Research Article

Smoking and Heberden Nodes: Analysis of Data from the Osteoarthritis Initiative

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Purpose. Dental hygienists, dentists, and other workforce providers who depend upon their hands for employment are acutely aware of the need to protect their hands to ensure a successful career. Recent research has suggested that smoking may be protective of hand osteoarthritis. The purpose of this study is to determine the association between smoking and Heberden's nodes. **Methods.** Data from the Osteoarthritis Initiative were used in a cross-sectional, secondary data analysis of self-reported current smoking/never smoking and the presence/absence of Heberden's nodes, the hard enlargements of the joints nearest the fingertips (distal interphalangeal joints). Analyses included descriptive statistics, Chi-square associations with Heberden's nodes, and logistic regressions. **Results.** In adjusted analysis, smoking had an adjusted odds ratio for Heberden's nodes of 0.832 [95% confidence interval: 0.60, 1.14] which failed to reach significance ($P = .2488$). In the selected model, females were more likely than males to have Heberden's nodes; non-Hispanic Blacks were less likely than non-Hispanic Whites to have Heberden's nodes; and older age groups were more likely than the youngest age group to have Heberden's nodes. **Conclusion.** Smoking did not provide protection against Heberden's nodes in this study of US participants in the Osteoarthritis Initiative.

1. Introduction

Osteoarthritis is the most common form of arthritis involving entire joints (cartilage, joint lining, ligaments, and underlying bone) [1] and mainly affecting the axial skeleton and large appendicular joints [2]. Over 21% of US adults (an estimated 46.4 million) have osteoarthritis [3]. When considering lifetime risk of symptomatic osteoarthritis, researchers reported nearly 50% of adults will develop osteoarthritis by age of 85 years [4]. Many of the epidemiological researchers for osteoarthritis have considered various predictors and associated morbidities involved with osteoarthritis. It has been associated with body mass index [5], low Vitamin D [6, 7], and increased consumption of soft drinks in men [8] and in women with limited milk consumption [9], not breastfeeding [10], and giving birth [10]. Inconclusive and contradictory associations have been reported concerning associations of osteoarthritis and sex in which some researchers

found positive associations [7, 11, 12] while others did not [13] and with smoking in which some researchers found positive associations [14], others found protective associations [15, 16], and others did not find any association [13].

Hand osteoarthritis is highly prevalent, impacts function, and leads to considerable pain, stiffness, and disability [17, 18]. There are 26.2% of women and 13.4% of men aged 71 years and above who have hand osteoarthritis [19]. In an age-sex standardized analysis, researchers reported an incidence of hand osteoarthritis of 100/100,000 person-years (as compared with 88/100,000 person-years for the hip) [20]. Nevertheless, epidemiological studies of hand osteoarthritis are limited [18, 19]. Hands often develop hard tissue enlargements. If the enlargements involve the joints nearest the fingertips, which are the distal interphalangeal joints, the enlargements are termed Heberden's nodes. If the enlargements involve the 2nd joints from the fingertips, which are the proximal interphalangeal joints, the enlargements are termed Bouchard's nodes.

Hand osteoarthritis has been defined as the presence of (1) hand pain/aching/stiffness; (2) at least 2 bony nodes on the 2nd/3rd distal/proximal interphalangeal/first trapeziometacarpal (base of thumb) joints; (3) less than 3 swollen metacarpophalangeal joints; and (4) at least 2 Heberden's nodes, or deformity of at least 2 of the 2nd/3rd distal/proximal interphalangeal/first trapeziometacarpal joints [21]. The disease process for hand osteoarthritis is poorly understood, and it is yet to be determined if metabolic factors are involved [18]. Some researchers have indicated that the hard tissue enlargements on the distal interphalangeal joints, Heberden's nodes, may be genetic markers for general arthritis [22]. If this is the case, an environmental factor, such as smoking, may have an epigenetic role [23].

Smoking is a potentially modifiable risk factor for many conditions and diseases including lung cancer and other cancers, coronary heart disease and other heart diseases, cerebrovascular disease and other vascular diseases, diabetes mellitus, respiratory diseases (including chronic obstructive pulmonary disease), rheumatoid arthritis, sudden unexplained infant death, inflammation, adverse effects on the immune system, and bone health [24]. Smoking causes more than 480,000 deaths annually in the US [24]. In a report of the U.S. Department of Health and Human Services (2014) [24], the authors indicated that smoking harms nearly every organ in the body. There is a biological plausibility that smoking is associated with hand osteoarthritis and one feature in particular—Heberden's nodes. Previous researchers have reported conflicting results as to the association of smoking and osteoarthritis in general and smoking with Heberden's nodes [2]. The purpose of this study is to determine the association of smoking and Heberden's nodes.

