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THE PREVALENCE OF EROSAVE OSTEOARTHRITIS IN CARPOMETACARPAL JOINTS AND ITS CLINICAL BURDEN IN SYMPTOMATIC COMMUNITY-DWELLING ADULTS

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Submitted
ABSTRACT

Objective
To estimate the prevalence of erosive disease in 1st carpometacarpal joints (CMCJs) and investigate its clinical impact compared with radiographic thumb base (TB) osteoarthritis.

Patient and methods
Standardised assessments with hand radiographs were performed in participants of two population-based cohort studies in North Staffordshire with hand symptoms lasting ≥1 day in the past month. Erosive disease was defined as the presence of eroded or remodelled phase in ≥1 interphalangeal joint (IPJ) or 1st CMCJ following the Verbruggen-Veys classification. Hand pain and function were assessed with AUSCAN. Prevalences were estimated by dividing the number of persons with erosive lesions by population size. Linear regression analyses were used to contrast clinical determinants between persons with erosions and with radiographic TB osteoarthritis. Results were presented as mean differences with 95% confidence intervals (95%CI), adjusted for age and sex.

Results
1076 participants were studied (60% women, mean age 64.7 years (SD 8.3); 24 persons had erosive disease in the TB. The prevalence of erosive disease in 1st CMCJs was 2.2% (95%CI 1.4, 3.3). Only 0.5% (95%CI 0.2, 1.2) had erosive disease affecting IPJs and 1st CMCJs combined. More persons with erosive disease of 1st CMCJs reported pain in their TB than persons with radiographic TB osteoarthritis, AUSCAN pain and function scores were similar.

Conclusion
Erosive disease of 1st CMCJs was present in 2.2% of subjects with hand pain and was often not accompanied by erosions in IPJs. Erosive disease was associated with TB pain, but not with the level of pain, when compared with radiographic TB osteoarthritis.
Osteoarthritis (OA) of the thumb base is defined as OA in the first carpometacarpal joint (1st CMCJ) with or without scaphotrapezoid joint (STJ) OA. It often occurs together with OA at other sites in the hand, however isolated OA of 1st CMCJ is also described. The prevalence of radiographic 1st CMCJ or STJ OA is described as up to 35.8% in the general population aged > 55 years, whereas prevalences of symptomatic 1st CMCJ OA in adults from the general population aged over 60 or 70 years are estimated at 1.9% and 4.1%, respectively. Thumb base OA can be recognized radiographically by osteophytes, joint space narrowing, sclerosis and cysts.

The clinical burden of 1st CMCJ OA is considerable. Radiographic thumb base OA has the highest association with hand pain compared with other hand OA joint groups. Radiographic thumb base OA is also associated with a risk of reduced grip strength. Studies on self-reported pain and disability showed that the burden is highest in patients with combined finger and thumb base OA. The presence of 1st CMCJ OA contributed more to pain and disability than interphalangeal joints (IPJs) OA in a population with symptomatic hand OA.

More recently, erosive hand OA has become a focus of interest. The pathophysiology of erosive OA is unclear and whether erosive OA should be considered as a separate disease entity or a more severe stage of hand OA is also unclear. Most previous studies on erosive OA have focused on the IPJs. Information on the presence of erosions in 1st CMCJs remains scarce, despite the availability of a standardized (OARSI) scoring method. In 1968, Peter et al. already described that erosive OA can involve the 1st CMCJ occasionally. In 1990, Cobby et al. reported that erosions in 1st CMCJ can be present in OA patients up to 51% in combination with erosions of metacarpalphalangeal joints and STJs. No specific frequency for erosive disease in 1st CMCJs only was given in that study. No knowledge is available whether erosive OA in the IPJs is a different phenotype than erosive disease in the thumb base.

Erosive OA is a radiographic subset of hand OA with a higher clinical burden (pain, functional limitations) than non-erosive hand OA. It is unclear what the clinical impact is of erosive disease in the thumb base.

