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Subjective Crepitus as a Risk Factor for Incident Symptomatic Knee Osteoarthritis: Data from the Osteoarthritis Initiative

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Abstract

Objective—Subjective crepitus is the complaint of hearing grating, cracking or popping sounds in and/or around a joint. We aimed to evaluate whether there is an association between crepitus and incident symptomatic knee osteoarthritis (SOA) in the Osteoarthritis Initiative (OAI), a multicenter longitudinal U.S. cohort.

Methods—Knees without baseline SOA were included. Crepitus frequency was assessed using a question from the Knee Injury and Osteoarthritis Outcome Score (KOOS) at baseline, 12-, 24-, and 36-month visits. Frequent knee pain and radiographs were assessed at baseline and annual visits up to 48-months. Radiographic OA (ROA) was tibiofemoral Kellgren and Lawrence (KL) grade ≥ 2. SOA was a knee with both frequent symptoms and ROA. We performed a repeated measures analysis with a predictor of crepitus and outcome of incident SOA, adjusting for age, sex, and BMI where never complaining of crepitus was the referent group.

Results—3495 participants (42.2% male) with mean age of 61.1 (9.2) years, mean BMI of 28.2 (4.7) kg/m^2. Odds of incident SOA was higher with greater frequency of crepitus (never, rarely, sometimes, often, always); adjusted odds ratios were (referent), 1.5, 1.8, 2.2, 3.0 (p for trend < 0.0001). The group at OAI baseline with ROA but without symptoms contributed 26% of the observations, but over 75% of the incident SOA cases.

Conclusion—Among those without SOA, subjective knee crepitus predicts incident SOA longitudinally, with most cases occurring in those with pre-existing tibiofemoral ROA but without

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frequent knee pain. An important limitation is that patellofemoral OA was not systematically evaluated within the OAI. Subjective crepitus offers utility for identification of at-risk individuals, predictive modeling, and future research.

INTRODUCTION

Osteoarthritis (OA) is the most common form of arthritis and one of the leading causes of chronic pain and disability. It is highly prevalent in the United States, afflicting an estimated 30.8 million adults annually in 2008–2011 (1). Because the population of those aged 65 and older is expected to grow and 35% of the overall adult population is obese (2, 3) OA prevalence will likely increase because older age and obesity are potent risk factors for knee OA (4–9). Symptomatic knee OA (SOA), defined as radiographic evidence of OA plus frequent pain, has an estimated prevalence of about 16% in US adults 60 years and older (10), with higher prevalence as age and BMI increase (11).

In the clinical setting, patients frequently ask whether crepitus should be concerning to them or not. Subjective crepitus is the complaint of hearing grating, cracking or popping sounds in and/or around a joint. Although this is a common sign in the clinical setting (12) and has been shown to be associated with prevalent OA based on contemporaneous MRI and radiographs (13–15), it is unclear whether the complaint of crepitus is predictive of worsening OA. In this study, we aim to evaluate whether subjective crepitus is predictive of incident SOA. If we find an association, this will support the idea that crepitus is a clinically important complaint that predicts who will develop SOA. Therefore, the objective of this study was to evaluate whether there is an association between crepitus and incident symptomatic knee osteoarthritis.

PATIENTS AND METHODS

Study Design

We performed a person-based longitudinal study, evaluating the right knee only, using data from the Osteoarthritis Initiative (OAI).

Sample Selection

Study participants were selected from the OAI, a longitudinal, observational study of knee OA conducted at four clinical sites: Memorial Hospital of Rhode Island (Pawtucket, RI), Ohio State University (Columbus, OH), University of Pittsburgh (Pittsburgh, PA), and University of Maryland/Johns Hopkins University (Baltimore, MD). At the time of OAI enrollment (February 2004 – May 2006), participants were 45 to 79 years of age. Body Mass Index (BMI) was assessed at baseline. Presence of crepitus and symptoms were assessed at baseline and annual follow-up visits. Knees with pre-existing SOA or arthroplasty at baseline were excluded.

Subjective Crepitus Assessment

At OAI baseline, 12-, 24-, and 36-month clinic visits, crepitus frequency (never, rarely, sometimes, often, and always) was assessed using question 2 of the Knee injury and

Osteoarthritis Outcome Score (KOOS) (16) symptoms question, “Do you feel grinding, hear clicking or any other type of noise when your right knee moves?”.

