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Progression of hand osteoarthritis over 2 years: a clinical and radiological follow-up study

S Botha-Scheepers,1 N Riyazi,1 I Watt,2 F R Rosendaal,3 E Slagboom,4 N Bellamy,5 F C Breedveld,1 M Kloppenburg1

ABSTRACT

Objectives: To investigate the course of hand osteoarthritis over 2 years by currently available outcome measures.

Methods: 189 participants of the Genetics, Arthrosis and Progression (GARP) study with hand osteoarthritis were followed for 2 years. Self-reported hand pain and functional limitations were assessed with the Australian/Canadian osteoarthritis hand index (AUSCAN LK 3.0). Pain intensity upon lateral pressure in the interphalangeal and thumb base joints was graded on a four-point scale. Osteophytes (0−3) and joint space narrowing (JSN) (0−3) was scored at baseline and after 2 years in interphalangeal and thumb base joints. Standardised response means (SRM) were calculated.

Results: 172 (91%) patients completed the 2-year follow-up (mean age 60.5 years, 78.5% women). Statistically significant increases in self-reported pain and function scores, in pain intensity scores as well as in osteophyte and JSN total scores were seen over 2 years. SRM were 0.25, 0.23, 0.67, 0.34 and 0.35, respectively, for self-reported pain and function scores, pain intensity scores, osteophyte and JSN total scores. Radiological progression was not associated with changes in self-reported pain and function. Women in an early post-menopausal stage were especially at risk of progressing radiologically.

Conclusions: Currently available outcome measures were able to assess progression over the relatively short time period of 2 years. Radiographic outcomes were more responsive than self-reported outcomes. Pain intensity upon lateral pressure seems to be a responsive measure but needs validation.

Hand osteoarthritis is a common joint disorder leading to considerable pain and with substantial impact on hand function.1,2 The disease course of patients with hand osteoarthritis, especially over the mid to long term, is, however, largely unknown. Therapy for hand osteoarthritis is limited.3 This is partly related to the lack of randomised controlled trials (RCT) in hand osteoarthritis.4 Moreover the few RCT that have been performed were discredited by a lack of standardised outcome assessments.5

A task force of the Osteoarthritis Research Society International (OARS) recently published guidelines and recommendations for clinical trials in hand osteoarthritis.5 Pain and physical function were recommended as the core clinical outcome measures for trials in hand osteoarthritis and should be assessed with reliable, valid and responsive instruments specific to hand osteoarthritis. The Australian/Canadian osteoarthritis hand index (AUSCAN LK 3.0).7–9 which is a self-administered multidimensional questionnaire, is such an instrument. It has been successfully used both in cross-sectional studies and in short-term clinical trials. Its ability to detect changes in pain and function in hand osteoarthritis over a few years is not known. Pain intensity assessment upon joint pressure during a physical examination is considered a useful instrument; however, it is not frequently used.10

Serial standard radiographs are considered the imaging modality of choice when assessing the progression of structural damage in hand osteoarthritis over time. The few published studies on radiological progression of hand osteoarthritis were mostly population-based studies and concerned extensive periods of time.11–14 The radiographic course of hand osteoarthritis patients over a mid to long term and the factors that predispose to a rapidly progressive course remain poorly evaluated.

To obtain more insight into the disease course of patients with hand osteoarthritis and to investigate whether currently available instruments can detect changes in clinical and radiological outcome measures over the mid to long term, we conducted a prospective observational study over a period of 2 years in hand osteoarthritis patients.

METHODS

Study description

The Genetics, Arthrosis and Progression (GARP) study is a prospective longitudinal cohort study, aimed at identifying determinants of osteoarthritis susceptibility and progression.15 The study population consists of white sib pairs with osteoarthritis at multiple sites. The GARP study was approved by the Medical Ethics Committee of the Leiden University Medical Centre. This well-characterised patient population also enabled us to investigate progression in a subset of hand osteoarthritis patients.

