The Prevalence, Incidence, and Progression of Hand Osteoarthritis in Relation to Body Mass Index, Smoking, and Alcohol Consumption

Ida K. Haugen, Karin Magnusson, Aleksandra Turkiewicz, and Martin Englund

ABSTRACT. ***Objective.*** To estimate the extent that overweight/obesity, smoking, and alcohol are associated with prevalence and longitudinal changes of radiographic hand osteoarthritis (OA).

Methods. Participants from the Osteoarthritis Initiative (n = 1232) were included, of whom 994 had 4-year followup data. In analyses on incident hand OA, only persons without hand OA at baseline were included (n = 406). Our exposure variables were overweight/obesity [body mass index (BMI), waist circumference], smoking (current/former, smoking pack-yrs), and alcohol consumption (drinks/week). Using linear and logistic regression analyses, we analyzed possible associations between baseline exposure variables and radiographic hand OA severity, erosive hand OA, incidence of hand OA, and radiographic changes. Analyses were adjusted for age, sex, and education.

Results. Neither overweight nor obesity were associated with hand OA. Current smoking was associated with less hand OA in cross-sectional analyses, whereas longitudinal analyses suggested higher odds of incident hand OA in current smokers (OR 2.20, 95% CI 1.02–4.77). Moderate alcohol consumption was associated with higher Kellgren-Lawrence sum score at baseline (1–3 drinks: 1.55, 95% CI 0.43–2.67) and increasing sum score during 4-year followup (4–7 drinks: 0.33, 95% CI 0.01–0.64). Moderate alcohol consumption (1–7 drinks/week) was associated with 2-fold higher odds of erosive hand OA, which was statistically significant. Additional adjustment for BMI gave similar strengths of associations.

Conclusion. Overweight/obesity were not associated with hand OA. Contrasting results were observed for smoking and hand OA, suggesting lack of association. Moderate alcohol consumption was associated with hand OA severity, radiographic changes, and erosive hand OA, warranting further investigation. (J Rheumatol First Release July 15 2017; doi:10.3899/jrheum.170026)

Key Indexing Terms:
HAND OSTEOARTHRITIS OBESITY EPIDEMIOLOGY RISK FACTORS

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Hand osteoarthritis (OA) affects a large proportion of the general population[1], and may lead to severe pain and physical disability[2,3]. Since no disease-modifying drugs exist, it is important to focus our attention on modifiable risk factors to reduce the risk of developing hand OA.

Previous studies have indicated that obesity is a risk factor for hand OA[4,5,6], and perhaps erosive hand OA in particular[7]. Because the mechanical effects of obesity do not have the same effect on the loading of finger joints, the associations may be related to systemic effects of obesity[8,9,10]. However, most previous studies are cross-sectional[4,8,9], leading to uncertainty about causality. Longitudinal studies are needed to analyze the association between obesity and hand OA. Using longitudinal data from a large database from the region of Catalonia in Spain, Reyes, *et al* recently reported that obesity was a risk factor for OA development in the hands, hips, and especially the knees[11]. Confirmation of obesity as a risk factor for hand OA is important because weight-reducing interventions could possibly reduce the risk of hand OA.

The association between smoking and OA is complex.

Smoking may increase the risk of OA through damage to cartilage and stimulate generalized inflammation. Nicotine may also inhibit the expression of cytokines and proteins, including collagen, bone morphogenetic protein, and growth factors[12,13]. On the other hand, clinical studies have suggested a decreased risk of OA in smokers, which may be related to lower weight and lower bone mineral density[14]. Inverse associations between smoking and OA have in particular been reported in hospital-based case-control studies[15]. Hence, the association may be due to selection bias, because smoking is a strong risk factor for several severe diseases requiring hospitalization (e.g., cancer, lung, and cardiovascular diseases)[16]. By focusing on hand OA, we will be able to study the direct effect of smoking that is not mediated through body weight. Few hand OA studies have been performed with contrasting results[17,18,19]. Because of the cross-sectional study design of previous studies, longitudinal studies are important to strengthen the evidence on the possible protective effect of smoking on hand OA development.

