage ankle OA, those with primary OA were older (mean 65 yrs) compared with the posttraumatic OA group (mean 58 yrs, p = 0.02)[6]. Among individuals with symptomatic knee OA, those with any evidence of ankle abnormality by scintigraphy were slightly older than those with normal ankles (65.4 vs 62.9 yrs, p = 0.20)[13]. Finally, in a study of organ donors, the severity of cartilage degeneration was associated with age, although this was more marked for the knee compared with the ankle[17].

While the association between knee OA and obesity is well established, it is less clear for other sites, particularly

Table 4. Adjusted OR and 95% CI (n = 1702 ankles*) for exploratory associations between covariates and KL 1 or more.

Characteristic	OR[1] (95% CI)	Adjusted OR[2] (95% CI)
Age ≥ 70 yrs	0.81 (0.64–1.03)	0.86 (0.68–1.09)
Age < 70 yrs	Referent	Referent
BMI ≥ 30 kg/m^2	2.00 (1.58–2.52)†	2.13 (1.66–2.73)†
BMI < 30 kg/m^2	Referent	Referent
Women	0.49 (0.38–0.64)†	0.47 (0.36–0.61)†
Men	Referent	Referent
African American	0.83 (0.65–1.06)	0.75 (0.58–0.98)†
White	Referent	Referent
Ankle injury	1.57 (1.06–2.31)†	1.50 (1.02–2.22)†
No injury	Referent	Referent
Ankle symptoms	1.82 (1.32–2.51)†	1.64 (1.18–2.29)†
No ankle symptoms	Referent	Referent

* n = 864 individuals/1728 ankles; missing data on injury (10 individuals/20 ankles), symptoms (1 individual/2 ankles), or KL (4 ankles) results in 1702 ankles available for complete case analysis. † Statistically significant. [1] Adjusted only for intraperson correlation using generalized estimating equations. [2] Adjusted for intraperson correlation and all other listed covariates. KL: Kellgren-Lawrence arthritis grading scale; BMI: body mass index.

the ankle. In a study of 1411 adults visiting a single orthopedic foot and ankle specialist, the odds of having ankle or foot OA were increased by 50% in overweight/obese versus normal weight individuals, although this association was not statistically significant[18]. Another study of patients with endstage ankle OA in a tertiary care setting found no difference in BMI among those with posttraumatic, secondary, or primary OA[6]. Body habitus was not associated with the severity of ankle cartilage degeneration among organ donors[17]. The symptomatic knee cohort described by Kraus, *et al* was obese on average [BMI 31.3 (6.7) kg/m^2], and compared with those with normal ankles, those with any ankle scintigraphic abnormality were significantly heavier (33.7 kg/m^2 vs 30.2 kg/m^2, $p = 0.0025$)[13].

Our results support the known relationship between injury and OA at the ankle[4,6], with a somewhat smaller magnitude. In our cohort, 11% reported any injury, increasing to about 20% among those with radiographic ankle OA, with an adjusted OR of about 2. In the study by Kraus, *et al*, patients with symptomatic knee OA could identify prior ankle injury or surgery only 9% of the time, despite the high prevalence of ankle abnormalities and OA[13]. In contrast, in the clinical studies of endstage ankle OA, three-quarters or more of patients are often categorized as having posttraumatic OA[6].

