Symmetry and clustering of symptomatic hand osteoarthritis in elderly men and women: the Framingham Study


Objective. While symmetry and clustering of radiographic hand osteoarthritis (OA) have been described in middle-aged women, these have not been studied in elderly individuals and similar investigations are lacking for symptomatic hand OA. The goal of this study was to study patterns of joint involvement in symptomatic hand OA among elderly Caucasian men and women.

Methods. Using data from the Framingham Osteoarthritis Study, we defined a joint as having symptomatic OA if it had symptoms and radiographic OA (Kellgren and Lawrence grade \( \geq 2 \)). We assessed clustering of symptomatic OA using a \( \chi^2 \)-test and evaluated the interrelationship of occurrence of symptomatic OA among different joints with generalized estimating equations.

Results. Of 976 subjects (age 71–99 yr, 36% men) examined, symptomatic OA more often affected multiple hand joints in an individual than would be expected by chance (\( P < 0.001 \)). The presence of symptomatic OA at a particular joint was strongly associated with symptomatic OA in the same joint of the opposite hand, followed by other joints in the same row of the same hand, and then other joints in the same ray of the same hand. The symmetrical pattern of symptomatic OA was more apparent in women than in men.

Conclusion. Our study demonstrates that symptomatic OA often affects multiple hand joints, and is more likely to cluster by row than by ray. The disease also occurs in a remarkably symmetrical pattern, especially in women.

Key words: Epidemiology, Hand, Osteoarthritis, Symptoms.

Osteoarthritis (OA) is the most common form of arthritis among the elderly [1]. Joints most affected by this disease are knees, hips and hands. Previous epidemiological studies have largely targeted radiographic OA, and most of them have concentrated on knee and hip joints [1–3]. While symptomatic OA should be a focus of studies because it causes disability and has formidable societal and public health impact, few studies have been conducted to study symptomatic OA, especially hand OA, among the elderly. As such, we know little about patterns of joint involvement and risk factors for symptomatic hand OA.

Studies of patterns of joint involvement in hand OA could shed light on our understanding of the aetiology of the disease. Several studies have reported that the prevalence of radiographic hand OA is higher in women than in men, and that distal interphalangeal joints are the most frequently affected joints [4–9]. In 1995, Egger et al. [10] evaluated the pattern of joint involvement of radiographic hand OA in middle-aged women. They found that radiographic OA often affects multiple joints of the hand, occurs symmetrically and is more likely to be clustered by row than by ray. Similar patterns were also reported by other investigators using bony scintigraphy [11, 12]. Several mechanisms have been postulated to explain the joint involvement pattern of hand OA, including mechanical stress [13], neuroendocrine factors [14, 15] and genetic predisposition [16].

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To date, few studies have assessed the pattern of joint involvement for symptomatic hand OA [11], the important clinical entity. As a result, similar kinds of descriptive epidemiological data on joint involvement pattern are lacking for symptomatic hand OA. Any evidence of patterns of joint involvement in symptomatic hand OA in a population-based study would provide a broader perspective on OA.

Using data from the Framingham Osteoarthritis Study, we describe the prevalence of symptomatic OA in different joint groups of the hand and examine the patterns of joint involvement of this disease among elderly men and women.

Materials and methods

The Framingham Study started in 1948 in Framingham, Massachusetts. The original cohort included 5209 subjects at the first examination. Subjects have been examined biennially since then. As part of an osteoarthritis study performed between 1992 and 1993, participants received posteroanterior (PA) radiographs of both hands and were queried about hand symptoms.

The interviewer-administered symptom survey was conducted at the Framingham Study clinic. The survey included questions on major joint complaints, including hand OA. A battery of questions was used to assess hand symptoms, including ‘on most days do you have pain, aching or stiffness in the joints of your hands or wrists?’, ‘in the past month have you had any pain, aching or stiffness in the joints of your hands or wrists?’, and ‘on most days, do you have pain, aching or stiffness in any of your joints?’. If a subject answered ‘yes’ to the third question, the interviewer then showed a diagram which illustrated all distal interphalangeal (DIP), proximal interphalangeal (PIP), metacarpophalangeal (MCP), thumb interphalangeal (IP) and thumb base joints in both hands, and asked the subject to mark the joint(s) that had pain, aching or stiffness. In the current analysis we used the third question to define the symptomatic hand OA because this question permitted us to assess joint-specific symptoms. We defined a row as DIP (or PIP, or MCP) joints in different digits on the same hand, and a ray as DIP (or PIP, or MCP) joints on the same digit.