Patient selection

In brief, 191 probands (aged 40–70 years) and 191 siblings with osteoarthritis at multiple sites in the hands or in two or more of the following joint sites: hand, spine (cervical or lumbar), knee or hip, were included at baseline after giving informed written consent. Sib pairs with at least one subject with symptomatic hip or knee osteoarthritis were eligible for the 2-year follow-up study. Patients with secondary osteoarthritis, familial syndromes with a clear Mendelian inheritance pattern or a shortened life expectancy were excluded. In the
present study, patients with clinical hand osteoarthritis (as defined below) or structural abnormalities due to hand osteoarthritis (multiple bony swellings or radiological osteoarthritis) were included. Clinical hand osteoarthritis was defined according to the American College of Rheumatology (ACR) criteria as hand pain or stiffness on most days of the preceding month in addition to three of the following four criteria: bony swelling of two or more of the 10 selected joints, including the bilateral distal interphalangeal joints (DIPJ), two plus three, the bilateral proximal interphalangeal joints (PIPJ) two plus three and the first carpometacarpal joints (CMCJ), bony swelling of two or more DIPJ, less than three swollen metacarpalpalangeal joints and deformity of at least one of the 10 selected joints.\(^1\)

### Hand pain and functional limitation

Self-reported hand pain and functional limitation were assessed at baseline and after 2 years by the pain (five items) and function (nine items) subscales of the AUSCAN LK 3.0.\(^6\) A time frame of the past 48 h was used and responses administrated on a five-point Likert scale (0 = none to 4 = extreme). During physical examination, pain upon lateral pressure in all interphalangeal joints (IPJ) and first CMCJ was graded on a four-point scale (0 = no tenderness; 1 = patient complained of pain; 2 = patient complained of pain and winced; 3 = patient complained of pain and withdrew the joint) for intensity. The pain intensity score (range 0–60) is a reduced version of the articular index for the assessment of osteoarthritis as described by Doyle et al.\(^7\) The observer was blinded for scores obtained during previous assessments.

### Radiological assessment of hand osteoarthritis

One radiographer obtained radiographs of the hands (dorsal-volar views, both hands radiographed separately) at baseline and after 2 years employing a standard protocol with a fixed film focus distance (1.15 m). The patient’s film envelope was placed on the radiographic cassette and upon that the patient’s fingers were stretched as much as possible. The contour was outlined on the envelope at the first visit and this outline was re-used on subsequent visits.

Baseline and 2-year radiographs of the hands were scored for osteophytes and joint space narrowing (JSN) (0–3) with the help of the OARSI atlas.\(^8\) All IPJ and first CMCJ were scored by consensus opinion of two readers (SB and IW). The maximum total scores for osteophytes and for JSN were 60. Films were read blinded for patient characteristics and paired without knowledge of the chronological order. The intrareader variability for the assessment of the radiographic severity of hand osteoarthritis, depicted by the intraclass correlation coefficient, was 0.98 for osteophytes and 0.92 for JSN. The intrareader variability was based on the examination of 20 pairs of hand radiographs, which were selected randomly throughout the duration of the study period. Selection of radiographs for rescoring was set up before the start of the scoring and was done by an independent individual. Radiological progression scores were calculated by adding the increases in JSN and osteophyte scores in the DIPJ, PIPJ, first IPJ and first CMCJ after 2 years. Radiological progression was defined by JSN or osteophyte progression scores of at least 1 over the 2 years.

### Statistical analysis

Data were analysed using SPSS, version 12.0. To evaluate the magnitude of the changes observed over 2 years and to compare the responsiveness of the instruments, standardised response means (SRM) were calculated as the mean change between baseline and 2 years divided by the standard deviation of the change.\(^9\)

Spearman rank correlations were used to correlate baseline parameters.

To assess the association between changes in self-reported pain and function scores (as dependent variables) as well as between changes in osteophyte and JSN total scores (as dependent variables), linear mixed models were used with a random intercept to adjust for the familial effect within the sib pairs. Estimates of fixed effects with 95% CI were reported.

