Prolonged morning stiffness is common in hand OA and does not preclude a diagnosis of hand osteoarthritis

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Brief Report

Prolonged morning stiffness is common in hand OA and does not preclude a diagnosis of hand osteoarthritis

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SUMMARY

Objective: Prolonged morning stiffness (>60 min) is considered a symptom of inflammatory arthritis, but has a poor discriminative ability. Knowledge about morning stiffness in patients with hand osteoarthritis (OA) is lacking. We therefore studied morning stiffness in patients with hand OA.
Design: Patients with primary hand OA according to their treating rheumatologist in the Hand OSTeoArthritis in Secondary care (HOSTAS) cohort were studied. Severity of morning stiffness was examined with Australian/Canadian hand OA index (AUSCAN) and presence and duration of morning stiffness were examined with a standardized questionnaire. Association of patient and disease characteristics with prolonged morning stiffness (>60 min) were analyzed with logistic regression.
Results: In total 519 of 538 patients had available data about duration of morning stiffness, of whom 89 (17%) had prolonged morning stiffness. Severity of stiffness was mild in 158 of 525 (30%), intermediate in 194 (37%), severe in 97 (18%) and extreme in 19 (4%) patients. Patients with prolonged morning stiffness reported more pain, worse physical function and had a reduced mental and physical quality of life. Patients with prolonged morning stiffness also had more severe radiographic disease, although the association did not reach statistical significance.
Conclusions: Prolonged and severe morning stiffness are frequently present in patients with hand OA. Patients with these symptoms report more pain in general and have a lower quality of life than patients that do not report these symptoms. Prolonged morning stiffness does not preclude a diagnosis of hand OA.

Introduction

Prolonged morning stiffness is commonly acknowledged as a symptom of inflammatory arthritis in general and rheumatoid arthritis (RA) in particular. It was part of the American College of Rheumatology (ACR) RA classification criteria in the past[1] and it is also part of the early referral recommendation for newly diagnosed RA[2]. Furthermore, prolonged morning stiffness is part of the EULAR defined characteristics describing arthralgia at risk for developing RA[3].

Short duration morning stiffness on the other hand is regarded as a symptom of osteoarthritis (OA) and short morning stiffness is included in the tree format of clinical ACR classification criteria of hip OA and classical format ACR classification of knee OA[4,5]. Morning stiffness is sometimes used as a clinical outcome measurement in OA trials[6] and patients with OA rank morning stiffness as second most important patient reported outcome (PRO) after pain.[7]

However, morning stiffness is hard to define, even by clinicians, and patients often have been forced to report a cut-off time[8]. Moreover, duration of morning stiffness was shown to be a poor discriminator between RA and noninflammatory joint diseases by Hazes *et al.*[9] Duration of morning stiffness was also a poor discriminator between active vs inactive disease in RA patients, whereas severity of morning stiffness was able to discriminate these two conditions[9].

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Studies describing the characteristics of stiffness or morning stiffness in patients with OA are few and mostly concern clinical trials using morning stiffness as outcome measurement[10]. And although in patients with hand OA, the presence of stiffness is considered a core symptom that can result in functional disability and probably diminished quality of life, knowledge about the characteristics of stiffness and morning stiffness in patients with hand OA is lacking. We therefore studied the presence of morning stiffness in patients with primary hand OA, its characteristics and whether prolonged morning stiffness is present in these patients.

Methods

Patients study population

Data from the Hand OSTeoArthritis in Secondary care (HOSTAS) study was used, in which consecutive patients with primary hand OA were included between 2009 and 2015. Details of study procedure and references were published before[11]. In short, hand OA was diagnosed by the treating rheumatologist, exclusion criteria were any other pathological condition explaining the hand symptoms such as RA, psoriasis and secondary OA. Written informed consent was obtained from all participants. The study was approved by the Leiden University Medical Center (LUMC) medical ethics committee. Demographics and clinical characteristics were collected by standardized questionnaires, including the Dutch-language version of the Australian/Canadian hand OA index (AUSCAN) assessing severity of stiffness after first awakening in the morning with 5 answer categories (none, mild, moderate, severe and extreme) and a morning stiffness question embedded in a hand questionnaire that inquired about "stiff joints from waking" with 4 answer categories for duration (none, <30 min, 30–60 min, >60 min) after which patients were asked to assign what joints were stiff on a hand diagram (Fig. 1). Quality of life was captured with short form (SF)-36 for health related quality of life (used to calculate norm based physical (PCS) and mental (MCS) component scales, using age- and sex-specific Dutch-population based norms, with higher scores indicating better outcomes). Trained research nurses performed the physical examination, assessing the distal interphalangeal (DIPJs), proximal interphalangeal (PIPJs), interphalangeal (IPJs), metacarpophalangeal (MCPJs) and first carpometacarpal (CMC1Js) joints of both hands (30 per patient) for pain upon palpation on a 0–3 scale. Fulfillment of the ACR criteria for clinical hand OA was determined. Patients were followed for up to 8 years with yearly questionnaires and two-yearly visits. Follow-up is on-going; at present median follow-up is 5 years (Inter Quartile Range (IQR); 3–8 years), 202 patients have concluded their 8 year visit.

