

EXTENDED REPORTS

Association of hand and knee osteoarthritis: evidence for a polyarticular disease subset

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Abstract

Objective—To examine the association between hand and knee osteoarthritis (OA) in a community based population.

Methods—Radiographs of 695 participants aged ≥ 40 years in the Baltimore Longitudinal Study of Aging were read for changes of OA, using Kellgren-Lawrence grade ≥ 2 as the case definition.

Results—Logistic regression analyses, adjusting for age, gender and body mass index, revealed a significant association between OA in the knee and the following joint groups: distal and proximal interphalangeal (DIP, PIP) and Hand2 (OA in two or more hand joint groups) for grade 2–4 and grade 3–4 disease, and the first carpometacarpal (CMC1) joint for grade 3–4 disease.

Conclusion—There is an association between OA in hand sites and the knee. The strength of the associations increases with increasing disease severity. For the PIP site, there is a trend toward increasing strength of association for increasing numbers of affected joints and bilateral disease.

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Generalised osteoarthritis (GOA) was reported as early as 1805 and was re-emphasised in 1952 by Kellgren and Moore.¹ In 1969, Lawrence described radiographic GOA, a polyarticular subset of osteoarthritis (OA), in a population based sample from Leigh and Wensleydale, England.² Two criteria were used for case definition: either three or more, or five or more joint groups with grade 2–4 OA (as defined in the *Atlas of Standard Radiographs*),³ among the joint groups visible on radiographs from the following sites: hand, foot, knee, pelvis, and cervical and lumbar spine. The concept of GOA was validated in other population based studies using radiographically defined OA,⁴ however none of the earlier studies reported the association of OA between specific joint groups. More recently, the co-occurrence of OA at two of three major OA sites (hands, knees, and hips) was examined in a clinic based population in whom OA was defined by radiographs and clinical symptoms.⁵ The only significant association was found between knee and hand OA in women.

The purpose of this study was to determine if the association between radiographic hand and tibiofemoral knee OA occurred more often than that which could be attributed to chance alone, after adjusting for age, which is the strongest known risk factor for OA, and body mass index, as a measure of obesity, which is a risk factor for radiographic OA in some joint sites.

Subjects and methods

STUDY POPULATION

All subjects in this study were participants in the Baltimore Longitudinal Study of Aging (BLSA), a multidisciplinary research project conducted at the Gerontology Research Center, National Institute on Aging in Baltimore, Maryland. The continuing research project began in 1958 and was limited to male participants until 1978, when women began to be enrolled. Participants are community dwelling volunteers of middle to upper socioeconomic status, who are evaluated at two year intervals. Radiographs of the hands have been taken quadrennially since inception of the research project, and knee radiographs were added to the examination procedure in 1985. Ninety six percent of the BLSA participants are white; they were aged from 18 to 93 years at entry to the study. This paper reports a study of a population (referred to hereafter as the study population) limited to white participants (426 men and 269 women aged 40 years and above) who had bilateral hand and knee radiographs, obtained at the same visit, from 1985 to 1991.

RADIOGRAPHS AND DEFINITIONS

Bilateral posteroanterior hand and bilateral standing anteroposterior tibiofemoral knee radiographs were read for the presence of OA as described in the *Atlas of Standard Radiographs*.³ The five point Kellgren-Lawrence scales used (0–4) were: grade 0 = normal; grade 1 = questionable; grade 2 = mild; grade 3 = moderate; grade 4 = severe. Definite OA was defined as Kellgren-Lawrence grade 2 or higher, present in at least one joint of a given group.⁶

Radiographs of each joint site were read by a separate radiologist (hand: WWS; knee: RR), blinded to the subject. Previously obtained inter-reader (and intra-reader) intra-class correlations for these investigators and joint

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sites were 0.74 (0.80) and 0.68 (0.87), respectively.^{7 8}

The following joint groups were examined: the knees, and the distal and proximal interphalangeal (DIP, PIP) and first carpometacarpal (CMC1) joints of the hands. For convenience, the occurrence of definite OA in at least two of the three hand joint groups was termed Hand2.

Anthropometric measurements were made of height (m) and body weight (kg). Obesity was measured as body mass index (BMI) ($\text{kg}/(\text{m})^2$).