In an earlier study we performed in the Rotterdam Study we detected erosive lesions in 1st CMCJ. However, due to the study design (where the selection of hand radiographs was focused on IPJs in this sample), these erosive lesions could not be investigated in more detail in that particular study.

The aims of the present study are to describe the frequency of erosive disease in 1st CMCJs with its co-occurrence of erosive disease in IPJs and the presence of concordant pain and radiographic OA in the same thumb base. Also clinical outcomes such as pain and function are compared between radiographic thumb base OA with erosive disease in the thumb base.
METHODS

Population and study design

Data were collected from the Clinical Assessment Study of the Hand (CAS-HA) and Knee (CAS-K), both prospective, population-based, observational cohort studies in North Staffordshire. Study protocols of these studies are described elsewhere in detail\textsuperscript{18,19}. In short, all adults aged $\geq$ 50 years registered with two general practices were invited to participate in a two-stage postal survey. When they indicated that they had experienced hand symptoms within $\leq$ 12 months on the first postal questionnaire, they were invited to the research clinic. Those who attended the research clinic were included in the CAS-HA study ($n=623$)\textsuperscript{18}. CAS-K participants ($n=819$) were recruited from a further three different general practices using recruitment methods identical to CAS-HA, except that participants were invited for a clinical assessment in the CAS-K study when they reported knee pain (rather than hand symptoms) within last year\textsuperscript{19}. Ethical approval was obtained from the North Staffordshire Local Research Ethics Committee and all participants gave written consent. Only CAS-HA or CAS-K participants who indicated that they experienced hand symptoms (pain, aching, stiffness) $\geq$ 1 day during last month are included in this paper.

Radiographic assessment and scoring

Plain radiographs were completed of each hand in posteroanterior (PA) view\textsuperscript{18}. Distal, proximal and thumb interphalangeal joint (DIPJ, PIPJ and 1$^{st}$IPJ) and 1$^{st}$CMCJ were scored by two trained assessors (MM scored $n=521$, JH scored $n=555$), blinded for clinical data. Joints were scored for presence and severity of OA with the Kellgren-Lawrence (KL) grade (range 0-4)\textsuperscript{20}. Both observers re-scored fifty pairs to calculate inter- and intra-observer reliability. Inter-observer reliability (kappa) for the presence of hand OA was 0.50 (percentage agreement (PA) 90%). The intra-observer reliability for presence of hand OA was excellent (kappa=0.92 and 0.85, PA 98% and 98% for reader 1 and 2, respectively).

Erosive disease were scored by the Verbruggen-Veys scoring system\textsuperscript{10} and defined as the presence of eroded (E-phase) or remodelled, irregular, sclerotic subchondral plates (R-phase) in DIPJs, PIPJs, 1$^{st}$IPJs and 1$^{st}$CMCJs. The Verbruggen-Veys scoring does not include 1$^{st}$IPJs and 1$^{st}$CMCJs; however the same rules for DIPJs/PIPJs were applied to these joints. Figures 1 and 2 show examples of erosive disease in 1$^{st}$CMCJs. Additionally the OARSI atlas\textsuperscript{7} was used as a guide to score 1$^{st}$CMCJs for erosions. Erosions were scored by a single reader (WK), blinded for clinical data. The intra-observer reliability for erosive disease as a dichotomous variable in the Verbruggen-Veys scoring method was excellent (kappa= 0.94)\textsuperscript{21}.

Sample selection for scoring erosive disease in hand radiographs

The majority of hand radiographs were scored for erosions; exceptions were those radiographs that had no or very few osteoarthritic features. The assumption was that erosions are not present in subjects with near normal radiographs. To determine the selection for scoring erosions, KL-scores in the DIPJs, PIPJs, 1$^{st}$ IPJs and 1$^{st}$CMCJs...
Figure 1 & 2: Examples of images with erosions of 1st CMC-joints.

were summed to form an overall score (KLsum) for every participant. The population was divided in subgroups by the summation scores (range 0-72). All radiographs in subgroups with KLsum ≥3 were scored. Random samples of at least 10% of subgroups with KLsum <3 were screened and no erosive OA was seen.