Baseline posteroanterior radiographs of both hands were scored for osteophytes and joint space narrowing (JSN) following the Osteoarthritis Research Society International atlas: DIPJs, PIPJs, and CMC1Js from 0 to 3; IPJs and scaphotrapeziotrapezoid joints (STTJs) 0 (absent) or 1 (present). Scores of osteophytes and JSN were totaled resulting in sum scores reflecting radiographic severity. In addition

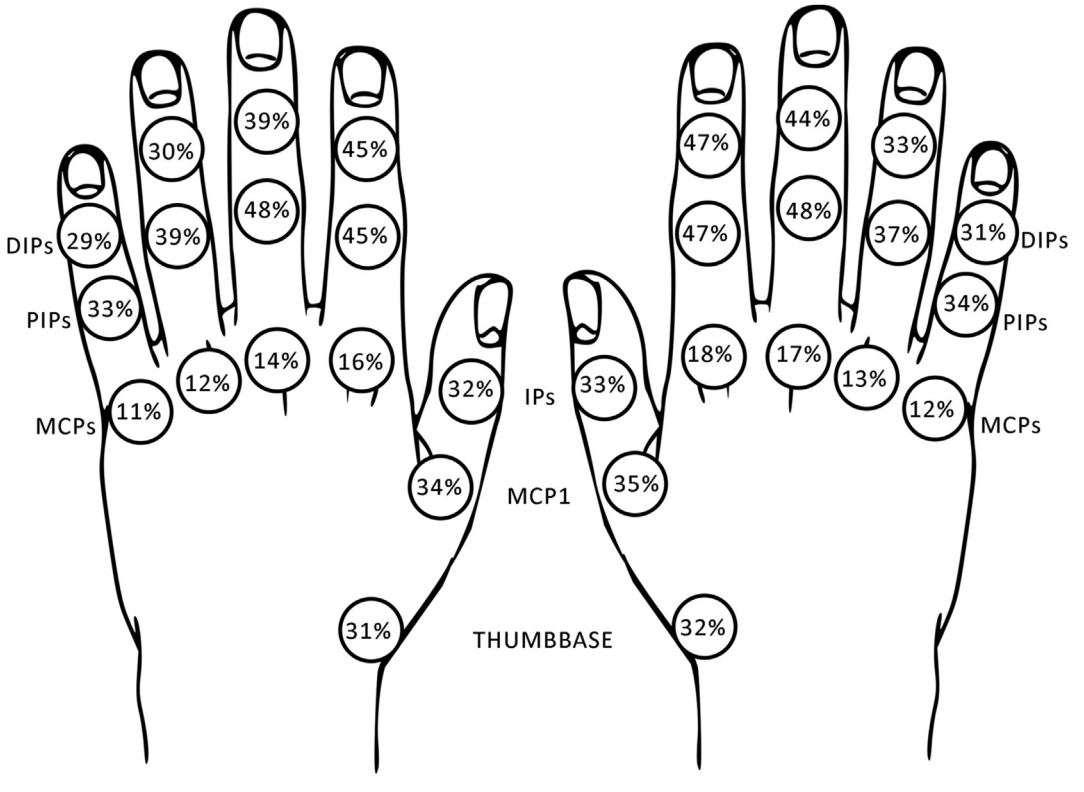

Fig. 1

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Percentage of patients having joint stiffness per joint. ***n*** = 528. DIP: distal interphalangeal joint, PIP: peripheral interphalangeal joint, MCP: metacarpal phalangeal joint.

DIPJs and PIPJs (16 joints per patient) were scored following Verbruggen-Veys (VV) anatomical phase scoring. Erosive disease was defined as having ≥1 joint in an erosive or remodeled phase. A single experienced reader (WD) scored all radiographs, blinded for demographic and clinical data, with high intraobserver reliability; intraclass correlation coefficient for different features was >0.9[11].