A study of mice suggested that chronic alcohol consumption induces OA-like pathological changes[20]. Previous studies have suggested that chronic excessive alcohol is associated with high-circulating levels of proinflammatory mediators[21], whereas moderate alcohol use may have antiinflammatory effects[22]. To our knowledge, few studies have analyzed the potential association between alcohol and OA in humans, suggesting no association with hip OA[23,24]. In the Norwegian cohort Musculoskeletal pain in Ullensaker STudy (MUST), drinkers demonstrated more finger joint inflammation than non-drinkers[25]. Because of convincing evidence that inflammation predicts future structural damage in OA[26,27,28], we anticipate a possible association between alcohol intake and the severity of radiographic OA.

Hence, the aims of our current study were to analyze whether overweight/obesity, smoking, and alcohol consumption were associated with hand OA in both cross-sectional and longitudinal analyses.

MATERIALS AND METHODS

Participants. The Osteoarthritis Initiative (OAI) is a multicenter prospective, observational cohort study in the United States, designed to identify biomarkers and risk factors for incident or progressive knee OA (www.oai.ucsf.edu). The study includes 4796 participants from ages 45–79 years and a diversity of ethnic backgrounds. At baseline, all participants have either established symptomatic knee OA ("Progression cohort"), have multiple risk factors for knee OA ("Incidence cohort"), or represent healthy reference subjects without typical OA risk factors ("Reference cohort"). General criteria for exclusion were systemic inflammatory arthritic diseases, bilateral endstage knee OA, inability to walk without aids, or magnetic resonance imaging (MRI) contraindications.

In our current study, originally designed to study early stage knee OA development, we included 1232 participants without any radiographic knee OA [i.e., bilateral Kellgren-Lawrence arthritis grading scale (KL) = 0] at baseline and available hand radiographs. Additional inclusion criteria for the early knee OA study were knee MRI available at 4 specified timepoints, although data from the knee MRI were not included in the current analyses on hand OA.

The institutional review boards (IRB) at each of the study sites [University of Pittsburgh IRB (IRB020552), Memorial Hospital of Rhode Island IRB (IRB00000171), University of Maryland Baltimore IRB (IRB00000233), Ohio State University Biomedical Sciences IRB (IRB00000294)] approved the study, and all participants gave informed consent.

Hand radiographs. The OAI participants underwent radiography of the dominant hand (frontal images of either unilateral hand only or bilateral hands also including the non-dominant hand) at baseline and 4-year followup. One medical doctor (IKH), who is a trained assessor of hand radiographs with 9 years of experience, scored the second to fifth distal interphalangeal (DIP), second to fifth proximal interphalangeal (PIP), thumb interphalangeal, first to fifth metacarpophalangeal (MCP), and first carpometacarpal (CMC) joints for the severity of OA according to a modified KL scale (0 = no OA, 1 = doubtful OA, 2 = mild OA, 3 = moderate OA, 4 = severe OA)[1,29]. The modification of the original scoring system refers to the scoring of clear joint space narrowing as present OA also in the absence of osteophytes. The absence/presence of central erosions was scored according to the Osteoarthritis Research Society International atlas[30].

The longitudinal radiographs were read in pairs with known time sequence to increase the likelihood of detecting clinically relevant changes without overestimation of nonrelevant differences[31]. We allowed 0.5 increments in case of progression, but not enough to be scored with a higher category, to increase the sensitivity to change.

After several weeks, the same investigator re-scored 25 hands from 25 randomly selected persons to assess intrareader reliability. The ICC (single measure 2-way mixed model, absolute agreement) was 0.82 (95% CI 0.53–0.93) for KL sum score. ICC values 0.80–1.00 are considered as very good reliability (i.e., same cutoffs as recommended for κ)[32].