Symptom Assessment

An affirmative response to the knee-specific frequent pain question, (“During the past 12 months, have you had pain, aching, or stiffness in or around your right knee on most days for at least one month? By most days, we mean more than half the days of a month.”) was used to define the presence of frequent symptoms. Symptoms (Sx) were ascertained at baseline, 12-, 24-, 36, and 48-month visits.

Additionally, at the OAI baseline visit, participants were asked to self-report knee-specific pain in reference to the last 7 days by completing the Western Ontario and McMaster (WOMAC) Universities Osteoarthritis Pain Scale (3.1 Likert version) (17). Possible pain scores range from 0 (no pain) to 20 (severe pain).

Acquisition of Knee Radiographs

Bilateral, fixed-flexion postero-anterior (PA) knee radiographs (18) were obtained at the OAI baseline and annual clinic visits through 48 months. Films were obtained in a standing position with knees flexed 20–30 degrees and feet rotated internally 10 degrees. A SynaFlexer plexiglass frame was used to fix the position of the knees and feet (19). Central readers assessed OA severity, Kellgren and Lawrence (KL) grade (0–4). Kappa coefficient for these measures ranged from 0.70–0.80 (20).

Analytic Approach

Outcome definition—Generalized Estimating Equations (GEE) only allow for adjustment for correlation across one variable (21). Because we planned repeated measures analyses and needed to adjust for correlations across visits, we would not have been able to adjust for correlation between knees within a person had we included both knees in the models. Therefore, we only included right knees in our analyses. Symptoms were defined by the Sx question. Radiographic OA (ROA) was tibiofemoral KL ≥ 2. Symptomatic OA (SOA) was defined as a knee that had both Sx and ROA. Any participant with a knee arthroplasty was identified as having Sx, ROA, and SOA.

Statistical analysis

SAS version 9.4 (SAS Institute Inc, Cary, NC, USA) was used for all analyses. To evaluate whether there was an association between baseline crepitus with WOMAC pain and KL grade, we performed Spearman correlations. We performed repeated measures logistic regression using GEE with an exchangeable correlation structure to adjust for correlations within person observations over time where the predictor was subjective crepitus frequency at baseline, month 12, 24, and 36 month visits and the outcome was incident right knee SOA one year subsequent to crepitus assessments. For instance, a participant who did not have SOA would be included in the analysis with a baseline crepitus assessment and SOA assessment at 12 months. If the participant did not develop SOA by the 12 month visit, his/her crepitus assessment at 12 months would be the predictor and the outcome of SOA at 24 months would be evaluated. This would continue until the participant developed SOA or

arrived at the 48 month visit, whichever came first. Each participant could contribute up to 4 observation periods. Once a participant developed incident SOA, he/she was censored from the analysis. The adjusted model included age, sex, and BMI. Cochran-Armitage tests were used to test for significance of trends (22, 23).

To better understand the groups that contributed to the association of crepitus with SOA, we performed post-hoc analyses divided into 3 subgroups based on their OAI baseline (at the time of enrollment into the OAI) ROA and symptoms (Sx) status: (1) those with ROA, but no frequent symptoms (+ROA, −Sx), (2) without ROA but with frequent symptoms (−ROA, +Sx), (3) without ROA and without frequent symptoms at baseline (−ROA, −Sx).

Because the natural history of OA is long, we were interested in seeing whether a longer follow up time (four years instead of one year) between assessment of crepitus and the outcome of SOA would show different results than our original analyses where we only allowed for one year of follow up. Thus, we repeated analyses with the predictor limited to crepitus at the OAI baseline visit and the outcome of interest of incident SOA ***by the OAI 48 month visit***. This meant that if a participant developed incident SOA at the 36 month visit, then he/she was identified as developing incident SOA by the 48 month visit. In these analyses, each participant contributed one observation.

We tested for interactions between crepitus with age, sex, and BMI. Because there were significant interactions for age and sex, we also present subgroup analyses evaluating men v. women, and younger (<65 years old) v. older (≥ 65 years old) participants.