Posteroanterior hand radiographs were taken with separate exposures of each hand, with the central ray on the third MCP joint. Two academically based bone and joint radiologists read radiographs using an atlas of individual radiographic features developed for the Framingham Osteoarthritis Study. Fifteen joints for each hand, including four DIPs, four PIPs, five MCPs, IP and thumb base, consisting of the carpometacarpal and scaphotrapezial joints, were evaluated for the presence of osteophytes, joint space narrowing, sclerosis and cysts. Each joint was graded for overall radiographic OA using a modified Kellgren and Lawrence (K&L) grade scaled 0–4.

A hand joint was considered as having symptomatic OA if it had a K&L grade of 2 or greater and the subject reported symptoms in the joint defined as a positive response to the joint-specific question. While the above definition constituted the primary way we defined thumb base symptomatic OA, we were concerned that some subjects could not differentiate on the hand diagram between the thumb base and the first MCP joint. Therefore, we tested another definition of thumb base symptomatic OA in which we characterized the joint as affected if there were symptoms reported there or in the first MCP, and if the thumb base’s K&L grade scored ≥ 2, while the adjacent first MCP’s K&L grade scored < 2.

For each joint group (eight DIPs, eight PIPs, 10 MCPs, two IPs and two thumb bases), we calculated sex-specific prevalence of symptomatic OA. Since the number of joints in each joint group varies, for each joint group we calculated the prevalence of symptomatic OA by using the number of joints with symptomatic OA divided by the total number of joints in that group. We compared the prevalence as well as average number of joints affected by symptomatic hand OA according to handedness status.

To test whether symptomatic OA is likely to cluster in multiple hand joints in some individuals, we divided subjects into five age groups: < 75, 75–79, 80–84, 85–89 and ≥ 90 yr, then obtained age- and sex-specific prevalences of symptomatic OA for each joint separately. We calculated the number of subjects who would have 0, 1, 2, 3, 4 or 5+ joints with symptomatic OA, assuming that the presence of this disease in different hand joints in a subject is independent. We compared the observed frequency of subjects with different numbers of joints affected with the expected frequency using a χ²-test.

To examine the interrelation of symptomatic OA occurrence among different hand joints, we used logistic regression to estimate the odds ratio (OR) of symptomatic OA in a particular joint according to the symptomatic OA status of other joints. In the regression model, we used symptomatic OA status of the same joint in the opposite hand, the joints in the same row of the same hand, and the joints in the same ray of the same hand to predict the symptomatic OA status of a particular joint. We used generalized estimating equations to account for the correlation among multiple joints in a hand.

To evaluate whether the association between the presence of symptomatic OA in a particular joint and the same joint in the opposite hand varies by gender, we estimated the odds ratios of having symptomatic OA in a given hand joint as a function of gender, the presence of OA in the same joint of the opposite hand and their interaction. Specifically, using the absence of symptomatic OA in the same joint of the opposite hand in men as the reference group, we created three indicator variables, i.e. presence of symptomatic OA in the same joint of the opposite hand in men, absence of symptomatic OA in the same joint of the opposite hand in women, and presence of symptomatic OA in the same joint of the opposite hand in women. We then calculated the proportion of excess increased prevalence of symptomatic OA in a particular joint that was due to the interdependent effect of these two factors [17, 18].

Finally, we also examined the joint involvement pattern of radiographic hand OA using the same approaches described above.

Results

Of the 1166 subjects who participated in the Framingham Osteoarthritis Study between 1992 and 1993, 1084 subjects obtained hand radiographs, 1099 answered survey questions and 1041 subjects completed both radiographs and survey. Excluded from the analysis were nine subjects with rheumatoid arthritis and 56 subjects with missing information on either radiographic scores or symptoms of some hand joints. The intra-observer reliabilities for K&L scoring averaged across hand joints were high for both radiologists (Reader 1: $k = 0.79$, $P < 0.001$; Reader 2: $k = 0.82$, $P < 0.001$).
The inter-observer reliability was 0.65 \( (P < 0.001) \) [6].