Overweight and obesity. The standing heights in millimeters (mm) and the weights in kilograms (kg) were measured without shoes and in lightweight clothing. The body mass index (BMI) was categorized into normal weight ($\leq$ 25.0 kg/m^2), overweight (25.1–29.9 kg/m^2) and obese ($\geq$ 30.0 kg/m^2). Underweight was present in only 9 persons, who were therefore included in the normal weight category. Self-reported BMI at age 25 years was similarly categorized into normal weight ($\leq$ 25.0 kg/m^2) and overweight (> 25.0 kg/m^2) because there were few persons with obesity. To identify the BMI load over time, we defined and calculated a cumulative BMI score as the area under the curve based on maximum 4 weight measurements at the following: age of 25 years, age when having lowest weight, age when having the highest weight, and current age. Because of the discrepancy between the self-reported height at age 25 years and the current measured height (5% reported a loss of $\geq$ 5 cm and 5% reported increased height of $\geq$ 3 cm as compared to age 25 yrs), we used the current height in the calculation of BMI at all 4 timepoints. The area was standardized by the current age minus 25, representing the earliest age of weight assessment. The abdominal (but not hip) circumference was measured in centimeters with 1 decimal.

Smoking. Participants were divided into 3 groups based on self-reported smoking status. Never smokers had smoked < 100 cigarettes in their entire life and never regular pipe, cigars, or cigarillos. Persons who had smoked > 100 cigarettes or reported regular pipe, cigar, or cigarillo smoking were divided into former or current smokers based on current smoking status.

The number of pack-years was calculated in cigarette smokers as the number of cigarettes per day divided by 20 and multiplied with the number of years of smoking (e.g., 10 cigarettes per day for 10 yrs = 5 pack-yrs). Never smokers were treated as having 0 pack-years. Pack-years of cigarettes were categorized into 0, 1–11, and 12 or more, with 12 being the 75% percentile.

Alcohol. The number of alcoholic drinks in a typical week the past 12 months was self-reported (0, < 1, 1–3, 4–7, 8–14, 15–21, 22–27, or $\geq$ 28 drinks/week). The latter 4 categories were merged into 1 category because of few observations.

Outcomes. The outcomes in the cross-sectional analyses were the KL sum

score and erosive hand OA [≥ 1 joint(s) with radiographic central erosions] in the second to fifth DIP and PIP joints in each hand. We excluded CMC-1 and MCP joints because they may be more strongly related to biomechanical stress[33,34].

In the longitudinal analyses, the main outcome was incident hand OA, defined as having ≥ 1 DIP or PIP joint(s) with KL grade ≥ 2 at followup. We included persons free of radiographic hand OA (KL grade ≤ 1) at baseline. In case of bilateral hand radiographs, we excluded both hands from the analyses if DIP or PIP OA was present in at least 1 hand. We repeated the analyses focusing on radiographic changes, including all participants with longitudinal data. The change of KL sum score in the second to fifth DIP and PIP joints was used as the outcome. Additionally, we performed analyses using incident erosive hand OA as the outcome in patients who had nonerosive disease at baseline. In case of bilateral hand radiographs, we excluded both hands from the analyses if erosions were present in at least 1 hand.

Statistical analyses. We performed linear regression analyses to assess the cross-sectional and longitudinal associations between the risk factors and KL sum score using Generalized Estimating Equations (GEE) to account for the dependency between hands within 1 person (in case of bilateral hand radiographs). We used robust standard errors because of mild heteroscedasticity of residuals. Where the GEE model did not converge (relevant for crude cross-sectional analyses only), we used linear regression with standard errors adjusted for clustering. To analyze the associations with presence/incidence of erosive hand OA and incidence of hand OA, we performed logistic regression analyses using GEE.

The analyses were adjusted for age, sex, and level of education. We repeated analyses with additional adjustment for current BMI.

We presented the results as effect estimates with 95% CI. Analyses were performed using Stata, version 13 (Stata Statistical Software: Release 13, StataCorp).

RESULTS

Sampling and baseline characteristics. In the cross-sectional analyses, we included 1232 participants with hand radiographs (n = 366 bilateral, 866 unilateral) at baseline (Table

Table 1. Baseline characteristics of the participants included in our cross-sectional analyses (n = 1232)* and longitudinal analyses on radiographic changes (n = 994)**, and incident OA (n = 406)***.