RESULTS

Of 4,796 OAI participants, those excluded from this study were 35 who already had arthroplasty at the time of OAI enrollment, 305 who did not have readings of Kellgren and Lawrence grade in the right knee at the baseline visit, 877 participants who had pre-existing SOA of the right knee at the baseline visit, 84 did not have any valid outcome measure assessments of SOA at any of the follow up visit time points. Thus 3,495 participants were eligible to be included in our study. In total, 750 observations had missing information on the outcome of SOA and were excluded from analyses, representing 6.3% of the overall 11,994 potential observations. An additional 7 observations had missing information on crepitus as a predictor.

Overall, 3,495 people contributed 11,237 observations to the analyses with the outcome of incident SOA one year subsequent to crepitus assessment (Table 1). Participants had a mean age of 61.1 (9.2) years and mean BMI of 28.2 (4.7) kg/m^2. 42.2% were male. Crepitus frequency prevalence overall included observations for the responses none, rarely, sometimes, often, and always were 7,313 (65.1%), 1,213 (10.8%), 1,701 (15.1%), 626 (5.6%), 384 (3.4%), respectively. Cross-sectionally at the baseline visit, there was a correlation between crepitus and WOMAC pain ($R = 0.33$, $p<0.0001$), but there was no correlation between the crepitus and Kellgren and Lawrence score ($R=0.03$, $p = 0.1$). Supplemental Table 1, available in the appendix, provides the distribution of crepitus frequency by Kellgren and Lawrence score.

The overall number of number of incident cases of SOA was 636 from 3495 individuals for an incidence rate of 18.1%. 258, 159, 126, and 93 incident SOA cases occurred in the first through fourth observation periods respectively. In the unadjusted and adjusted models, odds of subsequent development of incident SOA increased with increasing frequency of crepitus with a statistically significant p for trend (Table 1).

To better understand which groups contributed most to the incident SOA cases, we performed post-hoc subgroup analyses (Table 2) specifically evaluating those people with ROA but without symptoms at baseline (+ROA, −Sx), without ROA but with symptoms at baseline (−ROA, +Sx), and those without ROA or symptoms at baseline (−ROA, −Sx). The SOA incidence rate in those with ROA but without symptoms at baseline was 45.0% (488/1,085), in those without ROA but with symptoms at baseline was 10.2% (67/660), and in those without ROA or symptoms at baseline was 4.6% (81/1,750). In each of these groups, crepitus and WOMAC pain were correlated (R = 0.31, 0.20, and 0.25 respectively, all with p <0.0001) but crepitus and KL scores were not (R = −0.007 (p = 0.8), −0.01 (p = 0.7), 0.04 (p = 0.07) respectively). People with ROA but without symptoms at baseline showed similar results to that of the whole group and contributed 488/636 (76.7%) of the total incident SOA cases (Table 2). 213, 126, 84, and 65 incident SOA cases occurred in the first through 4th observation periods respectively. In the other two subgroups, there was no significant association between baseline crepitus and SOA (Table 2).

In the analyses with incident SOA over 4 years as the outcome, the same 3,495 participants were included, contributing one observation each. Crepitus frequency prevalence for the responses none, rarely, sometimes, often, and always was 2,195 (62.8%), 391 (11.2%), 561 (16.1%), 229 (6.6%), 119 (3.4%), respectively. In these analyses, we found a similar overall result where adjusted odds ratios for incident SOA were greater in those with greater crepitus frequency (Table 3). In the post-hoc analyses evaluating the subgroups that developed incident SOA (Table 4), again those with pre-existing ROA who did not have frequent knee symptoms, representing around one third of the overall sample, contributed most of the incident SOA cases (488/636 or 76.7% of cases). In the group that had pre-existing frequent knee symptoms but did not have ROA, representing the smallest subgroup, greater crepitus frequency was not predictive of SOA over 4 years, similar to the one year follow up analyses. The group that did not have pre-existing frequent knee symptoms and did not have ROA represented the largest proportion of observations 54.5% (6,127/11,237) (Table 4) had the lowest proportion of incident SOA, 4.6% (81/1750) (Table 4). In this group, crepitus was not associated with incident SOA in this group over one year, but it was in the 4-year analyses (p for trend = 0.03) (Table 4).

We found significant interactions between crepitus and sex as well as crepitus and age in the overall group and in the group of participants without ROA but without frequent knee symptoms at baseline (Table 5). Subgroup analyses of men v. women showed that although the overall number of incident cases of SOA was lower in men than in women, the association between crepitus and incident SOA revealed larger odds ratios (Table 6). Similarly, although there were fewer incident SOA cases in older participants, crepitus frequency indicated a larger odds ratio for incident SOA than in younger participants (Table 6). These subgroup analyses comparing men v. women and older v. younger participants

findings were similar in the group of participants with ROA but without frequent knee symptoms (Supplemental Table 2).