Logistic regression analyses were used to investigate risk factors for radiological progression. First, crude and adjusted odds ratios (OR; 95% CI) were calculated that were subsequently transformed into risk ratios (RR) using the formula described by Zhang and Yu\(^{10}\). This was done because OR for common outcomes are not good approximations of RR. To take

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**Table 1** Baseline characteristics of 172 patients with hand osteoarthritis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study population (n = 172)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years(^{\dagger})</td>
<td>59.7 (55.3–65.2)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>135 (78.5)</td>
</tr>
<tr>
<td>Post-menopausal, n (%)</td>
<td>117 (68.7)</td>
</tr>
<tr>
<td>Body mass index, kg/m(^2)</td>
<td>25.7 (23.6–28.1)</td>
</tr>
<tr>
<td>Hand osteoarthritis following ACR criteria, n (%)</td>
<td>129 (75.9)</td>
</tr>
<tr>
<td>Hand osteoarthritis subtypes, n (%)</td>
<td></td>
</tr>
<tr>
<td>DIPJ</td>
<td>76 (44.2)</td>
</tr>
<tr>
<td>PIPJ</td>
<td>66 (38.4)</td>
</tr>
<tr>
<td>First CMCJ</td>
<td>54 (31.4)</td>
</tr>
<tr>
<td>Right handed, n (%)</td>
<td>132 (76.7)</td>
</tr>
</tbody>
</table>

*Hand osteoarthritis was defined by the American College of Rheumatology (ACR) criteria for clinical hand osteoarthritis or the presence of structural abnormalities (multiple bony swellings or radiological osteoarthritis) in the hands.

\(^{\dagger}\)Values are medians (interquartile ranges) unless otherwise stated. CMCJ, carpometacarpal joint; DIPJ, distal interphalangeal joint; PIPJ, proximal interphalangeal joint.

**Table 2** Values at baseline and at the end and change scores over 2 years in 172 patients with hand osteoarthritis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline*</th>
<th>2 Years*</th>
<th>Change†</th>
<th>95% CI‡</th>
<th>SRM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-reported pain, range 0–20</td>
<td>6.2 (4.6)</td>
<td>7.2 (4.8)</td>
<td>1.0 (4.0)</td>
<td>0.4 to 1.6</td>
<td>0.25</td>
</tr>
<tr>
<td>Self-reported function, range 0–36</td>
<td>11.1 (8.8)</td>
<td>12.5 (9.1)</td>
<td>1.4 (6.1)</td>
<td>0.5 to 2.3</td>
<td>0.23</td>
</tr>
<tr>
<td>Pain intensity scores, range 0–60</td>
<td>3.9 (5.0)</td>
<td>8.1 (7.9)</td>
<td>4.2 (6.2)</td>
<td>3.2 to 5.1</td>
<td>0.67</td>
</tr>
<tr>
<td>Osteophyte total scores, range 0–60</td>
<td>9.3 (7.9)</td>
<td>9.7 (8.5)</td>
<td>0.4 (1.2)</td>
<td>0.2 to 0.6</td>
<td>0.35</td>
</tr>
<tr>
<td>JSN total scores, range 0–60</td>
<td>14.6 (10.5)</td>
<td>14.9 (10.9)</td>
<td>0.3 (1.0)</td>
<td>0.2 to 0.5</td>
<td>0.34</td>
</tr>
</tbody>
</table>

*Values are mean (SD).

†Mean change (SD) over 2 years.

‡95% CI of the change.

JSN, joint space narrowing; SRM, standardised response mean.
into account the intrafamily effect, robust standard errors were computed using the statistical program Stata, version 7.0.

Finally, linear mixed models were used to assess whether radiological progression was associated with changes in self-reported pain and function scores or in pain intensity scores (as dependent variables).

RESULTS

Population description

A total of 189 patients was included in the present study and 172 (91%) completed the 2-year follow-up. As depicted in table 1 the median age of the patients was 59.7 years and 78.5% were women. The majority of the patients (75%) met the ACR criteria for clinical hand osteoarthritis. Osteoarthritis occurred most often in the DIPJ.

Changes in hand pain and function scores

Self-reported pain and function scores, pain at physical examination and radiological scores at baseline and after 2 years of follow-up are presented in table 2. At baseline all parameters were correlated with each other; highest correlations were demonstrated for self-reported pain and function scores and for JSN and osteophytes (data not shown).