Characteristics	Cross-sectional	Longitudinal	Incident OA
Age, yrs, mean (SD)	58.4 (8.9)	58.4 (9.0)	54.7 (7.2)
Female, n (%)	718 (58)	572 (57.6)	233 (57.4)
BMI, kg/m^2, mean (SD)	26.8 (4.5)	26.8 (4.4)	26.8 (4.6)
BMI at age 25, kg/m^2, mean (SD)	22.5 (2.9)	22.6 (2.9)	22.5 (2.9)
Abdominal circumference, cm, mean (SD)	98.3 (12.8)	98.3 (12.7)	97.7 (13.0)
Above weight cutoff at IEI, n (%)[#]	264 (21.4)	216 (21.7)	94 (23.2)
Frequent pain at least 1 knee at IEI, n (%)[#]	477 (38.7)	365 (36.7)	176 (43.4)
Medication for knee symptoms previous 12 mos, n (%)[#]	528 (42.9)	402 (40.4)	178 (43.8)
Family history of knee replacement surgery, n (%)[#]	188 (15.3)	157 (15.8)	66 (16.3)
Knee injury or surgery, n (%)[#]	440 (35.7)	345 (34.7)	140 (34.5)
Engaged in at least 1 knee-bending activity, n (%)[#]	877 (71.2)	704 (70.8)	276 (68.0)
Education, n (%)			
Less than high school graduate	31 (2.5)	14 (1.4)	6 (1.5)
High school graduate	122 (9.9)	98 (9.9)	26 (6.4)
Some college	265 (21.5)	210 (21.1)	88 (21.7)
College graduate	263 (21.3)	216 (21.7)	91 (22.4)
Some graduate school	107 (8.7)	89 (9.0)	38 (9.4)
Graduate degree	436 (35.4)	363 (36.5)	154 (37.9)
Missing	8 (0.7)	4 (0.4)	3 (0.7)
Regular smokers of cigarettes, pipes, cigars, and/or cigarillos, n (%)			
Never	618 (50.2)	509 (51.2)	217 (53.5)
Former	500 (40.6)	411 (41.4)	147 (36.2)
Current	106 (8.6)	70 (7.0)	39 (9.6)
Missing	8 (0.7)	4 (0.4)	3 (0.7)
In cigarette smokers, pack-yrs, mean (SD)	20.0 (18.6)	19.3 (18.2)	17.8 (15.2)
Alcoholic drinks in typical week past 12 mos, n (%)			
0	208 (16.9)	161 (16.2)	86 (21.2)
< 1	451 (36.6)	367 (36.9)	138 (34.0)
1–3	201 (16.3)	167 (16.8)	56 (13.8)
4–7	191 (15.5)	154 (15.5)	72 (17.7)
≥ 8	173 (14.0)	141 (14.2)	51(12.6)
Missing	8 (0.65)	4 (0.4)	3 (0.7)
Hands with radiographic finger OA, ≥ 1 DIP/PIP joint with KL ≥ 2, n (%)	904/1598 (56.6)	733/1282 (57.2)	NA
KL sum score in the DIP and PIP joints for each hand, median (IQR)	4 (1–9)	4 (1–9)	NA
Hands with erosive hand OA, ≥ 1 DIP/PIP joint with erosions, n (%)	163/1598 (10.3)	136/1282 (10.7)	NA

*n = 1232 persons (n = 1598 hands) included in cross-sectional analyses. **n = 994 persons (n = 1282 hands) included in analyses on progression. ***n = 406 persons (n = 502 hands) included in analyses on incident OA. [#]Used for study eligibility. OA: osteoarthritis; BMI: body mass index; IEI: initial eligibility interview; DIP: distal interphalangeal; PIP: proximal interphalangeal; KL: Kellgren-Lawrence arthritis grading scale; IQR: interquartile range; NA: not applicable because no OA at baseline.

1). Longitudinal radiographs (n = 288 bilateral, n = 706 unilateral) were available for 994 persons. In analyses on incident OA, we included 406 persons with no DIP or PIP OA at baseline (n = 96 bilateral, n = 310 unilateral longitudinal radiographs; Table 1).

Most participants (n = 1064) belonged to the "Incidence cohort," whereas 69 and 99 were from the "Progression cohort" and the "Reference cohort," respectively. There were high frequencies of risk factors for knee OA assessed at the initial eligibility interview (Table 1).

