A Cross Sectional Study of the Association Between Sex, Smoking, and Other Lifestyle Factors and Osteoarthritis of the Hand

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ABSTRACT. ***Objective.*** To describe the association between sex, smoking, physical activity, occupation, and previous digit fracture and hand osteoarthritis (OA).

Methods. Cross sectional study of 522 subjects from 101 Tasmanian families (348 women, 174 men). Hand OA was assessed by 2 observers using the OARSI atlas for joint space narrowing and osteophytes at distal interphalangeal (DIP) and carpometacarpal joints as well as a score for Heberden's nodes based on hand photography. A structured questionnaire collected information regarding physical activity, sport participation, occupation, and smoking history.

Results. Women had a higher prevalence of hand OA and the increase with age was significantly higher for women at all sites (all $p < 0.05$). Ever smoking was associated with less frequent (OR 0.59, 95% CI 0.38, 0.92) and less severe Heberden's nodes (ß –0.60, 95% CI –1.03, –0.17), but not radiological disease. Recall of occupation, physical activity, and sport participation between the ages of 20 and 40 years had no association with the prevalence or severity of hand OA, while self-reported digital fracture was significantly associated with more common (OR 2.42, 95% CI 1.22, 4.83) and severe DIP joint disease (ß +3.92, 95% CI +1.50, +6.36). No factors were associated with carpometacarpal disease.

Conclusion. In this sample, women had a higher prevalence of hand OA at all sites as well as greater severity and a steeper age gradient (implying higher incidence rates). Smoking may decrease the risk of Heberden's nodes while having no effect on radiological hand OA, suggesting a differential effect possibly at the time of disease onset. With the exception of digital fracture, these data do not support a causal role for occupation or activity in earlier life with regard to hand OA. (J Rheumatol 2002;29:1719–24)

Key Indexing Terms:
OSTEOARTHRITIS SMOKING FRACTURE

Osteoarthritis (OA) is the leading musculoskeletal cause of disability in most Western countries[1]. While a genetic predisposition is well established[2-4], it is also likely that lifestyle or environmental factors play a significant role in the expression of the disease.

Age and sex have well described effects on the prevalence and severity of hand OA[5], but there is less information as to whether the age gradient is different between the sexes. One study has reported a higher incidence rate in women for symptomatic hand OA[6], while another has reported higher rates of radiographic hand OA at most sites[7]. The role of other lifestyle factors such as smoking and the effect of physical activity are less well established[8,9]. Smoking has been reported to have a protective effect on knee OA[10,11] but its effect on hand OA is controversial[11-13]. While OA is widely regarded as due to wear and tear, the evidence to support this is limited. Higher grip strength has been associated with the development of OA in most hand joints, with the exception of the distal interphalangeal (DIP) joints[14], while DIP OA may be more common in female textile workers whose work involves fine pincer grip[15], and paralysis appears to protect against hand OA[16]. In contrast to OA at other sites, few data are available on the effect of trauma on hand OA, with one report linking self-reported digital fracture with hand OA[12]. Lastly, obesity is also reported to be a significant risk factor for the development of knee OA[17-19], but its association with hand OA is less clear. Studies have reported no association between high body mass index (BMI) and hand OA in the elderly, while other studies found a positive association, particularly with carpometacarpal (CMC) OA[11,20-23]. The aim of this cross sectional family based study was to describe the associations between sex, smoking, physical activity, occupation, digit fracture, and BMI and the prevalence and severity of hand OA in Tasmanian men and women.

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MATERIALS AND METHODS

Patient selection. Tasmania is an island state of Australia with a population of 472,000[24]. It is primarily Caucasian in origin and genetically reflects a European population[25]. Rheumatology specialist services in Tasmania at the time of this study were primarily provided by 3 rheumatologists in partnership in the capital city of Hobart who have provided a statewide service since 1983. Index cases in this study were recruited from the records of this rheumatology practice. All subjects who had OA of the hand and a family history of at least one living relative with OA of the hand were invited with their families (both affected and unaffected) to take part in a study of the genetic and environmental factors associated with this disease. This study was granted ethical approval by the Royal Hobart Hospital ethics committee (human experimentation) and all subjects provided informed written consent.