The self-reported pain and function scores deteriorated significantly over 2 years (table 2). Corresponding SRM were 0.25 and 0.23, respectively. An increase in self-reported pain and function scores was present in 86 (50.0%) and 91 (52.9%) patients, respectively. Thirty-five (20.3%) and 20 (11.6%) patients had no change and 51 (29.7%) and 61 (35.5%) patients had a decrease in self-reported pain and function scores, respectively. Function scores increased with 0.9 (95% CI 0.7 to 1.1) per one score increase in pain scores ($p < 0.001$). There was a statistically significant deterioration in pain intensity scores from baseline to 2 years (table 2). The corresponding SRM was 0.67. A total of 128 (74.4%) patients had an increase, 19 (11.0%) patients had no change and 25 (14.5%) had a decrease in pain intensity scores.

Progression of hand osteoarthritis with regard to osteophytes and JSN

The osteophyte and JSN total scores deteriorated statistically significantly over 2 years (table 2). Corresponding SRM were 0.34 and 0.35, respectively.

Table 3 shows the distribution in JSN and osteophyte progression scores in the DIPJ, PIPJ, IPJ and first CMCJ over 2 years. Radiological progression was demonstrated in 21.5% of patients with respect to osteophytes and in 19.2% of patients with respect to JSN. Radiological progression was seen in a single joint group in 25 and 20 patients, in two joint groups in 10 and 11 patients and in more than two joints groups in two...
and two patients, for osteophytes and JSN, respectively. The most frequent joint group combination for JSN progression was the combination of PIPJ and first IPJ and for osteophyte progression the combination of DIPJ and PIPJ.

JSN progression scores were associated with osteophyte progression scores. JSN progression scores increased, with 0.6 (95% CI 0.3 to 0.9) per one score increase in osteophyte progression scores (p<0.001). In the DIPJ and PIPJ, changes in JSN scores were moderately correlated with changes in osteophyte scores (Spearman rank correlation coefficients 0.3, p<0.001 and 0.5, p<0.001, respectively). No such correlation was seen for the first IPJ and first CMCJ.

Radiological progression in relation to age, gender and post-menopausal stage

Progression of osteophytes tends to be more frequent in middle-aged patients than in the elderly and is more frequent in women than in men (table 4). A total of 117 post-menopausal women was analysed separately; women in an early post-menopausal stage more often had JSN and osteophyte progression when compared with women in a late post-menopausal stage. Age, gender and post-menopausal stage were not associated with clinical progression.

The relation between self-reported pain and function scores, pain intensity scores and radiological progression

Changes in self-reported pain and function scores and in pain intensity scores were not associated with progression of osteophytes or JSN over 2 years. Baseline AUSCAN pain scores were higher in patients with than without JSN progression over 2 years, with a mean difference (adjusted for age, gender and family effect) of 1.8 points (95% CI 0.2 to 3.4). No such difference was seen for pain at baseline and osteophyte progression over 2 years.

DISCUSSION

In the present study patients with hand osteoarthritis demonstrated a statistically significant deterioration in self-reported hand pain and function as well as in pain assessment at physical examination over the relatively short time period of 2 years. In addition, statistically significant radiological progression of hand osteoarthritis was detected over 2 years. Currently available instruments were thus responsive and could assess changes over 2 years. More than 50% of patients reported more pain and more limitation in function over 2 years, and 20% of patients demonstrated radiological progression over 2 years. Remarkably, radiological progression occurred more often in women in an early post-menopausal stage. Deterioration of hand pain and function over 2 years was not associated with radiological progression.

Little is known about the rate of progression of pain and functional limitation in hand osteoarthritis patients. The present study provides evidence for an increase in hand pain and a decline in hand function in a considerable proportion of patients over the relatively short period of 2 years. In this observational study the longitudinal performance of the AUSCAN over a period of 2 years demonstrated sufficient sensitivity to change. There was a strong association between changes in self-reported pain and self-reported function scores, but these were not associated with radiological progression of hand osteoarthritis. This discrepancy between changes in AUSCAN scores and radiological findings is in accordance with an earlier cross-sectional study. The disparity between symptoms and structural abnormalities has also been reported with other instruments for hand osteoarthritis outcome measures and in other osteoarthritis affected joints. Pain due to hand osteoarthritis may reflect various underlying mechanisms, such as structural abnormalities, disease activity, but also perceptions that a patient has about his or her joint problem. Therefore, it could be informative to measure pain not only by a self-reported pain measure but also in another way. We used a reduced version of the Doyle index to assess pain at physical examination in the hand joints. In the original article, the articular index was valid, reliable and responsive to change. The present study confirms its responsive quality. Further validation and assessment of intra and inter-observer reliability should be performed.