Radiographic changes during followup. After 4 years, 82/502 hands (16.3%) in 77/407 persons (19.0%) had developed at least 1 DIP or PIP joint(s) with incident radiographic OA. During the 4-year followup, radiographic changes in the DIP and PIP joints occurred in 721/1282 hands (56.2%) in 590/994 persons (59.4%). However, for most participants the changes were small with a median (interquartile range) change of the KL sum score for the DIP and PIP joints in each hand of 1 (0–2). At baseline, 136/1598 hands (8.5%) in 133/1232 persons (10.8%) had erosive hand OA. During followup, only 30/1127 hands (2.7%) in 28/844 persons (3.2%) developed incident erosive disease.

Associations between obesity and hand OA. Measures of obesity were not statistically significantly associated with OA in the DIP and PIP joints in either cross-sectional (Table 2) or longitudinal analyses (Table 3), and the estimated effect sizes were small, indicating no clinically relevant effect. Persons with overweight or obesity did not demonstrate higher odds of having erosive disease as compared with persons with normal weight (Table 2).

Associations between smoking and hand OA. Contrasting results were found for the associations between smoking and hand OA. Persons with a long history of smoking (≥ 12 pack-yrs) had lower KL sum score than non-smokers, but the uncertainty of the estimate was large (Table 2). In contrast, there was a tendency that smokers had increased odds of developing DIP or PIP OA, whereas no statistically significant association was found between smoking and changes in KL sum score (Table 3). Using erosive hand OA as the outcome, no statistically significant associations were found (Table 2).

Associations between alcohol consumption and hand OA. In cross-sectional analyses, moderate alcohol consumption was associated with more severe OA in the DIP and PIP joints. A statistically significant association was found for 1–3 alcoholic drinks per week, whereas the strength of associations was weaker and not statistically significant for lower and higher alcohol intake (Table 2). Similarly, statistically significant associations with presence of erosive hand OA were found for 1–3 and 4–7 drinks/week (Table 2).

In our longitudinal analyses, no statistically significant association was found for incident hand OA, whereas 4–7

Table 2. Baseline associations between overweight/obesity, smoking, and alcohol and the severity hand OA (KL sum score in DIP/PIP in each hand) and the presence of erosive hand OA.

Variables	KL Sum Score (95% CI)		Presence of Erosive Hand OA, OR (95% CI)	
	Crude Analyses	Adjusted Analyses*	Crude Analyses	Adjusted Analyses*
Current BMI, kg/m^2				
≤ 25.0	0.00 (Ref.)	0.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
25.1–29.9	0.63 (–0.25 to 1.51)	0.55 (–0.20 to 1.29)	0.86 (0.58–1.28)	0.95 (0.62–1.45)
≥ 30.0	–0.36 (–1.32 to 0.61)	0.58 (–0.30 to 1.46)	**0.42 (0.24–0.75)**	0.64 (0.35–1.17)
BMI at age 25 yrs, kg/m^2				
≤ 25.0	0.00 (Ref.)	0.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
> 25.0	–0.18 (–1.12 to 0.77)	0.63 (–0.27 to 1.52)	**0.57 (0.33–0.99)**	0.91 (0.50–1.68)
Cumulative BMI, per 5-unit increase	–0.10 (–0.61 to 0.41)	0.39 (–0.08 to 0.86)	**0.73 (0.56–0.95)**	0.91 (0.67–1.24)
Waist circumference, per 10-cm increase	0.21 (–0.07 to 0.48)	0.15 (–0.12 to 0.43)	0.94 (0.81–1.09)	0.92 (0.78–1.09)
Alcoholic drinks/week				
0	0.00 (Ref.)	0.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
< 1	0.69 (–0.32 to 1.70)	0.66 (0.29–1.61)	1.06 (0.59–1.91)	1.14 (0.61–2.10)
1–3	1.23 (–0.05 to 2.50)	**1.55 (0.43–2.67)**	1.55 (0.82–2.94)	**2.15 (1.09–4.24)**
4–7	**1.56 (0.11–3.00)**	1.07 (–0.07 to 2.20)	**1.95 (1.05–3.63)**	**2.24 (1.16–4.35)**
≥ 8	**1.40 (0.12–2.68)**	1.03 (–0.14 to 2.21)	1.03 (0.51–2.11)	1.20 (0.56–2.55)
Smoking pack-yrs				
0	0.00 (Ref.)	0.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
1–11	0.50 (–0.61 to 1.62)	0.06 (–0.84 to 0.96)	1.05 (0.64–1.73)	0.99 (0.59–1.69)
≥ 12	0.27 (–0.64 to 1.18)	–0.55 (–1.37 to 0.26)	1.05 (0.68–1.62)	0.83 (0.52–1.32)
Smoking				
Never	0.00 (Ref.)	0.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Former	0.58 (–0.25 to 1.40)	–0.31 (–1.00 to 0.39)	1.03 (0.71–1.50)	0.85 (0.57–1.27)
Current	**–1.46 (–2.52 to –0.40)**	–0.69 (–1.91 to 0.53)	**0.37 (0.14–0.97)**	0.54 (0.20–1.48)