Study protocol. Participants underwent a comprehensive protocol involving collection of blood as well as detailed assessment of hand OA, anthropometrics, environmental factors, pain, and function. Data in the form of a structured questionnaire were collected regarding smoking history, occupation, sport participation, physical activity (current and between the ages of 20 to 40 years), and history of digit fracture. Smoking history was recorded as ever smoked, age at which smoking commenced and ceased, and number of cigarettes smoked. Subjects recalled occupation, physical activity, and sport between the ages 20 to 40 years for analysis, as current occupation and physical activity may be modified by disability associated with the presence of OA. Subjects described type of occupation, e.g., farmer, clerical worker, cleaner, and a qualitative score (0 or 1) was given for the degree of mechanical stress to hand joints associated with the particular occupation and activity. Hence a high impact would score 1 and low impact would score 0. Sporting and physical activity were assessed both as yes/no, i.e., did they participate in sport or recreational activity, and as a qualitative assessment of the repetitive mechanical stress to the joints of the hand as a grade 0 (low impact) or grade 1 (high impact). This qualitative assessment was based on the type of sport played: rugby would be considered a high impact sport and swimming or soccer low impact sports. Previous digit fracture was assessed by self-report.

Weight was measured to the nearest 0.1 kg (with socks, shoes, and bulky clothes removed) using a single set of electronic scales (Seca Delta Model 707), which were calibrated using a known weight at the beginning of each clinic. Height was measured to the nearest 0.1 cm (with socks and shoes removed) using a stadiometer. BMI was calculated as weight (kg)/height (m)^2.

Assessment of hand OA. Hand OA was assessed in 2 ways: (1) A photo of both hands was taken by an Elicar Medical Macro MS2 camera. Photographs were scored as to the presence or absence of Heberden's nodes in each DIP joint by 2 investigators simultaneously without reference to radiographs (GJ, HC). Subjects were then classified with either presence or absence of disease and total score (0–8). Reproducibility was assessed one week apart in 50 photographs with an appropriate wide range of scores. (2) Radiographic disease was assessed using the Altman atlas[26] for joint space narrowing and osteophytes at DIP and CMC joints from a single anteroposterior radiograph of the hands performed according to a standardized protocol by the same 2 investigators simultaneously, with a single score obtained by consensus. The scores for each component at each joint could vary from 0 to 3. Subjects were then classified with either presence or absence of disease (0 vs 1 or greater) and total score at each anatomical site. Scores for DIP disease could vary from 0 to 48 and CMC disease from 0 to 12. Intraobserver reproducibility was assessed for both total osteophyte and joint space narrowing scores one week apart in radiographs from 45 different subjects with an appropriate wide range of scores.

The intraclass correlations for reproducibility of the Heberden's nodes and radiographic OA measures were all excellent[27]. Due to their lower reported prevalence[7] and relative rarity in our sample, erosion and deformity at proximal interphalangeals and other sites were not assessed.

Statistical analysis. Student's t test and Mann-Whitney U tests were utilized for comparison of means. Linear and logistic regression were used to analyze the effect of the various study factors on presence and severity of hand OA. To account for intrafamily correlations, mixed effect models were utilized for continuous variables and general estimating equations for dichotomous variables. All models were adjusted, where appropriate, for age, sex, age-sex interaction, BMI, and intrafamily correlation. Even though a number of dependent variables were ordinal, standard model assumptions were met in all cases. A p value < 0.05 (2 tailed) or a 95% confidence interval (CI) not including the null point were regarded as statistically significant. All statistical calculations were carried out on Stata version 7.0 for Windows (Stata Corp., College Station, TX, USA).

RESULTS

A total of 522 subjects from 101 families were studied (response rate 78%). There were 348 women and 174 men. Demographic details are provided in Table 1. There was a high prevalence of hand OA (44–70%), but there was wide variation in severity. Hand OA was both more common and more severe in women for all categories. In addition, the age gradient was steeper in women at all sites (Figure 1).

Table 2 shows the association between smoking, BMI, and hand OA. Ever smoking was associated with a significant reduction in the prevalence of Heberden's nodes, while no association was observed with radiological disease after adjustment for age, sex, their interaction term, BMI, and family status. Similarly, ever smoking was associated with fewer Heberden's nodes but there was no association with the severity of radiological hand OA. Current smoking was not associated with the severity or prevalence of any component of hand OA. Neither was there evidence of a dose response association with years of smoking or pack-years (data not shown). Being overweight or obese was associated with a significantly lower Heberden's node score but not with other sites (Table 3). There were no substantive differ-

Table 1. Characteristics of study participants. Data are presented as mean (standard deviation) unless otherwise specified.