**OA definitions**

The presence of pain in the thumb was determined from hand drawings; participants shaded areas where they had experienced pain lasting ≥1 day during past month. Radiographic thumb base OA was defined as KL-grade ≥2 in at least one 1st CMCJ or scaphotrapezoid joint (STJ). Symptomatic radiographic thumb base OA was defined as having radiographic thumb base OA combined with concordant pain of the thumb base. Erosive disease in the thumb base was defined as having ≥ 1 E- or R-phase in the 1st CMCJs. Erosive disease in the IPJs is defined as having at least 1 E- or R-phase in the DIPJ, PIPJ or 1st IPJ.
**Diagnosis of systemic inflammatory rheumatic diseases**

Medical records from general practitioners and the local Rheumatology hospital were reviewed to identify patients with systemic inflammatory rheumatic diseases (e.g. rheumatoid arthritis, psoriatic arthritis). Participants were categorized as having an inflammatory rheumatic disease when there was evidence of inflammatory changes on the radiographs, identified by a musculoskeletal radiologist.

**Clinical outcomes**

General characteristics of age and sex were recorded in postal surveys and height and weight were measured at the research clinics held at a local Rheumatology outpatients clinic.

**Hand pain and stiffness**

The pain and stiffness subscale of the Australian/Canadian Hand Osteoarthritis Index (AUSCAN) was completed by all participants (range 0-20 and 0-4, respectively). Self-reported pain was also assessed with the pain subscale of the Arthritis Impact Measurement Scales health status questionnaire (AIMS-2, range 0-10). Higher scores indicate more pain or stiffness.

**Hand function and performance**

Self-reported hand function was assessed with the function subscales of the AUSCAN (range 0-36) and AIMS-2 (range 0-10). Higher scores represent more limitation in hand function. The maximum gross and pinch grip strength was assessed with the JAMAR dynamometer (Sammons Preston, Chicago, IL) and B&L pinch gauge (B&L Engineering, Tustin, CA), respectively. In addition, the Grip Ability Test (GAT) was performed in the CAS-HA participants. The GAT consisted of 3 tasks (putting a flexigrip stocking over the non-dominant hand, putting a paperclip on an envelope, pouring water from a jug into a cup) which participants had to perform within 2-3 minutes. Scores are based on the time to complete the 3 tasks; higher scores correspond to poorer hand function. GAT scores of <20 are considered normal.

**General health perceptions**

General health perceptions were measured by the Short-Form 12 (SF-12), a widely used generic health status questionnaire yielding summary component scores for physical health (PCS, 0-100) and mental health (MCS, 0-100), where lower scores represent poorer perceived health and the population average is 50.

**Aesthetic and impact of hand problems**

Appearance of the hand was measured with the aesthetics subscale of the Michigan Hand Outcomes Questionnaire (MHQ, range 0-100). The impact of hand symptoms on health status was measured with the impact subscale of the AIMS-2 (range 0-10). Higher scores represent more satisfaction with aesthetics of the hand and a higher negative impact.
**Statistical analysis**

Prevalence of erosive disease of the thumb in the population with radiographic thumb base OA and concordant radiographic thumb base OA with pain is the proportion of individuals with erosive disease of the thumb. Associated 95% confidence intervals (95%CI) were calculated based on a binomial distribution.

Linear regression analyses were used to investigate differences in clinical characteristics between participants with and without erosive thumb base disease. The beta-estimate is presented as the mean difference (with 95%CI), adjusted for age and sex and in addition for the sum of KL-score of both 1st CMCJs (in order to adjust for the severity radiographic thumb base OA).

Data were analyzed with SPSS, version 20 (SPSS Inc, Chicago, Illinois).