*Adjusted for age, sex, and education (analysis of erosions adjusted for age and sex only owing to sparse data). Significant data are in bold face ($p < 0.05$). OA: osteoarthritis; KL: Kellgren-Lawrence arthritis grading scale; DIP: distal interphalangeal; PIP: proximal interphalangeal; BMI: body mass index.

Table 3. Associations between obesity, smoking, and alcohol and development and progression of OA in the DIP/PIP joints.

Variables	Hands, n (%)	Incident OA		OA Progression, Change in KL Sum Score (95% CI)	
		Crude Analyses, OR (95% CI)	Adjusted Analyses*, OR (95% CI)	Crude Analyses	Adjusted Analyses*
Current BMI, kg/m^2					
≤ 25.0	29 (15)	1.00 (Ref.)	1.0 (Ref.)	0.0 (Ref.)	0.0 (Ref.)
25.1–29.9	36 (18)	1.32 (0.76–2.30)	1.34 (0.76–2.35)	–0.06 (–0.27 to 0.14)	1.0 (–0.20 to 0.21)
≥ 30.0	17 (14)	1.01 (0.52–1.97)	1.05 (0.53–2.08)	**–0.30 (–0.53 to –0.07)**	–0.14 (–0.37 to 0.09)
BMI at age 25 yrs, kg/m^2					
≤ 25.0	64 (15)	1.00 (Ref.)	1.00 (Ref.)	0.00 (Ref.)	0.00 (Ref.)
> 25.0	18 (18)	1.23 (0.68–2.24)	1.29 (0.67–2.47)	–0.14 (–0.33 to 0.05)	0.08 (–0.11 to 0.28)
Cumulative BMI, per 5-unit increase	NA	1.00 (0.94–1.06)	1.01 (0.94–1.07)	**–0.15 (–0.26 to –0.04)**	–0.04 (–0.15 to 0.08)
Waist circumference, per 10-cm increase	NA	0.98 (0.81–1.19)	0.97 (0.79–1.18)	–0.07 (–0.14 to 0.01)	–0.04 (–0.12 to 0.03)
Alcoholic drinks/week					
0	18 (16)	1.00 (Ref.)	1.00 (Ref.)	0.00 (Ref.)	0.00 (Ref.)
< 1	26 (15)	0.91 (0.46–1.78)	0.89 (0.45–1.76)	0.17 (–0.07 to 0.42)	0.14 (–0.09 to 0.38)
1–3	9 (13)	0.82 (0.34–1.99)	0.82 (0.33–2.03)	0.27 (–0.03 to 0.56)	0.28 (–0.01 to 0.57)
4–7	17 (19)	1.25 (0.59–2.65)	1.21 (0.57–2.59)	**0.34 (0.02–0.67)**	**0.33 (0.01–0.64)**
≥ 8	12 (20)	1.26 (0.55–2.90)	1.24 (0.53–2.89)	0.18 (–0.10 to 0.46)	0.23 (–0.05 to 0.50)
Smoking pack-yrs					
0	35 (13)	1.00 (Ref.)	1.00 (Ref.)	0.00 (Ref.)	0.00 (Ref.)
1–11	21 (24)	**2.11 (1.13–3.96)**	**2.19 (1.16–4.14)**	0.22 (–0.01 to 0.46)	0.17 (–0.07 to 0.41)
≥ 12	22 (18)	1.50 (0.82–2.73)	1.50 (0.80–2.80)	0.15 (–0.07 to 0.38)	0.12 (–0.10 to 0.35)
Smoking					
Never	35 (13)	1.00 (Ref.)	1.00 (Ref.)	0.00 (Ref.)	0.00 (Ref.)
Former	34 (18)	1.37 (0.81–2.33)	1.38 (0.80–2.37)	0.10 (–0.09 to 0.29)	0.07 (–0.12 to 0.26)
Current	13 (25)	2.07 (0.98–4.36)	**2.20 (1.02–4.77)**	–0.02 (–0.33 to 0.30)	0.14 (–0.18 to 0.46)