2. Materials and Methods

2.1. Data Source. The data used in the preparation of this paper were obtained from the Osteoarthritis Initiative (OAI) database, which is available for public access at <http://www.oai.ucsf.edu/>. Specific datasets used were from the version 0.2.2 (2009) physical exam/measurements file: subject characteristics file; risk factors file; joint symptoms/function file; biomarkers file; and medical history file. The version V21 (2015) enrollee file was also used.

The researchers for the OAI conducted a longitudinal study at four clinical centers (Brown University School of Medicine/Memorial Hospital of Rhode Island in Pawtucket; The Ohio State University in Columbus; University of Pittsburgh in Pittsburgh; and University of Maryland/John Hopkins University in Baltimore) and one data collection center (University of California, San Francisco School of Medicine) in a design to develop public domain osteoarthritis research through the development and maintenance of an osteoarthritis natural history database containing biochemical, genetic, and imaging biomarkers for osteoarthritis [25]. Participant exclusion criteria included refusal to sign informed consent documents, self-reported prevalent rheumatoid arthritis, bilateral total knee replacement or expected bilateral knee replacement within 3 years, severe joint space narrowing in

both knees determined at baseline, pregnancy, the use of more than a single cane to aid in walking for more than 50% of the time, conditions which might cause an inability to participate in the entire length of the study, potential move from the clinic area within 3 years, enrollment as a participant in a double-blind randomized controlled study, inability to have a 3.0 Tesla MRI, or inability to provide a blood sample [25]. There were 4769 participants, aged 45–79 years, in the source data from which our sample was drawn. Additional documentation describing various aspects of the design and methods of the OAI is available at the OAI online website (<http://www.oai.ucsf.edu/>).

2.2. Participant Eligibility. Participants for this study were included if they (1) were current or never smokers; (2) provided a response to the question about any obvious hard bumps on the joints nearest to the fingertips; and (3) had complete data on the other variables of interest in the study (age, sex, race/ethnicity, alcohol use, educational level, comorbidities, height, weight, family history, physical summary score, and knee osteoarthritis). Participants were excluded if they were former smokers or if they did not provide a response concerning any obvious hard bumps on the joints nearest to the fingertips or had incomplete data on the other variables of interest in the study. From the 4769 participants in the OAI, there were 2723 participants who had data on all of the variables of interest and were therefore eligible for this study.

2.3. Key Dependent Variable. The presence or absence (yes, no) of Heberden's nodes was the key dependent variable. It was determined by the self-report of the participant of any obvious hard bumps on the joints nearest to the fingertips. This was a question asked during the initial eligibility interview.

2.4. Key Independent Variable. The key independent variable is smoking (current, never). Never smoking was determined by the self-report of the participant that he or she had never smoked 100 cigarettes (5 packs) in his or her life. A follow-up question of current smoking status identified current smokers. Former smokers were excluded from the study.

2.5. Other Variables. Also included in the analyses were sex (male, female); age (45 to less than 56 years, 56 to less than 66 years, and 66 years and above); race/ethnicity (non-Hispanic White, non-Hispanic Black, and Hispanic/other); education (high school graduate or less, more than high school graduate); body mass index (less than 25, 25 to less than 30, and 30 and above); Charlson index (0, 1, and above); and mother/father/sister/brother having had knee replacement (yes, no). The presence of knee osteoarthritis was determined by the right-side baseline radiographs scored on the composite quasi-Kellgren and Lawrence graded as (0) normal, (1) possible, (2) mild, (3) moderate, and (4) severe OA. Physical summary scores (categorized as quartiles) from the Medical Outcomes Study Short Form-12 version 2 physical summary scale were also included.

2.6. Statistical Analyses. The analyses for the study were conducted using SAS 9.2® software (SAS Institute, Chicago, IL). The data were analyzed for a description of the sample characteristics, bivariate analyses of the variables by Heberden's nodes, and logistic regression on Heberden's nodes. Unadjusted and adjusted logistic regressions were completed using the eligible participants as the domain in the analyses.