**RESULTS**

**Clinical characteristics and demographics**

The cohorts yielded a combined sample of 1442 potentially eligible participants. Participants with incomplete radiographs (n=56), without hand symptoms ≥1 day during last month (n=266) and those with inflammatory disease (n=44) were excluded (Figure 3), leaving a total of 1076 eligible participants (60% women, mean age 64.7 years (SD 8.3)).

![Flowchart of selection of CAS-K & CAS-HA participants for EOA analyses](image)

Figure 3: Flowchart of selection of CAS-K & CAS-HA participants for EOA analyses.
In 56% (n=605) pain was present in any left or right thumb base, of which 364 persons had bilateral thumb pain. Radiographic thumb base OA was present in 54% (n=585) of participants, of which 396 persons (67%) had bilateral radiographic thumb base OA. All STJs with a KL-grade ≥ 2, also had at least one 1st CMCJ with a KL-grade ≥ 2. Of all persons with radiographic thumb OA, 954 1st CMC joints had a KL-score of at least 2 (517 left 1st CMCJs, 437 right 1st CMCJs). Of these 954 joints, 493 joints were painful (262 left 1st CMCJs, 231 right 1st CMCJs). In 31% (n=331) of the participants, concordant thumb base pain and radiographic thumb base OA was seen (table 1).

**Occurrence and prevalence of erosive disease in the thumb base**

Of the 1076 individuals, 24 had at least one E- or R-phase in any 1st CMCJ. The prevalence of erosive disease in 1st CMCJ was 2.2% (95%CI 1.4, 3.3) (table 1).

Twenty-four patients had at least one erosive lesion in the 1st CMCJs with 4 persons having both 1st CMCJs involved. Of the 28 joints affected, 23 were an E-phase and 5 were an R-phase.

Of the 28 1st CMCJs with an erosive lesion, 22 joints were concordantly painful. These painful joints were present in 19 patients.

In 1.7% (n=18) of participants erosive disease was exclusively present in 1st CMCJs and only 0.5% (n=6) had erosive disease in both the IPJs and 1st CMCJs. Of the 1076 patients, 98 had EOA in 1 IPJ, 1st CMC or both (table 1).

In the population with radiographic thumb base OA, the prevalence of erosive disease was 4.1% (95%CI 2.6, 6.1), whereas in the population with concordant pain in the thumb base and radiographic thumb base OA a prevalence of 6.0% (95%CI 3.7, 9.2) was seen, as shown in table 2. The prevalence of erosive disease in the thumb base was higher for men than women in all groups.

### Table 1: Baseline characteristics of 1076 persons in the population with hand symptoms lasting ≥ 1 day during last month.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, no. (%)</td>
<td>650 (60)</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>64.7 (8.3)</td>
</tr>
<tr>
<td>BMI (kg/m²), mean (SD)</td>
<td>29.1 (5.1)</td>
</tr>
<tr>
<td>Pain in any left or right thumb base (TB), no. (%)</td>
<td>605 (56)</td>
</tr>
<tr>
<td>Radiographic TB OA, no. (%)*</td>
<td>585 (54)</td>
</tr>
<tr>
<td>Concordant TB pain and radiographic TB OA**, no (%)</td>
<td>331 (31)</td>
</tr>
<tr>
<td>Persons with erosive disease*** in any 1st CMCJs, no. (%)</td>
<td>24 (2.2)</td>
</tr>
<tr>
<td>Persons with erosive disease exclusively 1st CMC, no. (%)</td>
<td>18 (1.7)</td>
</tr>
<tr>
<td>Persons with erosive disease in 1st CMCJ combined with interphalangeal joints, no. (%)</td>
<td>6 (0.5)</td>
</tr>
<tr>
<td>Persons with erosive disease only in interphalangeal joints (DIPJ/PIPJ), no. (%)</td>
<td>74 (6.9)</td>
</tr>
</tbody>
</table>