*Adjusted for age, sex, and education. Significant data are in bold face ($p < 0.05$). OA: osteoarthritis; DIP: distal interphalangeal; PIP: proximal interphalangeal; KL: Kellgren-Lawrence arthritis grading scale; BMI: body mass index; NA: not applicable.

drinks/week was associated with radiographic changes during the 4-year followup period (Table 3). There was a trend that a higher number of drinks/week was associated with higher odds of incident erosive disease, but no statistically significant associations were found (data not shown).

The strength of associations between alcohol and hand OA severity/progression seemed stronger in women than men, although no statistically significant interaction was found with sex (data not shown).

All results remained similar after additional adjustment for current BMI.

DISCUSSION

In our prospective cohort study of risk factors for radiographic hand OA, we found no association between overweight/obesity and hand OA in either cross-sectional or longitudinal analyses. Current smoking was associated with incident but not with prevalent hand OA, which suggests an arbitrary positive finding. Moderate alcohol consumption was associated with prevalent hand OA, increasing severity during followup, as well as erosive hand OA. However, the lack of robust or dose-dependent associations emphasize that future studies are needed to analyze this possible association.

Our findings regarding the lack of an association between overweight and hand OA are in line with previous Norwegian studies of obesity and hand OA[35,36]. We were not able to find any clinically relevant associations between overweight and hand OA (including the erosive hand OA phenotype) in either cross-sectional or longitudinal analyses, which contradicts a common belief that overweight is a risk factor for hand OA[4]. Previously observed associations in cross-sectional studies may be spurious, e.g., because of the strong association between knee OA and high BMI. For instance, our results contradict the positive association observed in the Catalan register study wherein associations between overweight and obesity and incident clinical diagnoses of OA in hands, knees, and hips were analyzed in primary care records[11]. Measurement of BMI is more likely to occur in persons with risk of weight-related diseases, such as knee OA. Overweight is a well-known risk factor for knee OA, and persons with a diagnosis of knee OA may be more likely to also have OA diagnosed in other joints when a joint examination is performed. Overweight is also a risk factor for other diseases, such as metabolic syndrome and cardiovascular disease, which may lead to more frequent visits at the doctor and a higher likelihood of having their OA diagnosed. Further, overweight/obese persons may experience more pain than lean persons, leading to more frequent joint examinations and diagnoses of OA. Different results across studies may also relate to different definitions of OA. Clinical OA definitions with inclusion of pain may be more likely to show associations to overweight and obesity than sole radiographic defini-

tions because of the known associations between obesity and pain[37,38]. In OAI, the participants underwent the same examinations regardless of the exposure status, which leads to lower risk of differential misclassification of the outcome. An oversampling of persons with risk factors for knee OA in OAI may have affected our results. However, the mean BMI in our study is lower than in many population-based studies such as the Framingham study[1], probably because of exclusion of persons with prevalent knee OA. We also covered a wide range of BMI from normal weight to obesity and retrospective BMI earlier in life. In our present report we have studied persons with knees with KL grade 0 only. We cannot exclude the possibility that this selection may induce a bias resembling collider stratification bias[39], but we find it unlikely that the selection has diminished an association between BMI and hand OA if such association truly existed.