	Men, n = 174	Women, n = 348	p
Age, yrs	53.2 (14.0)	57.0 (15.0)	0.006*
Height, cm	174.5 (6.8)	159.8 (7.2)	< 0.001*
Weight, kg	84.1 (14.9)	69.8 (14.7)	< 0.001*
Body mass index, kg/m^2	27.5 (3.9)	27.3 (5.2)	> 0.05*
Heberden's nodes, %	44	66	< 0.001
CMC disease, %	44	65	< 0.001
DIP disease, %	57	70	0.003
Heberden's nodes score, 0–8	1.6 (2.4)	3.4 (3.2)	< 0.001
DIP score, 0–48	9.0 (11.2)	14.2 (14.4)	< 0.001
CMC score, 0–12	2.0 (3.3)	3.7 (3.7)	< 0.001
Met ACR criteria for hand OA, %	56	36	< 0.001
Ever smoker, %	64	48	< 0.001
Current smoker, %	19	17	> 0.05
High impact occupation	42	9	< 0.001
Sport (yes/no)	74	54	< 0.001
High impact sport (yes/no)	62	47	< 0.001
Self-reported digit fracture	32	9	< 0.001

* Unpaired t test, all others are Mann-Whitney U test.

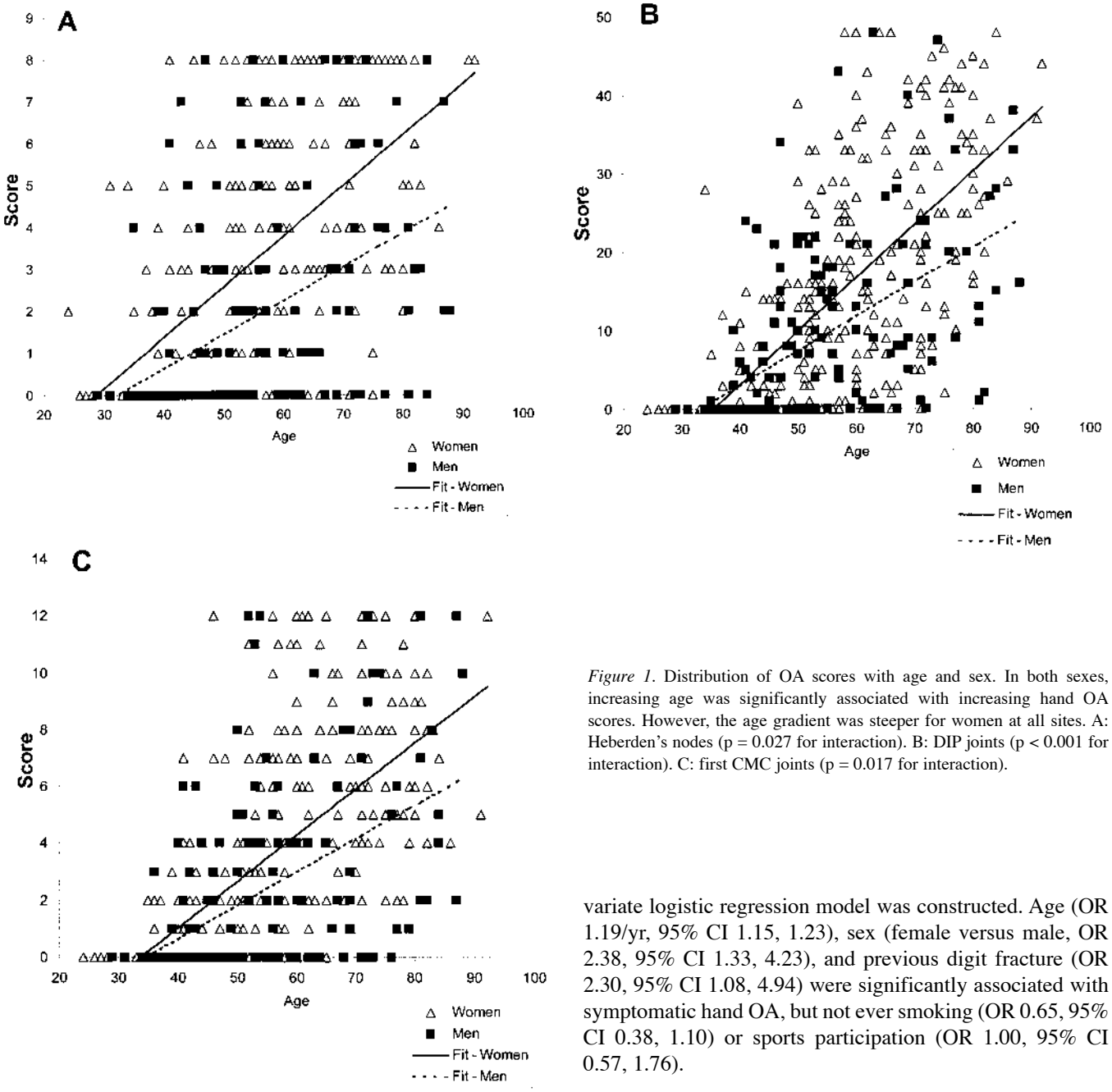

Figure 1. Distribution of OA scores with age and sex. In both sexes, increasing age was significantly associated with increasing hand OA scores. However, the age gradient was steeper for women at all sites. A: Heberden's nodes ($p = 0.027$ for interaction). B: DIP joints ($p < 0.001$ for interaction). C: first CMC joints ($p = 0.017$ for interaction).

ences if these analyses were restricted to men or women. Neither was there any significant correlation between BMI and prevalence or severity of hand OA at any site (data not shown).

The association of other lifestyle factors with the prevalence and severity of hand OA is described in Table 3. Self-reported digit fracture was significantly associated with increased prevalence and severity of hand OA. Occupation, high impact physical activity, and sport participation (age 20–40 years) had no significant association with hand OA. Using American College of Rheumatology (ACR) criteria for OA[28] as a marker for symptomatic hand OA, a multivariate logistic regression model was constructed. Age (OR 1.19/yr, 95% CI 1.15, 1.23), sex (female versus male, OR 2.38, 95% CI 1.33, 4.23), and previous digit fracture (OR 2.30, 95% CI 1.08, 4.94) were significantly associated with symptomatic hand OA, but not ever smoking (OR 0.65, 95% CI 0.38, 1.10) or sports participation (OR 1.00, 95% CI 0.57, 1.76).

DISCUSSION

In this cross sectional study of hand OA, we report significant associations with the prevalence and severity of hand OA for age, sex, age-sex interaction, and self-reported fracture for DIP OA; ever smoking for Heberden's nodes; and no significant association with obesity, physical activity, and occupation.