The characteristics of the remaining 976 subjects are presented in Table 1. The mean age of the study participants was 79.0 (range 71–99 yr old), with 32.5% men and 41.9% women being 80 yr and older. Radiographic OA occurred in 22.1% of hand joints in men and 32.7 of hand joints in women. Compared with men, women reported more clinical symptoms in their hand joints \( (P < 0.001) \) and had a higher proportion of hand joints involved by symptomatic OA \( (P < 0.001) \).

The prevalence of symptomatic OA for each hand joint group is presented in Table 2. Symptomatic hand OA occurred most frequently in DIP joints and was rarely seen in MCP joints in both men and women. For each hand joint group, women had a much higher prevalence of symptomatic OA than men. Using the modified definition of symptomatic OA in the thumb base, we found that 10 subjects complained of pain in the first MCP joint, but had radiographic OA only in the thumb base joint; and only one subject had pain in the thumb base joint but had radiographic OA in the first MCP joint. These results suggest even if subjects may have difficulty in differentiating pain in the thumb base from that in the first MCP joint, the number should be small.

No apparent increased prevalence of symptomatic OA was found in the dominant hand \( (OR = 1.1, 95\% CI: 0.9–1.2) \). The average number of joints affected by symptomatic OA in the dominant hand (0.62) was similar to that in the non-dominant hand (0.59) with a \( P \) value equal to 0.746.

Symptomatic OA clustered in hand joints in both men and women (Table 3). If we assume the presence of symptomatic OA in one hand joint was independent of the OA status of the other hand joints in a person, we would expect that less than five men should have four or more joints affected by symptomatic OA. In fact, we observed 17 men who had four or more joints involved with symptomatic OA. Similar findings were observed in women.

The interrelationship of the presence of symptomatic OA among hand joints is presented in Table 4. In both men and women, the strongest predictor for the presence of symptomatic OA in a particular joint was the disease status in the same joint of the opposite hand, followed by

**Table 1. Subject characteristics and proportion of hand joints with symptoms, radiographic and symptomatic OA in the Framingham Study**

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>Men (n = 351)</th>
<th>Women (n = 625)</th>
</tr>
</thead>
<tbody>
<tr>
<td>70–74</td>
<td>18.5</td>
<td>17.9</td>
</tr>
<tr>
<td>75–79</td>
<td>49.0</td>
<td>40.2</td>
</tr>
<tr>
<td>80–84</td>
<td>20.2</td>
<td>25.6</td>
</tr>
<tr>
<td>≥ 85</td>
<td>12.3</td>
<td>16.3</td>
</tr>
<tr>
<td>Hand joints with symptoms</td>
<td>4.6</td>
<td>9.5</td>
</tr>
<tr>
<td>Hand joints with radiographic OA</td>
<td>22.1</td>
<td>32.7</td>
</tr>
<tr>
<td>Hand joints with symptomatic OA</td>
<td>1.8</td>
<td>5.5</td>
</tr>
</tbody>
</table>

**Table 2. Prevalence of symptomatic OA in hand joint groups in the Framingham Study**

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of joints with symptomatic OA (prevalence %)</td>
<td>82 (2.9)</td>
<td>71 (2.5)</td>
</tr>
<tr>
<td>No. of joints with symptomatic OA (prevalence %)</td>
<td>468 (9.4)</td>
<td>363 (7.3)</td>
</tr>
</tbody>
</table>

**Table 3. Observed and expected number of subjects with joints involved by symptomatic OA by gender**

<table>
<thead>
<tr>
<th>Number of joints with symptomatic OA</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed</td>
<td>Expected</td>
<td>Observed</td>
</tr>
<tr>
<td>0</td>
<td>309</td>
<td>220.1</td>
</tr>
<tr>
<td>1</td>
<td>13</td>
<td>90.5</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>26.8</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>9.1</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>3.2</td>
</tr>
<tr>
<td>5+</td>
<td>12</td>
<td>1.3</td>
</tr>
</tbody>
</table>

**Table 4. Presence of symptomatic OA in a particular hand joint according to symptomatic OA status of other hand joints: adjusted odds ratios (with 95% CI)**

<table>
<thead>
<tr>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same joint, other hand</td>
<td>14.0 (3.4–58.5)</td>
</tr>
<tr>
<td>Same row, same hand</td>
<td>6.4 (4.3–9.4)</td>
</tr>
<tr>
<td>Same ray, same hand</td>
<td>5.3 (2.9–10.0)</td>
</tr>
</tbody>
</table>

*Adjusted for age.