3. Results and Discussion

The sample consisted of 2723 participants. There were 59.7% (1625) females, 78.9% (2148) non-Hispanic Whites, 19.0% (516) non-Hispanic Blacks, and 2.2% (59) Hispanic/other. In terms of age groups, there were 38.5% (1047) participants aged 45 to less than 56 years; 30.4% (827) aged 56 to less than 66 years; and 31.2% aged 66 years and above. There were 26.0% with a body mass index below 25 (normal weight); 38.7% with a body mass index between 25 and less than 30 (overweight); and 35.3% with a body mass index of 30 or above (obese). Most participants (76.2%) had a Charlson index of 0 and an education above high school (84.1%) and did not have a mother/father/sister/brother who had a knee replacement. There were 18.8% of participants who had a normal right knee radiographic evaluation and 5.5% of participants who had a severe right knee radiographic evaluation. There were 30.1% (819) of participants who reported having Heberden's nodes and 11.4% (310) of participants who reported current smoking. The Medical Outcomes Study Short Form-12 version 2 physical summary scale quartile cut-points were 43.06, 51.24, and 56.14 for 25%, 50%, and 75%, respectively. Details of the analyses are presented in Table 1.

Table 2 includes the results of the Chi-square analyses between Heberden's nodes and the variables. Smoking, the key independent variable of interest, was significantly related to Heberden's nodes ($P = .0006$). Other significant relationships with Heberden's nodes were with sex, race/ethnicity, age, body mass index, right knee radiographic evaluation, mother/father/sister/brother who had a knee replacement, education, and the Medical Outcomes Study Short Form-12 version 2 physical summary scale quartiles. Charlson index and alcohol usage failed to reach significance in association with Heberden's nodes.

Table 3 includes the results of the logistic regressions of smoking on Heberden's nodes. In unadjusted analysis, current smokers were less likely to have Heberden's nodes than never smokers (less than 5 packs/lifetime). The odds ratio for current smokers, as compared with never smokers, was 0.61 (95% confidence interval: 0.46, 0.81; $P = .0007$). When the other significant variables were included in the model, smoking was attenuated to an adjusted odds ratio of 0.83 [95% confidence interval: 0.60, 1.14] which failed to reach significance ($P = .2488$). In the selected model, females were more likely than males to have Heberden's nodes; non-Hispanic Blacks were less likely than non-Hispanic Whites to have Heberden's nodes; older age groups were more likely than the youngest age group to have Heberden's nodes; people in the lower quartiles on the Medical Outcomes Study Short Form-12 version 2 physical summary scale were more likely to have Heberden's nodes than people in the highest quartile;

TABLE 1: Sample description, Osteoarthritis Initiative data.

	Number	Percent
All	2723	100
Heberden's nodes		
Yes	819	30.1
No	1904	69.9
Smoking		
Yes, current	310	11.4
Never (<5 packs/lifetime)	2413	88.6
Sex		
Female	1625	59.7
Male	1098	40.3
Race/ethnicity		
Non-Hispanic White	2148	78.9
Non-Hispanic Black	516	18.9
Hispanic/other	59	2.2
Age in years		
45 to <56	1047	38.5
≥56 to <66	827	30.4
≥66	849	31.2
Body mass index		
<25 (normal weight)	709	26.0
≥25 to <30 (overweight)	1054	38.7
≥30 (obese)	960	35.3
Right knee radiographic evaluation		
Normal	512	18.8
Possible osteoarthritis	957	35.1
Mild	544	20.0
Moderate	559	20.5
Severe	151	5.5
Family history of osteoarthritis		
Yes	248	9.1
No	2475	90.9
Charlson index		
0	2074	76.2
≥1	649	23.8
Education		
High school or less	434	15.9
More than high school	2289	84.1
Alcohol use (drinks/week)		
0–3	2084	76.5
4–7	355	13.0
8–14	198	7.3
15 and above	86	3.2
¹ Medical Outcomes Study Short Form-12		
Quartile 1	655	24.1
Quartile 2	668	24.5
Quartile 3	643	23.6
Quartile 4	757	27.8

¹ Medical Outcomes Study Short Form-12 version 2 physical summary scale quartile cut-points: 25% = 43.06; 50% = 51.24; and 75% = 56.14.

and people with a BMI of 30 and above were less likely to have Heberden's nodes than people with a BMI of less than 25.

TABLE 2: Chi-square analysis of Heberden's nodes by the variables, Osteoarthritis Initiative data.