The significant age-sex interaction implies a higher incidence rate of hand OA in women at all sites. This confirms and extends observations of higher hand OA incidence in women[6,7]. Our data do not provide an explanation for this difference, suggesting a possible hormonal effect or sex

Table 2. Smoking, BMI, and hand OA.

	Presence of Disease, OR (95% CI)	Severity of Disease, β (95% CI)
Ever smoking (yes/no)		
Heberden's nodes	0.59 (0.38, 0.92)	–0.60 (–1.03, –0.17)
DIP disease	0.77 (0.47, 1.28)	–1.44 (–3.21, +0.33)
CMC disease	0.92 (0.58, 1.48)	–0.07 (–0.58, +0.44)
Current smoking (yes/no)		
Heberden's nodes	0.71 (0.42,1.22)	–0.33 (–0.90, +0.23)
DIP disease	1.01 (0.56, 1.81)	–0.09 (–2.39, +2.19)
CMC disease	1.28 (0.72, 2.28)	+0.19 (–0.47, +0.85)
BMI (≥ 25 vs < 25 kg/m^2)		
Heberden's nodes	0.69 (0.43, 1.12)	–0.50 (–0.97, –0.04)
Distal interphalangeal disease	1.22 (0.70, 2.14)	–0.25 (–2.13, +1.65)
Carpometacarpal disease	0.90 (0.54, 1.52)	–0.34 (–0.88, +0.21)

All coefficients are adjusted for age, sex, their interaction term, and intrafamily correlation.

Table 3. Association between environmental factors and hand OA. All coefficients adjusted for age, sex, age-sex interaction, BMI, and family status.

	Presence of Disease, OR (95% CI)	Severity of Disease, β (95% CI)
Self-reported digital fracture		
Heberden's nodes	0.99 (0.55, 1.77)	+0.48 (–0.11, +1.07)
DIP disease	2.42 (1.22, 4.83)	+3.84 (+1.48, +6.20)
CMC disease	1.63 (0.86, 3.10)	+0.43 (–0.26, +1.13)
High impact occupation (age 20–40 years)		
Heberden's nodes	1.13 (0.65, 1.97)	+0.01 (–0.54, +0.56)
DIP disease	1.29 (0.69, 2.43)	–0.11 (–2.33, +2.11)
CMC disease	0.73 (0.40, 1.33)	–0.26 (–0.90, +0.38)
High impact physical activity (age 20–40 yrs)		
Heberden's nodes	0.96 (0.54, 1.71)	–0.06 (–0.64, +0.52)
DIP disease	1.00 (0.53, 1.88)	–0.74 (–3.04, +1.56)
CMC disease	0.82 (0.45, 1.50)	–0.27 (–0.94, +0.40)
Sport participation (age 20–40 yrs)		
Heberden's nodes	0.93 (0.59, 1.45)	–0.23 (–0.69, +0.22)
DIP disease	1.29 (0.76, 2.17)	+0.14 (–1.67, +1.97)
CMC disease	0.86 (0.53, 1.40)	–0.00 (–0.53, +0.53)

dependent gene expression. Further investigation of this observation may shed light on the etiology of this common condition.