DISCUSSION

Within the OAI, a US based multi-center cohort, we found that subjective crepitus was predictive of incident symptomatic tibiofemoral osteoarthritis. The majority of incident cases of SOA occurred in the subgroup of people who had prevalent ROA at baseline but no frequent knee symptoms (+ROA, −Sx) where crepitus was predictive of the development of frequent knee pain within a year and over 4 years of observation. For those who had neither frequent symptoms nor ROA, crepitus was predictive of development of radiographic evidence of tibiofemoral OA over a longer time frame but not over one year of follow up. These findings suggest that crepitus is indeed a useful symptom to predict the development of SOA over time. To our knowledge, ours is the first study evaluating the association of crepitus with incident symptomatic knee OA.

Existing literature on crepitus is limited to the assessment of the physical exam finding of crepitus as compared to in our study where we studied the subjective complaint of crepitus. Further, existing studies have focused on cross-sectional associations, evaluating the contemporaneous implications of crepitus, not longitudinal associations as we have evaluated in our study. Crepitus by compartment on exam is associated with contemporaneous presence of compartment-specific osteophytes (24–26), meaning crepitus palpated in the patellofemoral compartment was predictive of patellofemoral osteophytes and crepitus in the medial and lateral tibiofemoral compartments were predictive of medial and lateral tibiofemoral osteophytes respectively. The association between crepitus and articular cartilage damage is less clear – two studies suggest that there is an association (25, 26) while the other does not (24). In one study, patellofemoral crepitus was also associated with patellofemoral cysts and bone marrow lesions as seen on magnetic resonance images (26). An important limitation to our study is that patellofemoral OA was not systematically evaluated within the OAI. Thus, within the context of this study, performed within the OAI, we were unable to tease out the role of the patellofemoral compartment in the relationship between crepitus and incident SOA. The lack of inclusion of the patellofemoral compartment in our assessment of ROA may provide an explanation for why baseline crepitus was not associated with KL grade in the overall group or in any of the subgroups. This is in contrast to the study by Crema et al (24) where skyline radiographs were included in the assessment of KL grade, which was associated with physical exam detected crepitus, in a cohort screened to have early knee OA. Investigation of these questions in a different cohort that has assessments of crepitus in addition to readings for patellofemoral OA will provide additional important insights into the clinical importance of crepitus.

In our study, we also found that there was a significant interaction of crepitus with age and crepitus with sex in the development of incident SOA. Crepitus frequency resulted in larger odds ratios for incident SOA in men v. women and in older v. younger participants. These findings suggest that crepitus may be screening for different pathologies in these different subgroups that lead to incident SOA. Nevertheless, crepitus is predictive of incident SOA in all the subgroups, indicating that that crepitus is clinically relevant in all these groups.

The assessment of crepitus used in our study was based on a question from the KOOS questionnaire. This simple assessment only depends on the patient self-reflecting the frequency that crepitus is present, eliminating the need to train staff who can perform an exam to assess crepitus. Although the KOOS question that assesses crepitus does not allow for attribution of the compartment from which crepitus emanates, we have found that it is predictive of the development of symptomatic tibiofemoral OA. Interestingly, we found crepitus to be associated with WOMAC pain among all groups, including the overall group and all subgroups, which might mean that crepitus is a manifestation of knee symptoms. Notably the correlations though significant were on the order of 0.2 – 0.3, not close to one, suggesting that crepitus and pain do represent different constructs. Perhaps selecting those with more crepitus from those with or without frequent knee pain is a way of selecting those with more knee symptoms.

An interesting finding in our study relates to the distribution of new cases of SOA among those without SOA at baseline. More than 75% of the incident SOA cases originated from those that had ROA but no frequent knee symptoms, despite this group constituting less than a third of the total number of participants at risk for SOA. The group with frequent knee symptoms but no ROA had a far fewer incident SOA cases, and did not show an association between crepitus frequency and incident SOA, even when evaluated over the longer 4 year follow up. The group with no pre-existing ROA or frequent knee symptoms did not show an association between crepitus and SOA over one year of follow-up, but did when evaluating longer follow-up. Because both symptoms and ROA would have been required to achieve an outcome of SOA in this group, there may not have been sufficient time to allow for both to occur over one year.

