EXTENDED REPORTS

Cigarette smoking and risk of osteoarthritis in women in the general population: the Chingford study

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Abstract

Previous studies have suggested that smoking might be protective against the development of osteoarthritis (OA) of the knee. A group of 1003 women aged 45–64 years (mean 54·2 years) from the Chingford general population survey were studied to examine the effect of cigarette smoking on the prevalence of radiologically confirmed OA at different sites. Standard anteroposterior radiographs of the hand and knee were available in 985 women. Disease classification was made on the basis of radiological OA and symptomatic radiological OA. Odds ratios were calculated and adjusted for age and body mass index.

A total of 463 (46·2%) women were ever smokers compared with 540 (53·8%) non-smokers. Ever smokers had consumed an average of 14·9 cigarettes a day for a mean of 25·7 years.

For radiological OA of the distal interphalangeal joint (DIP) (140 women), proximal interphalangeal joint (40 women), carpometacarpal joint (160 women), and knee joint (118, women) there was no reduced risk of OA in ever smokers. In the small number of subjects with generalised OA (22 women) there was a non-significant 40% reduction of radiological OA in ever smokers (odds ratio 0·63; 95% confidence interval 0·24 to 1·68). Results were similar for subjects with radiographic clinical OA, except the DIP joint which showed a positive association between smoking and Heberden's nodes (odds ratio 2·02, 95% confidence interval 1·89 to 3·42). Results were similar when analysed using current smokers against never smokers.

These results do not support an inverse association between cigarette smoking and OA in women. A possible inverse relation with the small subgroup of women with generalised OA and an effect of cigarettes on disease severity cannot, however, be discounted.

There may be some evidence to suggest that smoking has a protective effect on the development of osteoarthritis (OA), though few data are available. The Framingham OA cohort study in the USA reported lower rates of radiological knee OA in smokers compared with non-smokers.[1] Two studies have also reported higher rates of back pain in smokers.[2][3] Little is understood about the aetiology of OA and risk factors of the disease. Whether smoking affects cartilage, bone, or both, is not known. Some studies have shown that smoking is inversely associated with rheumatoid arthritis[4] and common mechanisms might act in other rheumatic diseases. Smoking is an important risk factor in many diseases and studying its role as a risk factor in OA is important in increasing our knowledge of the epidemiology of the disorder. We therefore carried out a population based cross sectional study of the association of smoking with OA in a large group of middle aged women. As risk factors for OA are generally joint specific,[5] we examined the effect of smoking on distinct joint sites in the hand and knee.

Subjects and methods

From an age/sex register of a large general practice of over 11 000 patients in Chingford, outer London all 1353 women in the age range 45–64 years (mean 54·2 years) were invited to participate in a study assessing musculoskeletal disease in the general population. Further details of this population have been published elsewhere.[6] In terms of smoking habits 29·6% of women in the Chingford population are current smokers compared with 35% of women in the UK.[7]

Women taking part in the study underwent a clinical examination of their hands by a single observer (DH), including clinical evidence of bony swelling of the interphalangeal joints and tenderness or pain on movement of the carpometacarpal (CMC) joints. These signs have been shown previously by ourselves and others to have good reproducibility.[8][9]

Osteoarthritis was classified radiologically using standard anteroposterior radiographs of the hands and weightbearing knees, which were taken at the same time as the clinical examination. Radiographs were scored blind to clinical details according to the method of Kellgren and Lawrence using the *Atlas of standard radiographs* by a single trained observer.[10] We have previously shown good reproducibility using this method.[11] A subject was considered positive for radiographic OA of the knee and CMC joints if at least a grade 2 Kellgren and Lawrence score was present on either side, and for the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints grade 2+ changes had to be present in two or more joints to be positive. The joint space of the knee was evaluated by digitised image analysis in the lateral and medial compartments.[12] As no agreed definition exists, for the purpose of this investigation generalised OA was defined as the combination of OA of the DIP, CMC, and knee joints.

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Table 1 Characteristics of 985 women with available radiographs. Results are mean (SD) values

Characteristic	Current smoker (n=297)	Previous smoker (n=166)	Non-smoker (n=540)
Age (years)	53·9 (6·01)	54·6 (6·44)	54·3 (5·92)
Weight (kg)	66·7 (12·74)	66·9 (9·94)	67·1 (11·89)
Height (m)	1·62 (0·6)	1·62 (0·6)	1·62 (0·6)
Body mass index	25·5 (4·52)	25·6 (3·91)	25·7 (4·30)
No of cigarettes smoked a day	14·3 (8·60)	16·1 (10·96)	—
No of years as a smoker	30·5 (10·58)	16·9 (9·47)	—

Radiographic clinical OA was defined as the presence of radiological changes in addition to symptoms or clinical signs. A standardised joint symptom questionnaire administered by a nurse was used to obtain details of symptoms (onset, duration, stiffness, current pain, and number of days each month of pain). The knees were considered to be symptomatic if joint pain was reported to be present for longer than one month in the last 10 years. The DIP and PIP joints were considered to be affected clinically if bony swelling was present on clinical examination and the CMC joints were considered to be affected clinically if pain on movement or tenderness was present. A standardised questionnaire administered by a nurse was used to obtain details of smoking, number of cigarettes smoked, and number of years smoked.