Statistical

Prolonged morning stiffness was defined as morning stiffness of more than 60 min. Crude odds ratios (ORs) with 95% confidence intervals (CI) were estimated with logistic regression to investigate the association between patient and disease characteristics and prolonged morning stiffness, with the latter as dependent and the patient and disease characteristics as the independent variables. Sensitivity analyses were performed adjusting for sex, body mass index (BMI) (kg/m^2) and age and, in the case of quality of life, also for AUSCAN pain on baseline. Pearson correlation coefficient was calculated to assess correlation between severity of morning stiffness and duration of stiffness. There was no indication of missing data being not at random. Analysis were performed for patients having complete data for the analysis in question. Numbers for each model are presented as notes in the tables.

Results

Patient characteristics and characteristics of stiffness

Characteristics of 538 patients included in the study are shown in Supplemental Table 1. Mean age was 61 years (SD 8.6), 86% female, mean BMI was 27 (SD 4.8) and 90% fulfilled ACR criteria for hand OA.

Morning stiffness was present in 449 patients (87%, $n = 519$). In 237 patients (46%) duration was <30 min, in 123 (24%) it was 30–60 min, and in 89 (17%) it was >60 min. When asked about severity of morning stiffness (AUSCAN stiffness), 468 (89%, $n = 525$) reported some stiffness, of whom 158 (30%) had mild, 194 (37%) had intermediate, 97 had severe (18%) and 19 (4%) had extreme morning stiffness. Correlation between duration of morning stiffness and morning stiffness severity was moderate with a Spearman's rho of 0.52 (Supplemental Table 2), whereas absolute agreement between presence of AUSCAN stiffness and presence of morning stiffness was 92%. Presence of stiffness was most frequent in second and third PIPs and DIPs (Fig. 1).

Characteristics of patients with long morning stiffness

Eighty nine patients (17%) had prolonged morning stiffness (>60 min). These patients had more radiographic damage and erosive disease than patients without prolonged morning stiffness, although these differences did not reach statistical significance. Patients with prolonged morning stiffness reported significantly more pain, had worse physical function and had significantly lower physical and mental quality of life as compared with patients without prolonged morning stiffness (Table I). Adjusting for BMI, sex and age and, in case of physical function and quality of life for AUSCAN pain, did not alter these results. Of patients with prolonged morning stiffness, one was diagnosed with RA during follow-up after 28 months.

Discussion

In this study we showed that prolonged morning stiffness is present in roughly one fifth of patients with primary hand OA and that presence of morning stiffness in these patients is associated with more pain, worse physical function and a reduced quality of life. Patients with prolonged morning stiffness had also longer symptom duration and more severe disease on hand radiographs, although these associations were not statistically significant.

$N = 519$	Morning stiffness >60 min		OR (95% CI)
	No $N = 430$	Yes $N = 89$	
Age, mean (SD) years	60.6 (8.3)	61.8 (9.2)	1.02 (0.99; 1.04)
Sex, *n* (%) women	374 (87)	73 (82)	1.46 (0.80; 2.69)
BMI,* mean (SD) kg/m^2	27 (4.8)	28 (4.5)	1.03 (0.98; 1.08)
Fulfilling ACR criteria, (*n* %)	391 (90)	79 (89)	0.79 (0.38; 1.64)
Duration of complaints,† median (IQR) years	5.2 (1.9–12)	5.4 (1.9–13)	1.02 (1.00; 1.05)
Osteophyte sum score,‡ median (IQR) (range 0–58)	9.0 (5.0–18)	13 (5.0–22)	1.02 (1.00; 1.05)
JSN sum score,‡ median (IQR) (range 0–58)	7.0 (2.0–17)	9.0 (4.0–18)	1.01 (0.99; 1.04)
Erosive disease, *n* (%)	119 (28)	31 (36)	1.44 (0.88; 2.34)
Soft swollen joint(s) present, *n* (%)	132 (30)	28 (32)	1.04 (0.63; 1.70)
AUSCAN pain,§ mean (SD) (range 0–20)	8.7 (4.2)	11.7 (4.1)	1.20 (1.12; 1.27)
AUSCAN function,§ mean (SD) (range 0–36)	14 (8.1)	21 (7.8)	1.11 (1.07–1.14)
SF-36**			
PCS, mean (SD) (range 0–100)	46 (7.9)	40 (8.3)	0.92 (0.89–0.95)
MCS, mean (SD) (range 0–100)	52 (8.0)	48 (10.6)	0.95 (0.93–0.98)

*$n = 511$, †$n = 493$, ‡$n = 515$, §$n = 516$, **$n = 503$. ACR = American college of Rheumatology criteria for hand OA. BMI = Body mass index. AUSCAN = Australian/Canadian osteoarthritis hand index. JSN = Joint Space Narrowing. SF-36 = Short-form 36, with norm based scores with a mean of 50 and SD of 10 using age and sex-specific Dutch population-based norms. MCS = mental component scale. PCS = physical component scale. OR = Odds ratio's with 1 unit of the independent variable as increment. CI = Confidence interval.