The biologic implications of the findings of our study in the context of existing literature are substantially assisted by the post-hoc analyses findings. The finding that crepitus is predictive of the development of frequent knee pain in as little time as one year among those who have ROA but no frequent knee pain suggests that crepitus is not just selecting out those who have an osteophyte, as all those with ROA by definition have an osteophyte on radiograph. There is some other risk factor that is being identified by the complaint of crepitus that predisposes to progression of symptoms. Further study of crepitus in the group with ROA but no frequent symptoms may help to clarify sources of pain in knee OA. The finding that crepitus is predictive of the development of tibiofemoral knee OA among those without ROA or frequent knee pain only after 4 years of observation, not with just one year of observation, suggests that perhaps in this group of people, crepitus is preferentially selecting out those who have patellofemoral osteophytes which cannot be evaluated on PA films of the knee, and those who have patellofemoral OA are more likely to develop tibiofemoral OA over a longer period of observation. This would be an interesting hypothesis to test in another cohort where patellofemoral OA status is available. Additionally, as magnetic resonance imaging is more sensitive than radiographs, a longitudinal study focusing on the magnetic resonance imaging findings in this group of participants who have crepitus as a predictor of incident SOA may be informative in identifying early imaging markers of OA.

In summary, subjective crepitus is a simple and effective assessment that is predictive of longitudinal development of SOA. It may offer utility for identification of at-risk individuals, predictive modeling, and future clinical and epidemiologic research. Future research should consider performing subgroup analyses based on ROA and Sx status to potentially assist with increasing our understanding of the biologic implications of primary analyses. In the right setting, selection of individuals with prevalent ROA but without frequent knee symptoms may strengthen the statistical power for studies evaluating incident SOA as an outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Significance & Innovations

- This is the first study to find an association between self-reported crepitus and incident symptomatic knee osteoarthritis.
- Among those who developed SOA, more than 75% had prevalent ROA but no frequent knee pain at baseline. Selecting individuals with ROA but without frequent knee symptoms may increase power in studies evaluating incident SOA.
- Subjective knee crepitus can be used clinically to identify individuals at risk for SOA, potentially assisting with earlier diagnosis and ultimately intervention.

Table 1

Overall association of crepitus with incident tibiofemoral SOA 1 year after crepitus assessment

		Incident SOA	Unadjusted Odds Ratio for Incident SOA	Adjusted Odds Ratio for Incident SOA*
All those without SOA at baseline	11237 observations from 3495 people	Total cases = 636		
Crepitus Frequency	Never	332/7313 (4.5%)	Ref	Ref
	Rarely	79/1213 (6.5%)	1.5 (1.1 – 1.9)	1.5 (1.2 – 2.0)
	Sometimes	130/1701 (7.6%)	1.7 (1.4 – 2.1)	1.8 (1.4 – 2.2)
	Often	52/626 (8.3%)	1.9 (1.4 – 2.6)	2.2 (1.6 – 3.0)
	Always	43/384 (11.2%)	2.6 (1.9 – 3.7)	3.0 (2.1 – 4.3)
			p for trend < 0.0001	*p for trend < 0.0001*

*adjusted for age, sex, and BMI.

Table 2

Subgroup associations of crepitus with incident tibiofemoral SOA 1 year after crepitus assessment