To our knowledge, our present study represents the first longitudinal study focusing on smoking and hand OA. No consistent results were demonstrated. We found a nonsignificant trend toward less severe hand OA in smokers in the cross-sectional analyses, which is in line with previous studies on knee and hand OA[15,40]. A previous cross-sectional study focusing on hand OA found significantly fewer Heberden nodes, but not less radiographic disease, in smokers[19], whereas data from the MUST study has suggested an inverse association between smoking and the severity of radiographic hand OA[25]. However, the clinical value is doubtful with relatively small differences between never-smokers and persons with long history of smoking in our current study. Further, the inverse association was not confirmed in the longitudinal analyses, which indicates that a causal association is doubtful. No dose-response association was found with a statistically significant 2-fold increase for 1–11 smoking pack-years only, and a lower estimate for ≥ 12 smoking pack-years. Our contrasting results are in line with a recent OAI study on smoking and knee OA, demonstrating less severe knee OA in smokers as compared to never smokers in cross-sectional analyses, whereas longitudinal analyses demonstrated no robust associations[41].

In our current study, we observed an association between moderate alcohol consumption and the severity of radiographic hand OA, the odds of having erosive hand OA, and changes in KL sum score. However, the associations were weaker and not statistically significant for persons with higher alcohol use. These results contradict the hypothesis that moderate alcohol use is antiinflammatory, whereas chronic heavy consumption is proinflammatory[22]. We cannot exclude the possibility that persons underestimate the number of drinks per week, which may influence these possible dose-response associations. In recent analyses of the MUST study, a similar association was found between moderate frequency of alcohol intake and prevalent ultrasound-detected synovitis, but not prevalent radiographic OA[25]. The association with synovitis could not be analyzed in our present study because there was no examination of joint inflammation. However, synovitis is a risk factor for radiographic progression[26,27,28] and may occur in early disease[42]. Further, persons with erosive hand OA demonstrate more joint inflammation than persons with nonerosive disease[43]. Hence, the results from the 2 studies may conform. In longitudinal analyses, the change in KL sum score increased with increasing number of alcoholic drinks with statistically significant association for 4–7 drinks per week. No statistically significant association was found for incident disease (including incident erosive disease), which may be related to lack of power.

When it comes to overweight/obesity, smoking, and alcohol and their possible effect on hand OA development, it is challenging to draw conclusions. The risk factors may be interrelated in ways that are unique to different persons and, therefore, challenging to identify without having very large sample sizes. The exposures may also relate differently to different joint structures and to different steps in OA progression. Further, mediation by metabolic or hormonal factors is possible. The associations should be further studied between lifestyle risk factors, other OA features than those seen by radiographs, and pain.

Our hand OA definition was based on radiographic evidence of OA in the DIP and PIP joints. Isolated MCP OA (without DIP/PIP OA) was uncommon, and inclusion of MCP OA in our definition would not change the results. Including CMC OA in our definition of hand OA gave similar results (data not shown).

Weaknesses of our study were the reliance on self-reported data for smoking, alcohol consumption, and previous weight[44]. However, objective measurement of these exposures during many years is not feasible. We did not have data on the past intake of alcohol. Our study had a short followup time, which may not be sufficient for observing slow progressing hand OA. We had a limited number of persons without hand OA at baseline and incident hand OA at followup, and we may have had limited power to detect statistically significant associations. Finally, bias regarding selection of the study sample with oversampling of risk factors for knee OA may have affected our results. In our longitudinal analyses on changes in KL sum scores, we also included participants with prevalent hand OA, which may lead to collider stratification bias. This type of bias is frequently reflected in an estimate indicating lack of association. However, the strengths of our present study were a high number of participants and the ability to study incident hand OA in an ethnically diverse study sample. We also used several measures of current and previous anthropometric data as well as detailed smoking data.

We found that overweight/obesity was not associated with hand OA in either cross-sectional or longitudinal analyses. Our longitudinal analyses suggest no protective effect of smoking, and the reverse associations in cross-sectional

analyses are likely because of selection bias or lack of temporal assessment of exposures and outcomes. The observed association between moderate alcohol consumption and prevalent OA and radiographic changes during followup warrants further investigation, especially with focus on the erosive hand OA phenotype.

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