ANALYSIS
Subjects were divided into three categories for analysis: ever smokers (a combination of previous and current smokers), current smokers, and never smokers. Previous smokers were defined as having more than five cigarettes a day

for more than five years. In each smoking category subjects with radiological OA and radiographic clinical OA were compared with controls who had no radiological evidence at any site in their hands or knees. Odds ratios and 95% confidence intervals were calculated and adjustment for potential confounding variables was performed by logistic regression using the PC software package EGRET (SERC, Seattle). All the odds ratios given are adjusted for age and body mass index. Age and body mass index were treated as continuous variables for regression analysis.

Results
Of the 1353 women invited to participate, 1003 were examined, six died, 66 moved away, and 278 refused to take part or did not respond. This gave a crude response rate of 74%, adjusted 78%. Eighteen women did not have radiographs taken for a variety of reasons. Table 1 gives the mean characteristics of the 985 women with available radiographs screened divided into smoking categories for comparison. A total of 29·6% of the women were current smokers, 16·6% previous smokers, and 53·8% non-smokers. The mean number of cigarettes smoked each day was 14·9 for an average of 25·7 years.

Table 2 gives the prevalence of OA at different sites. The occurrence of radiological OA at each site was 14·2% at DIP joints, 4·2% at PIP joints, 16·8% at CMC joints, 12% at the knee joints, and 2·2% for generalised OA. The occurrence approximately halved when analysis was restricted to those with radiographic findings and clinical signs or symptoms (table 2).

Table 3 gives the age and body mass index adjusted odds ratios for the effect of smoking at different joint sites. For radiological OA at any site there was no significant association of smoking and risk of OA. There was a 34–38% increased risk for CMC, DIP, and knee joint OA associated with ever smoking, however, and generalised OA showed a 40% reduction of risk, though confidence intervals included unity at all sites. Results were similar for women with radiographic clinical OA, except for the DIP joints which showed a positive association of risk of Heberden's nodes in ever smokers (odds ratio 2·02; 95% confidence interval 1·89 to 3·42). Analysis was also repeated using current smoking as the exposure variable against never smokers and no major differences in the results were noted (table 4).

In this study group the number of women with severe disease (Kellgren and Lawrence grade 3+) was too small to calculate odds ratios accurately, though there was no suggestion of

Table 2 Prevalence of radiographically defined osteoarthritis (OA) and radiological and clinical OA based on 985 subjects. Values are No (%)

Joints affected	Radiological OA	Radiological and clinical OA
Distal interphalangeal	140 (14·2)	96 (9·6)
Proximal interphalangeal	40 (4·2)	22 (2·2)
Carpometacarpal	160 (16·8)	93 (9·3)
Knee	118 (12·0)	58 (5·8)
Generalised OA	22 (2·2)	8 (0·8)

Table 3 Adjusted odds ratio and 95% confidence intervals for ever smokers v never smokers at different joint sites based on 985 subjects. Numbers as in table 2, compared with 619 controls with no osteoarthritis at any site

Joints affected	Radiological osteoarthritis	Radiological and clinical osteoarthritis
Distal interphalangeal	1.34 (0·88 to 2·04)	2.02 (1·89 to 3·42)
Proximal interphalangeal	1.01 (0·54 to 1·89)	1.26 (0·48 to 3·27)
Carpometacarpal	1·34 (0·77 to 1·67)	1·24 (0·74 to 2·08)
Knee	1.36 (0·88 to 2·10)	1.38 (0·77 to 2·49)
Generalised OA	0.64 (0·24 to 1·68)	—*

*Insufficient numbers.