DATA ANALYSIS

Separate multiple logistic regression analyses were used to estimate the odds ratio for the association of knee OA with OA at each hand site: knee OA was the dependent variable; the independent variables were BMI, which is continuous; age, which is ordinal (by decade); gender, and OA at each hand site, which are dichotomous. The reference group for all of the knee OA and hand site OA association analyses was no involvement of the respective hand sites. Interaction terms consisted of combinations of the independent variables. For the DIP and PIP hand sites, the contribution of increasing numbers of affected digits, and unilateral or bilateral disease was compared with no affected digits at the respective site.

Two sets of dummy variables were created: the first set was to test the association of interphalangeal (IP) and knee OA in two joint increments of affected IP joints; the second set was to test the association of IP and knee OA using two groupings of unilateral and bilateral IP OA. In group I, the dummy variables were created for unilateral or bilateral OA of one or

more affected digits, respectively. In group II, hand OA was further broken down into the following dummy variables: one affected digit; more than one affected digit unilateral disease; one affected digit on each hand; bilateral hand joint OA, two or more affected digits present on at least one hand. The dummy variables in each group were analysed using no affected hand joint digits as the reference.

Logistic regression analyses were performed using Statistical Analysis Systems, Release 6.07, SAS Institute, Cary, North Carolina.

Results

The study population consisted of 426 white men and 269 white women, aged 40–89 years (mean 64 (SD 12) years for men; mean 65 (13) years for women). Figure 1 shows the age and gender specific prevalence of grade 2–4 OA for each joint group studied. The DIP joint was the most frequent site of OA involvement in both genders and all age groups. Hand OA was significantly more prevalent in women at age 60 and older at each hand site, especially the CMC1. The prevalence of grade 2–4 knee OA was comparable in men and women. Figure 1 also demonstrates the strong association between increasing age and increasing OA prevalence at each joint site.

Figure 2 shows the overall prevalence of grade 2–4 polyarticular OA by sites involved. The combination of DIP and knee involvement had the greatest prevalence: 29.4% for men and 32.6% for women. The combination of three joint groups (Hand2 plus knee OA) was not uncommon, with a prevalence of 22.0% for men and 26.0% for women. An age associated increase in grade 2–4 hand and knee polyarticular OA occurred at significance levels of $p \leq 0.0001$, regardless of the hand site involved

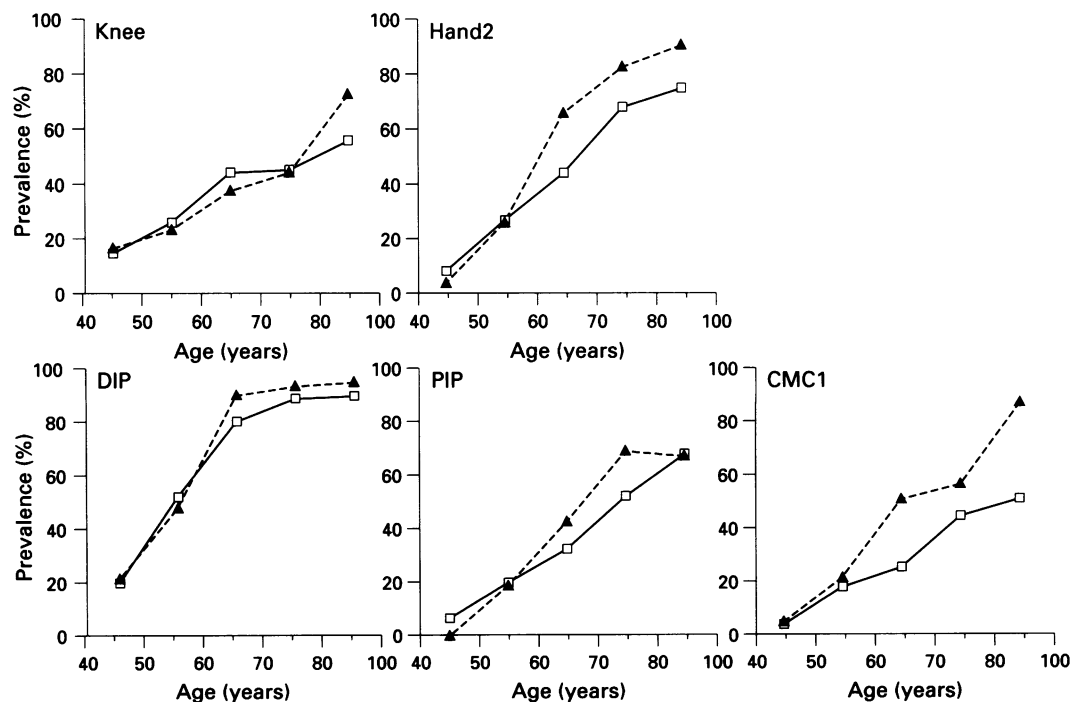


Figure 1 Age and gender specific prevalence of radiographic changes of grade 2–4 osteoarthritis in the knee, two or more hand joint groups (Hand2), distal and proximal interphalangeal (DIP, PIP), and carpometacarpal (CMC1) joints. □ = Men; ▲ = women.