Heberden's nodes	Yes	Row %	No.	Row %	P value
Smoking					.0006
Yes, current	67	21.6	243	78.4	
Never (<5 packs/lifetime)	752	31.2	1661	68.8	
Sex					<.0001
Female	647	39.8	978	60.2	
Male	172	15.7	926	84.3	
Race/ethnicity					<.0001
Non-Hispanic White	706	32.9	1442	67.1	
Non-Hispanic Black	90	17.4	426	82.6	
Hispanic/other	23	39.0	36	61.0	
Age					<.0001
45 to <56	187	17.9	860	82.1	
≥56 to <66	269	32.5	558	67.5	
≥66	363	42.8	486	57.2	
Body mass index					<.0001
<25 (normal weight)	247	34.8	462	65.2	
≥25 to <30 (overweight)	330	31.3	724	68.7	
≥30 (obese)	242	25.2	718	74.8	
Right knee radiographic evaluation					.0190
Normal	124	24.2	388	75.8	
Possible osteoarthritis	288	30.1	669	69.9	
Mild	178	32.7	366	67.3	
Moderate	181	32.4	378	67.6	
Severe	48	31.8	103	68.2	
Family history of osteoarthritis					.0172
Yes	91	36.7	157	63.5	
No	728	29.4	1747	70.6	
Charlson index					.7836
0	621	29.9	1453	70.1	
≥1	198	30.5	451	69.5	
Education					.0017
High school or less	158	36.4	276	63.6	
More than high school	661	28.9	1628	71.1	
Alcohol use (drinks/week)					.1025
0-3	646	31.0	1438	69.0	
4-7	104	29.3	251	70.7	
8-14	45	22.7	153	77.3	
15 and above	24	27.9	62	72.1	
¹ MOS SF-12 quartiles					.0037
Quartile 1	218	33.3	437	66.7	
Quartile 2	217	32.5	451	67.5	
Quartile 3	193	30.0	450	70.0	
Quartile 4	191	25.2	566	74.8	

¹Medical Outcomes Study Short Form-12 version 2 physical summary scale.

The purpose of this study was to explore the association of smoking and Heberden's nodes. The results were that the adjusted odds ratio for smoking on Heberden's nodes failed to reach significance ($P = .2337$). Interaction analysis with family history did not change the results. However, female smokers and female nonsmokers were more likely to have

TABLE 3: Odds ratios and 95% confidence intervals from logistic regression on Heberden's nodes, Osteoarthritis Initiative data.

	Odds ratio [confidence interval]	P value
<i>Unadjusted</i>		
Smoking		
Yes, current	0.61 [0.46, 0.81]	.0007
Never (<5 packs/lifetime)	Referent	
<i>Adjusted model</i>		
Smoking		.2488
Yes, current	0.83 [0.60, 1.14]	
Never (<5 packs/lifetime)	Referent	
Sex		<.0001
Female	3.65 [2.98, 4.48]	
Male	Referent	
Race/ethnicity		
Non-Hispanic White	Referent	
Non-Hispanic Black	0.38 [0.29, 0.49]	<.0001
Hispanic/other	1.12 [0.61, 2.08]	.7094
Age		
45 to <56	Referent	
≥56 to <66	1.97 [1.57, 2.48]	<.0001
≥66	2.81 [2.22, 3.55]	<.0001
Body mass index		
<25 (normal weight)	Referent	
≥25 to <30 (overweight)	1.02 [0.81, 1.27]	.8988
≥30 (obese)	0.72 [0.57, 0.93]	.0105
Right knee radiographic evaluation		
Normal	Referent	
Possible osteoarthritis	1.16 [0.89, 1.52]	.2722
Mild	1.22 [0.90, 1.65]	.1984
Moderate	1.16 [0.86, 1.58]	.3359
Severe	1.17 [0.74, 1.84]	.4998
Family history of osteoarthritis		
Yes	1.24 [0.92, 1.69]	.1625
No	Referent	
Education		
High school or less	1.16 [0.91, 1.50]	.2372
More than high school	Referent	
MOS SF-12 quartiles ¹		
Quartile 1	1.53 [1.18, 1.98]	.0015
Quartile 2	1.40 [1.09, 1.80]	.0096
Quartile 3	1.28 [0.99, 1.64]	.0577
Quartile 4	Referent	

¹Medical Outcomes Study Short Form-12 version 2 physical summary scale.

Heberden's nodes than male nonsmokers (AOR = 2.95 and 3.69, resp.; $P < .0001$); and smokers aged 45-56 years, smokers aged 56 years and above, and nonsmokers aged

56 years and above were more likely to have Heberden's nodes than young nonsmokers (AOR = 1.24, 1.94, 3.00, resp.).