SD, standard deviation; BMI, Body Mass Index; OA, osteoarthritis; DIPJ, distal interphalangeal joint; PIPJ, proximal interphalangeal joint; * = presence of Kellgren and Lawrence grade ≥ 2 in at least one joint with KL≥2 in carpometacarpal joint (1st CMCJ) or scaphotrapezoid joint (STJ) in any hand; ** = Radiographic TB OA combined with thumb pain, *** = at least having one eroded (E-phase) or remodelled joint (R-phase), according to the Verbruggen-Veys scoring method.
Clinical burden of erosive disease in 1st CMCJs in relation to radiographic thumb base OA

All those with erosive disease of the thumb had radiographic thumb base OA, patients with erosive disease of the 1st CMCJs reported more often thumb pain than those with radiographic thumb base OA, also after adjustment for age and sex (mean difference 22.4% (95%CI 6.9, 37.8)) (table 3). Patients with erosive disease of the thumb were slightly older than those with radiographic thumb base OA (table 3). KL-scores of the 1st CMCJs were also higher in those with erosive disease of the thumb than those with radiographic thumb base OA (mean difference 2.6 (95% CI 1.7, 3.4)), as shown in table 3. Persons with erosive disease in the thumb reported higher values for pain on the AUSCAN and function on both AUSCAN and AIMS-2, and lower scores for power and pulp grip, GAT, perceived physical health and appearance of their hands (table 3).

Clinical burden of erosive disease in thumb in relation to radiographic thumb base OA in the same thumb

Nineteen out of 24 patients with erosive disease of the thumb had concordant pain in the thumb base, whereas 311 persons with radiographic thumb base OA reported concordant pain (mean difference 23.7% (95% CI 7.0, 40.5)). However, when the level of pain was compared between the persons with radiographic thumb base OA and concordant pain no difference was found in pain, stiffness, functional limitations as assessed by AUSCAN, power grip, pulp pinch strength and performance of the GAT. Also no relevant differences were seen in the AIMS-2 Impact subscale, PCS and MCS between patients with erosive disease in the thumb and those with concordant pain and radiographic OA in thumb base (data not shown).
Clinical burden of erosive disease in 1st CMCJs in relation to erosive OA of interphalangeal joints

Erosive disease in 1st CMCJs was more often present in men than in women, which is especially remarkable since erosive OA of IPJs was most prevalent in women. No large differences were found in pain, stiffness, functional limitations, performance tests, appearance and impact between persons with erosive disease in the thumb and those with erosive disease in the IPJs (data not shown).
DISCUSSION

We studied the prevalence of erosive disease in 1st CMCJs in 1076 individuals from a population based cohort, and found a prevalence of 2.2% in persons from the general population with hand symptoms. Only a few people had both erosive OA in the IPJs and erosive disease in the 1st CMCJs, while the rest have erosive lesions in 1st CMCJs or in IPJs exclusively. Persons with erosive disease in the 1st CMCJs reported more often pain in the affected joint and had higher sum scores of the KL-grade in 1st CMCJs compared with persons with radiographic thumb base OA; males tended to be more often affected by erosive disease in the 1st CMCJs. No differences in the level of hand pain, stiffness or functional limitations were seen between persons with erosive lesions in 1st CMCJs and persons with concordant pain and radiographic OA of the thumb base.

As expected, the prevalence of erosive lesions in 1st CMCJs is low in the general population with hand symptoms. We found that 4.1% of adults aged ≥ 50 years with radiographic thumb base OA have erosive lesions in 1st CMCJs. A striking finding was that erosive lesions in 1st CMCJ were more prevalent in males, in contrast to interphalangeal erosive OA that affected women more often16,28. Age could confound the results, however strenuous manual activities in males have previously been linked to thumb base OA29 and those occupational exposures prevalent in the local population (e.g. occupations in the pottery industry) could also explain the gender difference. Fontana et al. reported in a case-control study that occupational risk factors (such as manual occupations or professions with repetitive thumb use) were not associated with a higher prevalence of OA in 1st CMCJs30. Specific studies that have analysed the prevalence of erosive OA of the thumb in relation to manual occupation are yet not available in the literature. Further studies are needed to confirm these findings.