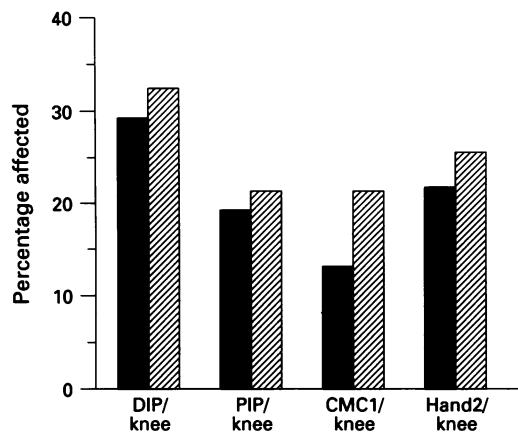


Figure 2 Proportion of subjects with radiographic changes of grade 2–4 osteoarthritis at multiple sites in men (■) and women (▨). Abbreviations as in figure 1.

(data not shown). The crude odds ratios, unadjusted for age, gender or BMI, showed significant association at all sites (table 1).

When data for both genders are combined, an association between grade 2–4 knee and hand OA was seen in this population at all joint sites, except the CMC1, even after adjusting for the effects of age, BMI and gender

Table 1 Crude odds ratios (OR) and 95% confidence intervals (CI) for the association of grade 2–4 hand and knee osteoarthritis derived from multiple logistic regression analyses

Joint groups	OR (95% CI)
Knee and DIP	3.23 (2.21 to 4.74)***
Knee and PIP	2.87 (2.08 to 3.95)***
Knee and CMC1	2.12 (1.53 to 2.92)***
Knee and Hand2	4.67 (2.99 to 7.29)***

Significance of association: ***p < 0.001.

Table 2 Age adjusted odds ratios (OR), and age and BMI adjusted OR, and 95% confidence intervals (CI) for the association of grade 2–4 hand and knee osteoarthritis derived from multiple logistic regression analyses

Joint groups	OR (95% CI)		
	Combined†	Men	Women
<i>Age adjusted data</i>			
Knee and DIP	1.85 (1.20 to 2.84)**	1.63 (0.97 to 2.74)	2.41 (1.09 to 5.32)*
Knee and PIP	1.87 (1.31 to 2.66)***	2.18 (1.39 to 3.41)***	1.41 (0.78 to 2.53)
Knee and CMC1	1.33 (0.93 to 1.92)	1.28 (0.80 to 2.05)	1.36 (0.76 to 2.46)
Knee and Hand2§	2.43 (1.44 to 4.13)**	2.28 (1.23 to 4.21)**	3.02 (1.04 to 8.78)*
<i>Age and BMI adjusted data</i>			
Knee and DIP	1.71 (1.10 to 2.65)*	1.56 (0.92 to 2.63)	2.11 (0.94 to 4.74)
Knee and PIP	1.76 (1.23 to 2.53)**	2.03 (1.29 to 3.19)**	1.39 (0.76 to 2.55)
Knee and CMC1	1.32 (0.91 to 1.91)	1.27 (0.79 to 2.04)	1.38 (0.75 to 2.52)
Knee and Hand2§	2.16 (1.26 to 3.69)**	2.09 (1.12 to 3.90)*	2.50 (0.83 to 7.48)

†Adjusted for gender. §Reference group is no hand joint involvement. Significance of associations: *p < 0.05; **p < 0.01; ***p < 0.001.