Ever smoking was associated with both a 40% reduction in the prevalence of Heberden's nodes as well as a lower Heberden's node score, but was not associated with radiological disease. Further, current smoking was not associated with any of the 3 compartments of hand OA. Neither was there any evidence of a dose response. This effect may be due to smoking having differential effects on target tissue, i.e., soft tissue in contrast to bone or cartilage. Smoking may result in less Heberden's node formation by an antiangiogenic effect at the time of disease initiation, which suggests Heberden's nodes have a somewhat different pathogenesis to joint space narrowing or osteophyte formation. However, these findings contrast with the study of Hart, *et al*, who reported in a community based study of women that ever smoking had a positive relationship with both Heberden's nodes and radiographic disease[13]. Consistent with our study, most studies report no association between radiographic hand OA and smoking, although significant associations at other sites have been reported[11,12].

Previous digit fracture was common in our population (especially in men) and was significantly associated with both the prevalence and severity of DIP OA but not at any other sites. This predominantly involved the digit affected by the fracture, and the size of the effect was both substantial and similar to that reported in premenopausal women[29]. The role of injury in the etiology of OA at other sites, in particular the knee and hip, is well established. However,

the mechanism by which previous fracture increases prevalence and severity of hand OA is unclear, especially as most fractures do not affect the joint. Previous self-reported fracture did not appear to be acting as a marker of increased physical activity or increased exposure to high impact activities, because there was no change in risk of OA with these factors. No role for mechanical factors in the development or severity of hand OA was observed in this study. Neither occupation nor high impact physical activity were found to be significantly associated with hand OA, with no trends suggesting either a major increase or decrease. This analysis was based on self-reported activity and occupation between the ages of 20 to 40, which may be subject to misclassification. However, we purposely kept the classification simple and qualitative to make this recall more accurate. Nevertheless, these data do not allow more detailed comparisons between different occupations and sports as a wide range of occupations and physical activities were described. Further, there are no well validated methods to quantify these in terms of stress and mechanical loading to joints, indicating the need for prospective studies in presymptomatic subjects.

Lastly, obesity had weak and inconsistent protective associations with hand OA in this study, which are not suggestive of a causal association. There are conflicting results in the literature regarding the association of obesity with hand OA[20-23]. The weight bearing effect of obesity is unlikely to explain the effect of obesity on hand OA.

This study has number of potential limitations. First, the study was primarily designed as a family study into the genetics of OA of the hand. As a result, the prevalence of arthritis was higher and almost certainly more severe than in the general population. Such studies are not available in Australia but this assertion is consistent with the few population based studies reported to date[5-8]. The result of this has been greater power to look at disease in general and especially more severe disease. It is not possible to generalize from this study about the prevalence of arthritis of the hand. However, this is less of a problem in an etiologic study, which looks at exposure outcome associations. Indeed, Miettinen[30] states that for these associations to be generalizable to other populations, 3 key criteria need to be met regarding selection, sample size, and adequate distribution of study factors, all of which are met by this study, suggesting that our findings may be generalizable to other Caucasian populations. In addition, assessment of exposure in this study was mainly by self-administered questionnaire, which leads to a significant potential for misclassification. This is most likely to apply to the physical activity data (as outlined above), but less so for smoking or self-reported digital fracture, and thus may explain some of the nonsignificant results. In contrast, the potential for misclassification of the radiographic outcome measure is lower, as the intraobserver variation was excellent, most likely due to the use of a radiographic atlas[26]. However, this measure was semiquantitative and further refinement of OA assessment by modalities such as magnetic resonance imaging may lead to greater power to examine exposure outcome associations.

In conclusion, women have a higher prevalence of hand OA at all sites, as well as greater severity and a steeper age gradient in this sample (implying higher incidence rates). Smoking may decrease the risk of Heberden's nodes, while having no effect on radiological hand OA, suggesting a differential effect possibly at the time of disease onset. Lastly, with the exception of digital fracture, these data do not support a causal role for occupation or activity in earlier life with regard to hand OA.

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