This study also showed that the co-occurrence of erosive lesions in 1st CMCJs with IPJs is rarely present; most erosive lesions in the 1st CMCJ occurred isolated without erosions in the IPJs. This was an interesting finding, since it can give us insight in the pattern of occurrence of erosions in hand joints and whether erosive disease in 1st CMCJs behaves differently from erosive lesions in IPJs only. At the moment, it is unclear whether erosive OA in general is a separate entity from hand OA (e.g. a disease with a systemic pathogenesis) or whether it is a severe subset of OA. Recently, Haugen et al. reported that erosions of the hand was associated with a higher odds of knee subchondral bone attrition (compared with persons with no OA in the DIPJ/PIPJ), which is considered as a result of bone remodelling due to biomechanical stress and appears radiographically like central erosions of IPJs31. They also reported that erosive hand OA is not associated with bone mineral density (BMD), which was used as a proxy for systemic bone changes. These results suggested that erosive OA may be a result of mechanical load through the joints leading to a more severe disease. However, Zoli et al. reported that erosive OA is associated with lower BMD suggesting that persons with erosive OA are more likely to develop osteoporosis32. Other studies showed that factors such as higher C-reactive protein33, an increased power Doppler signal and synovitis on ultrasound is associated with erosive OA34,35, and familial predisposition36 suggesting an underlying systemic cause for erosive OA.

The additional value of the present study was that detailed assessments of the hand were collected (e.g. clinical examination, AUSCAN, AIMS-2 and SF-12). This
made it possible to quantify pain, functional limitation and health status in erosive disease in a general population with hand symptoms in more detail than previous studies have allowed. Although we found a difference in the prevalence of concordant pain between persons with erosive disease and radiographic OA in the thumb, there was no difference found in the level of hand pain, stiffness or functional limitations on both AUSCAN and AIMS-2 subscales nor in grip strength, pinch grip strength, PCS, and MCS. An explanation could be that other patient effects that contribute to pain, such as genetic or psychosocial factors (e.g. expectation and experience of patients) are also influencing the scores on these questionnaires and therefore could not discriminate these groups.

Persons with erosive disease of the thumb did not report poorer overall perceived physical health than persons with concordant pain and radiographic OA of the thumb base, as reflected by the PCS. No older studies on erosive lesions of 1st CMCJs and health status are available. Bijsterbosch et al. reported no difference in health-related quality of life in persons with erosive OA of the IPJs compared with persons with non-erosive OA, but no subgroup analysis with erosive disease in 1st CMCJs was available.

Several limitations in the present study deserve mentioning. Although both cohorts gathered comparable data, they were assembled in subtly different ways – one on the basis of knee symptoms, the other on the basis of hand symptoms in the past 12 months. Biased estimates from the knee cohort would be a concern although the difference in prevalence estimates between the two cohorts was not large which justifies their combination. Another limitation could be the methods used to determine the presence of erosive disease in 1st CMCJs. Until present there is no consensus about how erosive disease in the thumb should be defined and whether it should be considered as the same phenotype as interphalangeal erosive OA. An under- or overestimation of the prevalences is possible, since the hand drawings for indicating pain in the thumb were not restricted to the thumb base. Finally, the absolute number of persons with erosive lesions in 1st CMCJs was not large and may be too small to detect differences in the clinical outcome measures when compared with persons with concordant pain and radiographic OA of the thumb base. Studies with larger numbers of erosive disease in 1st CMCJs are needed to confirm these findings.

In conclusion, we have identified erosive lesions in 1st CMCJs, mostly isolated without involvement with interphalangeal erosive OA. Although no statistic differences in hand pain or function was found in persons with erosive disease in thumb base compared with those with radiographic thumb base OA, a difference in the prevalence of pain was seen. We hope our systematic description of erosive OA in 1st CMCJs will facilitate further investigations in this topic.

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REFERENCE LIST