Table 3 Age adjusted odds ratios (OR), and age and BMI adjusted OR, and 95% confidence intervals (CI) for the association of grade 3–4 hand and knee osteoarthritis derived from multiple logistic regression analyses

Joint groups	OR (95% CI)		
	Combined†	Men	Women
<i>Age adjusted data</i>			
Knee and DIP	6.84 (1.39 to 33.64)*	4.31 (0.80 to 23.17)	NC
Knee and PIP	5.55 (2.11 to 14.60)***	3.11 (0.91 to 10.69)	16.64 (2.80 to 98.90)**
Knee and CMC1	3.63 (1.67 to 7.90)**	2.93 (1.10 to 7.80)*	5.37 (1.38 to 20.85)*
Knee and Hand2§	16.41 (3.28 to 82.02)***	8.49 (1.50 to 48.02)*	NC
<i>Age and BMI adjusted data</i>			
Knee and DIP	7.62 (1.52 to 38.63)*	6.51 (0.99 to 42.82)	NC
Knee and PIP	5.16 (1.92 to 13.87)**	2.45 (0.67 to 8.93)	17.55 (2.90 to 106.12)**
Knee and CMC1	4.10 (1.83 to 9.19)***	3.48 (1.24 to 9.79)*	5.46 (1.41 to 21.18)*
Knee and Hand2§	19.51 (3.78 to 100.74)***	9.58 (1.61 to 57.09)*	NC

†Adjusted for gender. §Reference group is no hand joint involvement. NC = No convergence. Significance of associations: *p < 0.05; **p < 0.01; ***p < 0.001.

(table 2). The gender specific odds ratios for polyarticular OA (derived from separate age and BMI adjusted logistic regression analyses for each gender), differed from each other in statistical significance at the knee plus PIP and Hand2 sites for grade 2–4 disease. However, these gender specific differences were not significant when interaction was tested in logistic regression analyses of the entire study population using the independent variables age, gender, BMI, and hand site OA, plus an interaction term incorporating gender and hand site OA (data not shown). Adjusting for BMI decreases the point estimates for almost all of the analyses; however, the significance of the hand and knee OA associations remained substantially the same (table 2). For grade 3–4 disease, the point estimates for association were greater throughout, especially for women, and were statistically significant for all hand sites when both genders were combined, even after adjustment for age and BMI (table 3).

Figure 3 presents data that suggest a trend of incremental increases in the odds ratio point estimates for association between increased numbers of affected interphalangeal joints and knee OA. For DIP OA, where only one digit was affected unilaterally or bilaterally, or more than one digit was affected unilaterally, there was no significant association with knee OA (table 4). However, there was a significant association between knee OA and bilateral DIP OA involving more than two digits. For PIP OA, there was no significant association between unilateral disease of one or more digits and knee OA. However, bilateral disease involving at least one digit of each hand was significantly associated with knee OA.

Discussion

The main finding of this study is the association between radiographically defined hand joint and tibiofemoral knee OA in a healthy, community dwelling population, after adjusting for age, gender, and BMI. The trends in age and gender specific prevalence of hand and knee OA sites in this study are similar to those reported in other population based studies of radiographic OA.^{4 6 9–15} In studies in which hand, feet, knee, hip, and spine radiographs were available, non-nodal GOA was slightly more common in men than in women, and nodal GOA and severity of OA at individual sites were more common in women. Grade 2–4 polyarticular OA at the DIP, PIP, CMC1, and Hand2 plus knee OA sites had greater prevalences in women in our study (fig 2). However, associations of OA between specific joint groups were not reported in the earlier polyarticular OA studies² and data concerning Heberden's nodes have not been analysed in the BLSA cohort.

Although we found a significant association between hand and knee OA in both men and women in our study, Cushnaghan and Dieppe found an association in women only.⁵ This difference may be attributable to the different composition of the study populations: healthy community volunteer compared with clinic