Table I

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Characteristics of patients with and without prolonged (>60 min) morning stiffness

To our knowledge the present study is the first to show the prevalence of prolonged morning stiffness in hand OA and its association with disease characteristics. Therefore, other studies are necessary to verify our results. In line with our results, a previous hand OA study showed that stiffness in general is associated with pain in patients[12], and a previous RA study showed correlations between morning stiffness and lower physical health-related quality of life[13]. In another study aiming to select clinical characteristics for classification purposes, duration of morning stiffness was inversely associated with hand OA although AUC was low[14]. Our study is the first to show that prolonged morning stiffness in patients with hand OA is associated with a lower health-related quality of life, independent of pain. It is therefore important to assess stiffness in patient care and clinical trials, because it could be a potential target for interventions such as physical therapy[10].

Patients with prolonged morning stiffness did not differ much on other characteristics, although they seemed to have more severe radiographic disease. The etiology of prolonged morning stiffness is unclear, but it is hypothesized to reflect inflammation and is thought to be the result of the circadian rhythm of proinflammatory cytokines[15]. Although inflammation plays a significant role in hand OA, understanding the etiology of morning stiffness with this 'circadian rhythm of proinflammatory cytokines hypothesis' is hard, because in hand OA, such a rhythm has not been described. Another explanation might be that for patients it is very hard to describe the phenomenon of morning stiffness and define its duration[8]. The simple question whether morning stiffness is present and what its duration is, might therefore be insufficient to discriminate between morning stiffness that is inflammatory in character and morning stiffness that is not. The latter may have a more structural etiology such as bone and/or soft tissue deformity, although we could not find a significant association with radiographic severity. Furthermore, patients with hand OA may define the duration of morning stiffness longer that 60 minutes when it is more or less constant throughout the day or when it is present after each period of inactivity. In clinical practice, these refinements can be made clear by an interview of the treating physician, but such refinements are lacking in standardized questionnaires, such as used in most clinical studies including the present.

Another explanation may be that the patients in our cohort with prolonged morning stiffness may have had an underlying inflammatory rheumatic disease. However, the presence of such a disease at baseline was reason for exclusion. During follow-up only 1 of 89 patients with prolonged morning stiffness developed RA after 28 months and we think it unlikely that this explains the presence of prolonged morning stiffness in our patients.

It thus seems that prolonged morning stiffness as defined by standardized questionnaires does not preclude a diagnosis of hand OA. These findings are in line with previous research from Hazes *et al.*, who found that prolonged morning stiffness did not discriminate between patients with RA and patients with non-inflammatory arthritis including OA[9]. In our study a control group was lacking and we could therefore not study sensitivity and specificity of the presence of prolonged morning stiffness. However, the goal of this study was not to show that prolonged morning stiffness should be used as a positive diagnostic criterion, but rather one should be careful to use it as a negative criterion. A more thorough interviewing technique such as used by most physicians in daily practice might be more discriminative, however this is a very speculative hypothesis that needs further study.

In conclusion, prolonged morning stiffness of more than 60 minutes can be present in patients with hand OA and is associated with more pain, worse physical function and a lower quality of life. Its presence should not preclude a diagnosis of hand OA.

Data availability

Due to privacy and ethical concerns data are not publicly available. Data are available from the corresponding author upon reasonable request.

Contributions

Conception and design of the study (LAvdS, MK), acquisition of data (LAvdS, MK), analysis and interpretation of data (LAvdS, IKH, DF, MK). All authors are involved in drafting the manuscript for intellectual content, and approved the final version. LAvdS takes full responsibility for the integrity of the work as a whole, from inception to finished article.

Declaration of interest

M.K. reports research grants from the Dutch Arthritis Society and EULAR, consultancy fees from Abbvie, Pfizer, Kiniksa, Flexion, Galapagos, Jansen, CHDR, Novartis, UCB and royalty fees from Wolter Kluwer and Springer Verlag, all paid to her department. She is board member of OARSI, member of EULAR Council and President of the Dutch Society for Rheumatology. All other authors report no conflicts of interest.

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2022.10.022.

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