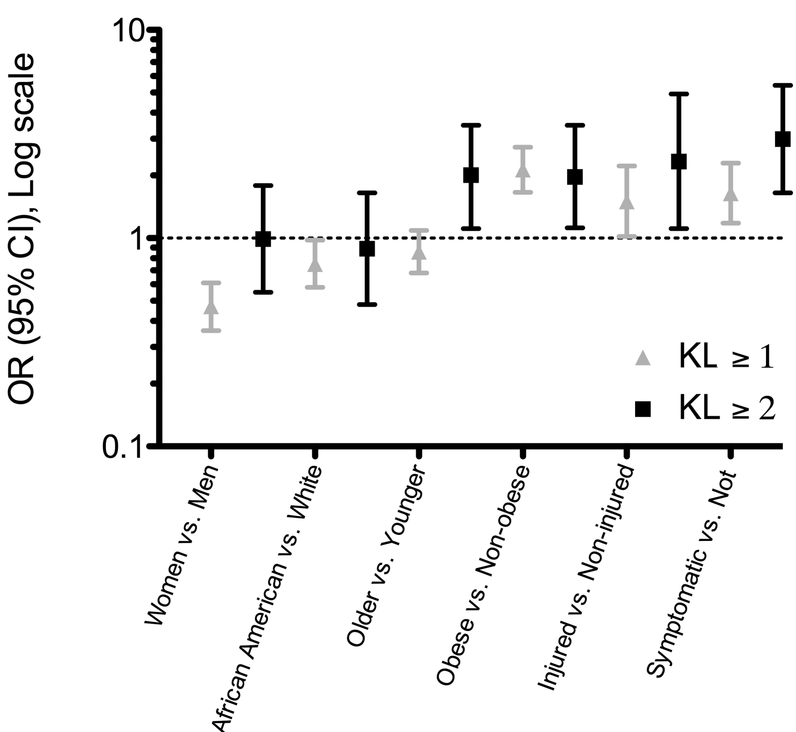

Figure 2. Graphic representation of the adjusted OR and 95% CI from Table 3 and Table 4, showing the consistency of the results for the outcomes of KL 1 or more (gray triangles) and KL 2 or more (black squares) for each category of comparison (X-axis) on the Log 10 scale. KL: Kellgren-Lawrence arthritis grading scale.

We also identified a cross-sectional association between ankle symptoms and the presence of radiographic ankle OA that is again in agreement with prior work[9,13], although this aspect is often not considered because the clinical cohorts tend to be of symptomatic endstage patients and do not use standard radiographic criteria.

Even though there were no significant differences by sex and race in the main analysis, the odds of having at least 1 ankle with a KL ≥ 1 (vs both with KL = 0) were significantly lower among African Americans and women. There are no prior studies of radiographic ankle OA among African Americans, to our knowledge, but differences in use of total ankle arthroplasty has been reported, with whites 4 times as likely to receive this procedure compared with African Americans[19]; it is not known whether this is because of differences in prevalence or to racial disparities in utilization and access to care, which have been well-documented for other joint replacement procedures. Valderrabano, *et al* reported a similar ratio of men and women with posttraumatic OA, although more men than women had primary OA (25 men vs 11 women)[6]. Kraus, *et al* found no difference in the frequency of scintigraphic ankle abnormalities by sex[13]. Among healthy organ donors, there was a trend toward delayed cartilage degeneration in women compared with men[17].

Our study has many strengths, including the use of data from a large and well-characterized, community-based cohort that was not selected for foot or ankle issues, the inclusion of African American and white men and women, and the use of standardized, weight-bearing ankle radiographs read with high reliability by a single musculoskeletal radiologist with decades of experience. Although we provide the first epidemiologic data on the frequency of ankle OA in the community, our cohort is older (mean age 72 yrs, range 55–94 yrs), and our results may not be generalizable to younger populations. Another limitation is the lack of detailed data on the specifics of the ankle injuries, such as type and severity. Our current analysis is cross-sectional, restricting our ability to make inferences about causality. However, this cross-sectional approach provides useful insights into the frequency of ankle OA and associated factors that (1) support more clinical attention for this joint, especially among those with symptoms, prior injury, and obesity, and (2) will inform longitudinal assessments (the next phase of our work with future followup in this cohort).

Ankle OA may be more common than previously thought. A better understanding, including longitudinal studies, of both traumatic and nontraumatic etiologies of ankle OA may allow for more effective preventive measures in at-risk individuals and therapeutic interventions earlier in the disease process for those with ankle OA.

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