		Incident SOA	Unadjusted Odds Ratio for Incident SOA	Adjusted Odds Ratio for Incident SOA*
People with ROA but without symptoms at baseline.	2973 observations from 1085 people	Total cases = 488		
(+ROA, −Sx)				
	Never	251/1952 (12.9%)	Ref	Ref
	Rarely	63/327 (19.3%)	1.6 (1.2 – 2.2)	1.6 (1.2 – 2.1)
	Sometimes	98/428 (22.9%)	2.0 (1.5 – 2.6)	1.9 (1.4 – 2.5)
	Often	43/153 (28.1%)	2.6 (1.8 – 3.8)	2.5 (1.7 – 3.6)
	Always	33/113 (29.2%)	2.8 (1.8 – 4.2)	2.8 (1.8 – 4.4)
			p for trend < 0.0001	*p for trend < 0.0001*
People without ROA but with symptoms at baseline.	2137 observations from 660 people	Total Cases = 67		
(−ROA, +Sx)				
	Never	30/1049 (2.9%)	Ref	Ref
	Rarely	6/239 (2.5%)	0.9 (0.4 – 2.1)	1.0 (0.4 – 2.4)
	Sometimes	15/485 (3.1%)	1.1 (0.6 – 2.0)	1.0 (0.5 – 2.1)
	Often	7/210 (3.3%)	1.2 (0.5 – 2.7)	1.2 (0.5 – 2.9)
	Always	9/154 (5.8%)	2.1 (1.0 – 4.6)	1.8 (0.8 – 4.2)
			p for trend = 0.2	*p for trend = 0.3*
People without ROA and symptoms at baseline.	6127 observations from 1750 people	Total Cases = 81		
(−ROA, −Sx)				
	Never	51/4312 (1.2%)	Ref	Ref
	Rarely	10/647 (1.5%)	1.3 (0.7 – 2.6)	1.4 (0.7 – 2.7)
	Sometimes	17/788 (2.2%)	1.8 (1.1 – 3.2)	1.8 (1.0 – 3.3)
	Often	2/263 (0.8%)	0.6 (0.2 – 2.6)	0.8 (0.2 – 3.2)
	Always	1/117 (0.9%)	0.7 (0.1 – 5.3)	0.8 (0.1 – 6.2)
			p for trend = 0.3	*p for trend = 0.3*

*adjusted for age, sex, and BMI.

Table 3

Overall association of crepitus with incident tibiofemoral SOA over 4 years

		Incident SOA	Unadjusted Odds Ratio for Incident SOA	Adjusted Odds Ratio for Incident SOA*
All those without SOA at baseline	3495 people	Total cases = 636		
Crepitus Frequency	Never	338/2195 (15.4%)	Ref	Ref
	Rarely	81/391 (20.7%)	1.4 (1.1–1.9)	1.5 (1.1–2.0)
	Sometimes	114/561 (20.3%)	1.4 (1.1–1.8)	1.5 (1.2–1.9)
	Often	61/229 (26.6%)	2.0 (1.5–2.7)	2.2 (1.6–3.0)
	Always	42/119 (35.3%)	3.0 (2.0–4.4)	3.8 (2.5–5.7)
			p for trend < 0.0001	*p for trend < 0.0001*

*adjusted for age, sex, and BMI.

Table 4

Subgroup associations of crepitus with incident tibiofemoral SOA over 4 years

		Incident SOA	Unadjusted Odds Ratio for Incident SOA	Adjusted Odds Ratio for Incident SOA*
People with ROA but without symptoms at baseline.	1085 people	Total cases = 488		
(+ROA, −Sx)				
	Never	261/669 (39.0%)	Ref	Ref
	Rarely	63/127 (49.6%)	1.5 (1.1–2.3)	1.5 (1.0–2.3)
	Sometimes	84/171 (49.1%)	1.5 (1.1–2.1)	1.5 (1.0–2.1)
	Often	48/77 (62.3%)	2.6 (1.6–4.2)	2.4 (1.5–3.9)
	Always	32/41 (78.0%)	5.6 (2.6–11.8)	5.5 (2.5–11.8)
			p for trend < 0.0001	*p for trend < 0.0001*
People without ROA but with symptoms at baseline.	660 people	Total Cases = 67		
(ROA, +Sx)				
	Never	29/298 (9.7%)	Ref	Ref
	Rarely	7/67 (10.5%)	1.1 (0.5–2.6)	1.2 (0.5–2.8)
	Sometimes	15/169 (8.9%)	0.9 (0.5–1.7)	0.9 (0.5–1.8)
	Often	7/72 (9.7%)	1.0 (0.4–2.4)	1.1 (0.4–2.7)
	Always	9/54 (16.7%)	1.9 (0.8–4.2)	2.0 (0.8–4.8)
			p for trend = 0.4	*p for trend = 0.4*
People without ROA and symptoms at baseline.	1750 people	Total Cases = 81		
(−ROA, −Sx)				
	Never	48/1228 (3.9%)	Ref	Ref
	Rarely	11/197 (5.6%)	1.5 (0.7–2.9)	1.5 (0.8–3.0)
	Sometimes	15/221 (6.8%)	1.8 (1.0–3.3)	1.9 (1.0–3.4)
	Often	6/80 (7.5%)	2.0 (0.8–4.8)	2.2 (0.9–5.4)
	Always	1/24 (4.2%)	1.1 (0.1–8.1)	1.1 (0.1–8.7)
			p for trend=0.04	*p for trend =0.03*

*adjusted for age, sex, and BMI.