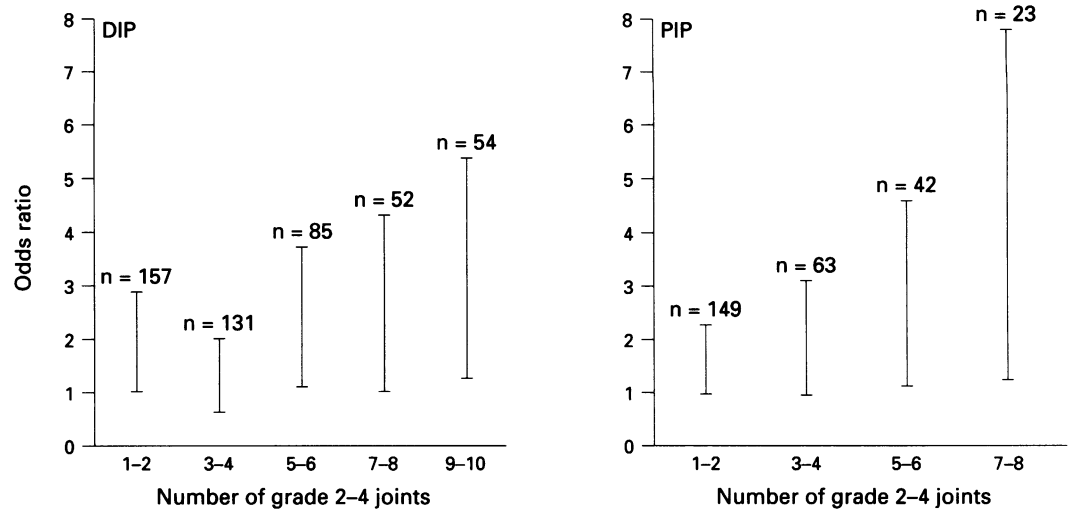


Figure 3 Odds ratios and confidence intervals of association for number of grade 2-4 affected DIP joints and grade 2-4 knee OA (left), and for number of grade 2-4 affected PIP joints and grade 2-4 knee OA (right). × = Point estimate.

based. Different case definitions (symptomatic radiographic disease versus radiographic disease) may also have contributed, as gender specific differences in symptom reporting have been documented.¹⁶ However, the possibility of a gender difference in the occurrence of polyarticular OA should not be disregarded. Although the differences in the gender specific odds ratios in our study did not achieve statistical significance when a gender-by-hand site interaction variable was added to the logistic regression model for the entire study population, there may not have been a sufficient number cases of polyarticular OA in the younger and sometimes the eldest age strata to allow detection of an interaction.¹⁷ Investigation of the significance of this trend would require analysis of larger samples from the same or comparable populations.

The strengths of association for the various unilateral and bilateral DIP joint OA variables were comparable (table 4); the lack of significance for unilateral or bilateral single digit DIP OA, and multidigit unilateral OA, probably reflects the small numbers of affected participants. For PIP OA, there was a trend toward increasing association for numbers of joints involved and bilateral disease (fig 3, table 4). The wider confidence interval for one digit bilateral disease, overlapping that for bilateral disease with more than two digits, may account for the greater odds ratio point estimate of the former.

Table 4 Age and BMI adjusted odds ratios (OR) and 95% confidence intervals (CI) for the association of knee and single or multidigit hand osteoarthritis (OA) derived from multiple logistic regression analyses

Analysis by dummy variable group	DIP		PIP	
	OR (95% CI)	Number in group	OR (95% CI)	Number in group
I. No OA§		216		418
≥ 1 digit unilateral OA	1.73 (1.01 to 2.95)*	119	1.45 (0.93 to 2.24)	133
≥ 1 digit bilateral OA	1.70 (1.07 to 2.70)*	360	2.18 (1.40 to 3.39)***	144
II. No OA§		216		418
1 digit unilateral OA	1.74 (0.97 to 3.12)	87	1.34 (0.83 to 2.17)	102
> 1 digit unilateral OA	1.68 (0.73 to 3.87)	32	1.81 (0.83 to 3.93)	31
1 digit bilateral OA	1.79 (0.88 to 3.63)	48	2.73 (1.09 to 6.87)*	22
Bilateral OA with ≥ 2 digits on ≥ 1 hand	1.68 (1.04 to 2.71)*	312	2.09 (1.30 to 3.34)**	122

§Reference group.

Significance of associations: *p < 0.05; **p < 0.01; ***p < 0.001.

The lack of lateral or skyline views of the knee for assessment of patellofemoral joint OA is a limitation of this study, and may have resulted in misclassification of some of the participants to the group without knee OA.¹⁸ Another constraint of the study is the use of the Kellgren-Lawrence OA grading system, which ranks osteophytes over joint space narrowing for assigning grade severity.³ Despite recent questions regarding the significance of osteophytes in disease progression,¹⁹⁻²³ the Kellgren-Lawrence scale remains the standard for case definition. The Kellgren-Lawrence scale was, furthermore, used to attain grading system comparability with earlier polyarticular OA studies.

In summary, this study examined the association between radiographic changes of hand and knee OA in a healthy, community dwelling population. The findings include significant associations between radiographic OA at the DIP, PIP, and CMC1 joints, and the knee. The strength of these associations increased with disease severity and, for the PIP site, there was a trend toward increasing strength of association with increasing numbers of affected joints and bilateral disease.

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