The literature has few studies involving the relationship between hand osteoarthritis and smoking, [26]. There are even fewer studies between Heberden's nodes and smoking with which we could compare our results. This study's results are similar to results of Haara et al. [26] who studied Kellgren and Lawrence Grade 2 + osteoarthritis in any finger and smokers who smoked 20 or more cigarettes per day. The results in that study included an adjusted odds ratio of 0.72 [95% confidence interval: 0.48, 1.09] [26]. In a study of 443 Chuvashian (Russian) men, no association of smoking and hand osteoarthritis was determined (Chi-square $P = .49$) [27].

This study's results are also similar to the risk ratio for current smoking on hand osteoarthritis in which the adjusted odds ratio was 0.99 [95% confidence interval: 0.75, 1.31] [28]. The definition for smoking exposure (i.e., current smoking and never smoking) used by Wilder et al. [28] was the same as the definition used for this study. However, protective results of smoking with Heberden's nodes in women [29] and protective results of smoking and osteoarthritis in knees and large joints are also reported in the literature [15, 16, 30]. It has been suggested that there is a differential effect of nicotine on human chondrocyte glycosaminoglycan and collagen synthesis [31].

3.1. Plausible Biological Mechanism. It has been reported that the relationship of smoking with Heberden's nodes and osteoarthritis is variable [2] and that the etiology of osteoarthritis may be different at different body sites [16]. Additionally, the effects of nicotine may also be different at different body sites [16]. Although nicotine was shown to be beneficial to chondrocyte metabolism, it was also shown to destroy chondrocytes at the intervertebral disk, but not at the knee [31–33].

4. Conclusion

Workforce losses due to hand osteoarthritis would place a great burden on society. This is particularly true for health-care access to care issues in which certain professions require repetitive motions (such as with dental hygiene). The public health impact is a concern, especially for high risk, special needs populations. Hand osteoarthritis and its implications may become a factor in recruitment to various professions and workforce numbers. Determining and understanding factors associated with hand osteoarthritis and factors not implicated with hand osteoarthritis are important for individuals and for workforce preparation.

We failed to reject the null hypothesis of no difference in the number of Heberden nodes among individuals who smoke and individuals who do not smoke; we did not provide any clear evidence of a protective effect of smoking. These findings are similar to the findings of many studies of smoking and hand osteoarthritis but are not similar to previous findings concerning Heberden's nodes in which smoking was protective. The implications of this study are that smoking has

not shown any beneficial effects in protecting the hands. With current knowledge of the harms of smoking, this study adds to the mounting knowledge in the literature that there are few benefits and many known harms of smoking.

Additional Points

The researchers of the OAI intended to provide a wide longitudinal database for public use; it was not intended to be nationally representative. As a result, the number of smokers in the study is not representative of the nation (11.4% in the sample as compared with 17.8% nationally) [34]. This was a limitation of the available data. There are limited studies available to determine if the smoking exposure in studying osteoarthritis should be current smoking, as is needed for studies of myocardial infarctions, or if it should be pack-years/total duration, as is needed for studies of lung cancer [28]; therefore this limitation also applies to this study.

Ethical Approval

This cross-sectional study, a secondary data analysis (nonhuman subject research) of the OAI data, was acknowledged by the West Virginia University Institutional Review Board (Protocol no. 1509861595) and did not include experimentation involving human subjects or animals. The West Virginia University Institutional Review Board does not approve nor disapprove research which involves nonhuman subjects, such as this project; however the members of the Board review the protocol, acknowledge the review, and keep the protocol on file. The research was conducted in full accordance with the World Medical Association Declaration of Helsinki.

As with any study which relies upon self-report, there is the possibility of misclassification due to inaccurate report of smoking, Heberden's nodes, or the other self-reported variables. Self-reported data remains a weakness of all cross-sectional studies. However, overall, the large sample made it possible to include many additional variables in the model in the explanation of the relationship of smoking and Heberden's nodes. Additionally, the data were quality data intended for secondary data analysis.

Disclosure

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the paper. The OAI is a public-private partnership comprised of five contracts (N01-AR-2-2258; N01-AR-2-2259; N01-AR-2-2260; N01-AR-2-2261; and N01-AR-2-2262) funded by the National Institutes of Health, a branch of the Department of Health and Human Services, and conducted by the OAI Study Investigators. Private funding partners include Merck Research Laboratories; Novartis Pharmaceuticals Corporation, GlaxoSmithKline; and Pfizer, Inc. Private sector funding for the OAI is managed by the Foundation for the National Institutes of Health. This paper

was prepared using an OAI public use dataset and does not necessarily reflect the opinions or views of the OAI investigators, the NIH, or the private funding partners.

Competing Interests

The authors declare that they have no competing interests.

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