**Table 5. Joint involvement pattern in symptomatic hand OA**

<table>
<thead>
<tr>
<th>Joint involvement pattern</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated single joint</td>
<td>14.0 (3.4–58.5)</td>
<td>17.5 (10.8–28.3)</td>
</tr>
<tr>
<td>Multiple joints involved</td>
<td>6.4 (4.3–9.4)</td>
<td>5.2 (4.5–6.0)</td>
</tr>
</tbody>
</table>

*Alternative definition of symptomatic thumb base OA in which the joint is defined as having symptomatic OA if either the thumb base or the adjacent first MCP joint had symptoms and the K&L grade scored ≥ 2 in the thumb base and < 2 in the adjacent first MCP joint.
the joints in the same row of the same hand, and then by the joints in the same ray of the same hand.

Symptomatic hand OA showed more symmetry in women than men (Table 5). Compared with a joint with no symptomatic OA in the same joint of the opposite hand in men, the prevalence of symptomatic OA in a particular joint was 14 times higher if the same joint in the opposite hand in men was affected by symptomatic OA, 1.7 times higher if the same joint in the opposite hand in women was unaffected, and 29.8 times higher if the same joint in the opposite hand in women was affected. The excess increased prevalence of symptomatic OA at a particular joint that was attributable to the combined effect of female gender and presence of OA in the contralateral joint was 50.4% (95% CI: 15.2–85.7%), suggesting that the effect of the presence of symptomatic hand OA in the same joint of the opposite hand is significantly modified by gender.

Similar patterns of joint involvement were also observed for radiographic hand OA. Radiographic OA was most commonly seen in DIP joints, followed by PIP and then MCP joints. No difference was found in the number of joints affected by radiographic OA between the dominant hand (n = 3.5) and the non-dominant hand (n = 3.5). Like symptomatic OA, radiographic OA was more strongly clustered in a row (OR = 2.5, 95% CI: 2.3–2.7 in men; OR = 2.9, 95% CI: 2.8–3.0 in women) than in a ray (OR = 1.3, 95% CI: 1.2–1.5 in men, OR = 1.3, 95% CI: 1.2–1.4 in women). Radiographic OA also showed a strong symmetrical phenomenon in both men and women (OR = 8.5, 95% CI: 7.0–10.3 in men; OR = 7.5, 95% CI: 6.5–8.5 in women).

### Discussion

In this population-based study of symptomatic hand OA, we found the disease was common in an elderly Caucasian population, especially among women. Symptomatic OA often involved multiple hand joints, with DIP joints most frequently affected. Symptomatic OA was more likely to cluster by row than by ray. It often occurred symmetrically, and this effect was stronger in women than men.

Our results of joint involvement pattern of radiographic hand OA are consistent with previous findings [5–12]. While radiographs accurately reflect advanced bony changes of OA, and thus provide a valuable tool to study the aetiology of radiographic hand OA, studies have showed that clinical signs and symptoms correlate poorly with radiographic changes in the population [19, 20]. In the current study, of the hand joints with clinical symptoms, 39.7% in men and 57.7% in women had radiographic OA; and of those joints with radiographic OA, only 8.3% in men and 16.7% in women had clinical symptoms. While many potential risk factors have been identified for radiographic hand OA, few risk factors for symptomatic hand OA have been identified, and factors differentiating symptomatic and radiographic disease are unknown [21]. We believe that symptomatic hand OA reflects the disease of clinical and public health interest and focusing on this entity avoids concerns about whether radiographic findings represent ‘disease’, and studies of the joint involvement pattern of symptomatic hand OA will shed light on our understanding of disease aetiology.

To our knowledge, few studies have assessed the joint involvement pattern of symptomatic hand OA. Macfarlane et al. [11] found that symptomatic hand OA assessed with scintigraphy showed considerable symmetry. However, the number of subjects in that study was small and participants were recruited from a rheumatology clinic. Several other studies also obtained information on both symptoms and radiographic or scintigraphic changes of the hand, but none of them specifically evaluated the joint involvement pattern of symptomatic hand OA [5, 9, 12]. We used both radiographic change and symptoms to define symptomatic hand OA and examined comprehensively the pattern of joint involvement of the disease using a population-based sample.