Table 5

Overall association of crepitus with incident tibiofemoral SOA over 4 years

All those without SOA at baseline	**3495 people**	**Total cases = 636**
Crepitus Frequency	Interactions	p-values
	Age	0.02
	Sex	0.009
	BMI	0.3
People with ROA but without symptoms at baseline.	1085 people	Total cases = 488
(+ROA, −Sx)	Interactions	p-values
	Age	0.008
	Sex	0.004
	BMI	0.7
People without ROA but with symptoms at baseline.	660 people	Total cases = 67
(−ROA, +Sx)	Interactions	p-values
	Age	0.3
	Sex	0.6
	BMI	0.3
People without ROA and symptoms at baseline.	1750 people	Total cases = 81
(−ROA, −Sx)	Interactions	p-values
	Age	0.8
	Sex	0.5
	BMI	0.7

*adjusted for age, sex, and BMI.

Table 6

Association of crepitus with incident tibiofemoral SOA over 4 years in subgroups of men, women, younger, and older participants.

		Incident SOA	Unadjusted Odds Ratio for Incident SOA	Adjusted Odds Ratio for Incident SOA
Men without SOA at baseline	1476 people	Total cases = 226		
Crepitus Frequency	Never	115/990 (11.6%)	Ref	Ref
	Rarely	34/161 (21.1%)	2.0 (1.3–3.1)	2.1 * (1.4–3.3)
	Sometimes	47/220 (21.4%)	2.1 (1.4–3.0)	2.3 * (1.6–3.4)
	Often	18/75 (24.0%)	2.4 (1.4–4.2)	2.7 * (1.5–4.8)
	Always	12/30 (40.0%)	5.1 (2.4–10.8)	6.8 * (3.1–14.7)
			p for trend < 0.0001	*p for trend < 0.0001*
Women without SOA at baseline	2019 people	Total cases = 410		
Crepitus Frequency	Never	223/1205 (18.5%)	Ref	Ref
	Rarely	47/230 (20.4%)	1.1 (0.8–1.6)	1.2 * (0.8–1.7)
	Sometimes	67/341 (19.7%)	1.1 (0.8–1.5)	1.2 * (0.8–1.6)
	Often	43/154 (27.9%)	1.7 (1.1–2.5)	1.9 * (1.3–2.9)
	Always	30/89 (33.7%)	2.2 (1.4–3.6)	3.0 * (1.8–4.9)
			p for trend = 0.0003	*p for trend < 0.0001*
Younger people (age<65) without SOA at baseline	2175 people	Total cases = 369		
Crepitus Frequency	Never	179/1236 (14.4%)	Ref	Ref
	Rarely	41/245 (16.7%)	1.2 (0.8–1.7)	1.1 ** (0.8–1.7)
	Sometimes	70/407 (17.2%)	1.2 (0.9–1.7)	1.2 ** (0.9–1.6)
	Often	45/186 (24.2%)	1.9 (1.3–2.7)	1.7 ** (1.2–2.5)
	Always	34/101 (33.7%)	3.0 (1.9–4.7)	3.1 ** (2.0–4.9)
			p for trend < 0.0001	*p for trend < 0.0001*
Older people (age≥65) without SOA at baseline	1320 people	Total cases = 267		
Crepitus Frequency	Never	159/959 (16.5%)	Ref	Ref
	Rarely	40/146 (27.4%)	1.9 (1.3–2.8)	2.0 ** (1.3–3.0)
	Sometimes	44/154 (28.6%)	2.0 (1.4–2.9)	1.9 ** (1.3–2.9)
	Often	16/43 (37.2%)	3.0 (1.6–5.7)	3.0 ** (1.5–5.8)
	Always	8/18 (44.4%)	4.0 (1.6–10.4)	3.9 ** (1.5–10.4)
			p for trend < 0.0001	*p for trend < 0.0001*

* adjusted for age and BMI

** adjusted for sex and BMI