Table 4 Adjusted odds ratios and 95% confidence intervals for current smokers v never smokers at different joint sites based on 985 subjects. Numbers as in table 2, compared with 619 controls with no osteoarthritis at any site

Joints affected	Radiological osteoarthritis	Radiological and clinical osteoarthritis
Distal interphalangeal	1.49 (0·92 to 2·41)	2.13 (1·18 to 3·85)
Proximal interphalangeal	1.16 (0·52 to 2·58)	1.50 (0·52 to 4·31)
Carpometacarpal	1·13 (0·72 to 1·78)	1·01 (0·54 to 1·88)
Knee	1.44 (0·87 to 2·38)	1.34 (0·68 to 2·64)
Generalised OA	0.63 (0·19 to 2·06)	—*

*Insufficient numbers.

major differences using this subgroup. For radiological OA of the knee joint in ever versus never smokers who were Kellgren and Lawrence grade 3+, the odds ratio was 1·25 (95% confidence interval 0·16 to 9·53). To examine whether the inclusion of sign positive, radiographically negative controls could have biased the results, we reanalysed the data for the knee joint and found no differences in the direction of the results. To examine any dose-response relations, smokers were divided into tertiles. The highest tertile of smoker, defined as consuming more than 20 cigarettes a day for 20 years, was compared with never smokers. No significant effect was seen. For heavy smokers odds ratio for the radiological OA of the knee joint was 1·09 (95% confidence interval 0·55 to 2·19), and for radiographic clinical OA of the knee joint the odds ratio was 1·46 (95% confidence interval 0·52 to 4·10). All results were adjusted for age and body mass index; additional adjustment for hysterectomy and parity status did not influence the results.

As the Kellgren and Lawrence grading system is dependent largely on osteophytes, we also examined whether joint space loss at the knee was associated with smoking. No differences were noted between smokers and non-smokers in the minimum joint space medially or laterally. Smokers were not found to report knee pain more often than non-smokers (odds ratio 1·11, 95% confidence interval 0·83 to 1·48).

Discussion
This cross sectional population study has shown no clear overall association of cigarette smoking and OA in women and does not confirm the Framlingham study data.[1] A protective effect of smoking on certain subgroups of OA cannot be excluded, however, given the suggestion of an inverse relation with smoking and generalised OA, a generalised systemic form of the disease.

The unexpected finding of an association with smoking and clinical Heberden's nodes which were radiographically positive is difficult to explain given the lack of radiological differences. One explanation might be that smokers have thinner or more bony fingers, and the diagnosis of bony swelling is therefore easier to make than in non-smokers. There was no significant weight difference in the smoking groups, however; non-smokers were only 0·2 units of body mass index heavier than current smokers.

The classification of OA still remains a problem in epidemiological studies.[13] In this study, however, women were classified primarily on a radiological basis using standard atlases and criteria with previously proved reproducibility. For the hand, clinical signs of tenderness and pain on movement were used to define clinical disease. Although these signs are prone to classification error, any error is likely to be random and would not have led to misclassification of the disease in any one direction. For the analysis subjects were classified by joints affected. It is well known that not all risk factors are common to all joints[5]—for example, obesity is a major risk factor for the knee, but less so for the hip or hand.

A potential problem in all population studies is response bias, if those responding were healthier and less likely to be smokers. The results and conclusions would only have been significantly altered if the 22% of non-responders were all heavy smokers without OA or never smokers with severe OA, and this scenario is extremely unlikely. With respect to generalisability, the Chingford population is broadly representative of women in the United Kingdom; the women are mainly white and of social class II–IV, with similar rates of smoking and obesity.

The sample size was sufficient to rule out any modest protective effect. Power calculations showed that with this number of cases of OA of the knee we had 80% power to detect a 40% protective effect of smoking at a 5% level of significance.

There are few other studies looking at the effect of smoking and OA. In an analysis of the Health and Nutrition Examination Survey (HANES) data, a modest protective effect was found for smoking. After adjusting for age, weight, and other confounding variables the confidence intervals included unity; for men the odds ratio was 0·79 (95% confidence interval 0·61 to 1·02) and for women the odds ratio was 0·85 (95% confidence interval 0·62 to 1·59).[14] These findings led to a further examination of the association by the same workers in the Framlingham data.[1] In this study subjects who were smokers in a first examination had a lower risk of subsequently developing OA of the knee 20 years later than non-smokers (relative risk 0·81; 95% confidence interval 0·66 to 0·99). It was unknown, however, whether smoking status at the first visit continued at the same rate up until knee examination 20 years later. Preliminary data from a Dutch follow up study of 135 women also found no association between smoking and risk of knee OA (odds ratio 1·03; 95% confidence interval 0·43 to 2·46).[15]

In summary, in this cross sectional population we found no clear protective effect of smoking for OA of the hands and knees in women. The data suggest a possible modest protective effect on the generalised form of OA, though risk may be slightly increased at other sites. As this study group did not include elderly subjects with severe disease we cannot draw conclusions on a possible effect of smoking and disease severity. Further work examining larger numbers of subjects with generalised nodal disease, which may be aetiologically distinct, may be worthwhile.

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