In the current study, we found that symptomatic hand OA showed a strong symmetrical pattern. The biological mechanisms for such a phenomenon are not fully understood. Studies have shown that mechanical factors, such as power grip or pincer grip, play important roles in the development of radiographic OA [13]. If local mechanical force does play a key role in the development of hand OA, one would expect that joints in the same row of the same hand, which would be subject to the same stressors, would have a stronger predicting power for symptomatic OA occurrence for a particular joint than the same joint of the opposite hand. That does not seem to be the case in our population or others. Our findings may therefore be construed as supporting the concept that genetic or some systemic factors may play more important roles in symptomatic hand OA than physical stressors.

The symmetry of disease occurrence has been invoked as an argument in favour of the genetic or systemic factors [14–16, 22]. Indeed, heritability of hand OA is high. In a twin study, investigators reported that, independent of known environmental and demographic factors, 59% (95% CI: 0.49–0.70) of hand OA variability might be attributed to genetic factors [16]. If symmetry, in part, represents heritability, then our finding of symmetrical hand involvement in older men and women suggests that genetic influence is a prominent source of

### Table 5. Odds ratios (with 95% CI)* of having symptomatic OA in a particular hand joint as a function of gender and status of symptomatic OA in the same joint of the opposite hand

<table>
<thead>
<tr>
<th>Presence of symptomatic OA in the same hand of the opposite hand</th>
<th>Gender</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>1.0 (reference)</td>
<td>1.7 (1.2, 2.5)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14.0 (7.1, 27.8)</td>
<td>29.8 (19.2, 46.3)</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age.
Joint involvement pattern in symptomatic hand OA

347

disease even later in life, a time when the heritability of other complex genetic diseases often falls [23, 24]. While we were unable to compare older and younger subjects in our sample, symmetry of hand OA in the older women in our sample was impressive. It was, however, substantially less prominent in older men, supporting the argument that heritability of hand OA in men is less than in women.

Kidd et al. [15] hypothesized that neurogenic factors might play a role in symmetry of hand OA. They speculated that some of the nerve fibres innervated in synovium may modulate the response of the synovial membrane to a variety of noxious stimuli by releasing neuropeptides. Synovial damage results in acute inflammation in the damaged joint and a neurogenically mediated infiltrate of inflammatory cells in the contralateral joint. Others have suggested that hormonal factors may cause a symmetrical pattern of hand OA [14]. We propose that symmetry in hand OA could also be a sign that particular hand joints, perhaps because of their location in the hand or their shape, are vulnerable to certain common physical stressors; thus inherited abnormal joint shape could serve as one explanation for the high heritability of hand OA.

Polyarticular joint involvement in hand OA has been recognized for a long time. In the early 1950s several investigators defined a specific subtype of radiographic OA, primary generalized OA, characterized by multiple joint involvement, with predilection for DIP and thumb base involvement [25, 26]. Results from a survey conducted in a working-class area of Northern England [4] showed that the prevalence of symptomatic hand OA was higher in women (2.7%) than in men (1.6%). These estimates were slightly lower than what we found in the Framingham Study. However, the difference may be explained by the older age of our subjects, as the majority of subjects in the survey in Northern England were young or middle-aged people. Similar to the findings of previous studies on radiographic hand OA, our study showed that symptomatic hand OA occurs in clusters, especially in rows rather than in rays. These findings imply that, in addition to genetic or systemic factors, local stressors probably play a role in causing symptomatic hand OA.

Our study had some limitations. Subjects in this study were elderly, with the youngest being over 70 yr. Thus, we were unable to estimate the proportion of joints involved by symptomatic OA among a middle-aged population. Second, the number of male subjects is relatively small; thus, the proportion estimate of joints involved by symptomatic OA, especially in MCP joints, may not be precise.

In conclusion, in this population-based study we found that the joint involvement pattern of symptomatic hand OA was similar to that reported in radiographic hand OA. Symptomatic hand OA often involved multiple hand joints, it occurred symmetrically and was more likely to be clustered by row than by ray. This pattern suggests that genetic factors may play an important role in the development of symptomatic hand OA.

Acknowledgements

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References