The present study is the largest longitudinal study in patients with hand osteoarthritis to date and is the first to show radiological progression over a relatively short period of 2 years. Three previous population-based studies did not demonstrate progression over the mid to long term of 2 years. Three studies have been performed in patients with hand osteoarthritis, the first performed by Verbruggen et al which performed a 10-year follow-up study of 59 patients with osteoarthritis of the hands or knees. Radiological progression of DIPJ, PIPJ and first CMCJ was recorded for osteophytes (38–59% of patients) and for JSN (39–48% of patients). Balblanc et al performed a small study comprising 15 patients with symptomatic osteoarthritis of DIPJ and/or PIPJ. Significant radiographic progression in JSN, osteophytes, sclerosis, cysts and subluxation was seen after 4 years’ follow-up. Finally, in a RCT by Verbruggen et al the 85 hand osteoarthritis patients on placebo medication showed radiological progression over 3 years, especially in the DIPJ and PIPJ. In summary, the three last studies showed radiological progression in hand osteoarthritis patients only after 5–5 years, whereas in the present study, progression was seen after 2 years. This may be ascribed to the smaller sample sizes in the earlier studies, the different scoring systems to assess radiological progression (Kellgren–Lawrence global scores, Kallman or Verbruggen and Veys scoring systems in contrast to a scoring system following the OARSI Atlas or a lack of standardisation in the acquisition of hand radiographs.

Identifying predisposing factors for radiological progression may help to distinguish patients with a high risk of rapid progression who might benefit most from future structure modifying treatment strategies. We found that progression of osteophytes tends to occur more in middle-aged than in elderly patients and more in women than in men. This is in accordance with findings from a 4-year longitudinal study in a 75–79-year olds by Bagge et al in which no radiological change was observed in approximately 95% of the hand joints. Such a reduced progression rate of hand osteoarthritis in older patients may suggest a “burnout” or self-limiting age-related phenomenon. In addition, Lane et al showed in a 5-year longitudinal study that the largest average radiological progression was seen in women, especially with regard to osteophytes. A relationship between hormonal changes of the menopause and the prevalence and incidence of osteoarthritis has been suggested in previous observational studies. The first few years of the post-menopausal period is characterised by complete dampening of ovarian function and accelerated bone loss. In perimenopausal women, an increased prevalence and incidence of osteoarthritis have been found, disproportional to age. Little is known, however, about the relation between the menopause and the progression of osteoarthritis. Therefore, we investigated whether the number of years after the final menstrual period...
was associated with radiological progression over 2 years. We found that post-menopausal women in an early stage (within 10 years after the last menstrual period) had a two to threefold increased risk of radiological progression of osteophytes and JSN compared with women in a later post-menopausal stage (≥10 years after the last menstrual period). These findings encourage further research into the role of female hormones in hand osteoarthritis and whether these could be a target for therapy in middle-aged women.

The present study has several limitations. The hand osteoarthritis patients in the present study all had familial osteoarthritis and a considerable proportion also had osteoarthritis at other joint sites. Whether this specific hand osteoarthritis phenotype has influenced the progression rate is not clear. To gain further insight into the disease course in hand osteoarthritis, studies in other hand osteoarthritis phenotypes are warranted. Radiographs were scored paired for progression with the films blinded for time sequence, which may have led to a possible underestimation of progression when compared with a scoring method with paired scoring with the films in time sequence. Any misclassification of progression in our study, however, would have been non-differential.

The present study demonstrated clinical as well as radiological deterioration in a considerable proportion of patients with hand osteoarthritis already after 2 years. Currently available instruments were sensitive to change and deserve to be used to be investigated new therapies. In particular, women at middle age seem to be in need of such new therapies. More studies are needed to explore further the relationship between self-reported and radiographic outcomes and the relationship with other domains such as biomarkers and other imaging modalities, not only in the mid-term, but also in the long-term.