Clinical aspects of hand osteoarthritis : are erosions of importance?

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PAIN IN HAND OSTEOARTHRITIS IS ASSOCIATED WITH INFLAMMATION: THE VALUE OF ULTRASOUND

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ABSTRACT

Objective

To investigate the association of ultrasound (US) features - gray scale (GS) synovitis, synovial thickening, effusion and power Doppler signal (PDS) - and symptoms in hand osteoarthritis (HOA).

Methods

Fifty-five consecutive patients (mean age 62 years, 87 % women) with HOA, fulfilling the American College of Rheumatology criteria, were assessed for pain upon palpation and filled in Australian/Canadian Osteoarthritis Index (AUSCAN) scores, visual analogue scale pain and Short Form-36 (SF-36). US was performed in all metacarpophalangeal, proximal interphalangeal, distal interphalangeal, first interphalangeal and first carpometacarpal joints and features semiquantitatively scored (0-3). Generalized equations estimations were used to calculate odds ratios (OR, with 95% confidence intervals (95%CI)) for the association between US features and pain per joint adjusted for relevant confounders. The association between US features summated scores and self-reported outcomes was studied by linear regression analysis.

Results

GS synovitis, effusion, synovial thickening and PDS were shown in 96%, 91%, 73% and 86% of patients, respectively. US features were dose-dependently associated with pain upon palpation (OR 4.5 (95%CI 2.2 to 9.0), 4.4 (2.0 to 9.4), 4.9 (2.2 to 11.0) and 4.1 (2.2 to 7.9)). GS synovitis was associated with AUSCAN pain, stiffness and SF-36, and effusion with AUSCAN pain.

Conclusions

GS synovitis, effusion, synovial thickening and PDS are associated with pain in HOA, suggesting a role for inflammation. Further follow-up studies are warranted.

INTRODUCTION

Hand osteoarthritis (HOA) causes considerable pain and disability[1,2]. The source of the pain is still unclear. Radiographic OA features show only a modest association with symptoms in HOA[3]. Radiography, however, is unable to visualize soft tissue such as synovitis and effusion. Ultrasonography (US) is an easy non-invasive procedure, with good availability and minimal discomfort for the patient, and can be used to study soft tissue in HOA.

A few studies on US in HOA have been published. They show that inflammatory features are often present in symptomatic HOA[4,5]. The association between pain and US features is still largely unknown.

The aim of the present study was to investigate the presence of inflammatory features and the association of US features - gray scale (GS) synovitis, synovial thickening, effusion and power Doppler signal (PDS) - with pain, function and health related quality of life (HRQoL) in HOA.

MATERIALS AND METHODS

Patient population and OA diagnosis

Consecutive patients were recruited from the rheumatology outpatient clinic of the Leiden University Medical Center, a secondary consultation centre for the region, in Leiden, the Netherlands from May 2008 until May 2009. Local medical ethics committee approval was obtained.

All patients met the American College of Rheumatology criteria for HOA and were at least 45 years of age[6]. Exclusion criteria were: trauma or an operation on the hands up to 6 months before inclusion, an intra-articular injection up to 3 months before inclusion, oral corticosteroids one month before inclusion, positive rheumatoid factor, carpal tunnel syndrome or another inflammatory joint disease. All patients gave informed consent.

Clinical assessment

Demographic characteristics were collected by standardised questionnaires. From all patients were obtained 100 mm visual analogue scale (VAS) and Australian/ Canadian Osteoarthritis Index (AUSCAN) pain, function and stiffness subscales over the preceding 48 hours[7].

HRQoL was assessed by the Short Form-36 (SF-36) physical component summary score (PCS), which was derived using norm-based data from the Dutch population. This means the score is standardised to a mean of 50 with a standard deviation of 10[8].

During physical examination, first carpometacarpal joints (CMCJs), first interphalangeal joints (IPJs), metacarpalphalangeal (MCPJs), proximal interphalangeal joints (PIPJs) and distal interphalangeal joints (DIPJs) from both hands were examined using the Doyle index[9]. No analgesics were allowed for 72 hours preceding the clinical and US assessment.

US procedure

US was performed on the same day as the clinical assessment by two ultrasonographers (MCK, WYK) in consensus, using a Toshiba Applio scanner (Toshiba Medical systems,

Tustin, California) with a 10-14 MHz linear array transducer. PDS was assessed with a pulse repetition frequency (PRF) of 13.2 kHz and a medium wall filter. Gain was adjusted until background signal was removed.

Hand joints were scanned on the dorsal side in longitudinal and transverse planes[10]. Features had to be present in both planes. Each joint was scored for GS synovitis defined as a composite of effusion and synovial thickening, as described[10].

In addition of GS synovitis, synovial thickening and effusion were scored separately. Synovial thickening and effusion were scored in accordance with the scoring system for rheumatoid arthritis[11]. The definition of synovial thickening and effusion followed the Outcome Measures in Rheumatoid Arthritis Clinical Trials definitions[12]. Synovial thickening is defined as an abnormal hypoechoic intra-articular material that is non-displaceable and poorly compressible and may exhibit PDS. Effusion is defined as an abnormal hypoechoic or anechoic intra-articular material that is displaceable and compressible and does not exhibit PDS.

All US features were scored using a semiquantative scale: 0=none, 1=mild, 2=moderate and 3=severe[10].

PDS and synovial thickening grade 3 was only seen in 2 and 8 joints, respectively. Therefore grade 2 and 3 were combined in the analyses.

Intraobserver variability was tested by performing a second US scan in 10% (randomly chosen) of patients on the same day after at least 5 hours. In between at least one other US assessment was performed. The ultrasonographers were blinded to clinical findings. The intraobserver variability, taking into account the severity of the score, depicted by the kappa value, was 0.73 for effusion, 0.73 for synovial thickening and 0.57 for PDS.

Statistical analysis

The association of US features with pain upon palpation of separate hand joints was studied using generalized estimated equations. Relative risks were presented as odds ratios (OR) with 95% confidence intervals (95%CI). In multivariate analyses, adjustments were made for patient effects and confounders. To investigate whether US features were independently associated with pain, adjustments were made for other US features. We compared summated scores of US features with self-reported pain, disability and HRQoL using linear regression analysis, adjusting for age, sex, body mass index (BMI) and US features when appropriate.

Data were analyzed using SPSS for Windows, version 16.0 (SPSS, Chicago, Illinois, USA).

RESULTS

Study population

Fifty-six patients with HOA were recruited. One patient received an intra-articular injection and was excluded. Hence 55 patients were analysed. Demographic and clinical characteristics are described in table 1. Mean age was 62 years and 87% were female. Mean AUSCAN and VAS pain scores were 9 and 50, respectively.

Table 1: Demographic and clinical characteristics of 55 patients with hand osteoarthritis (HOA).

Variable	HOA patients (n=55)
Age (years), mean (SD)	62.0 (8.9)
Female, number (%)	48 (87.3)
BMI (kg/m^2), mean (SD)	27.6 (4.5)
Symptom duration (years), median (range)	5.0 (0-55)
Painful joints upon palpation (no.), median (range)	9.0 (0-30)
VAS pain (mm), mean (SD)	50 (22.6)
AUSCAN pain (0-20), mean (SD)*	9.1 (4.2)
AUSCAN stiffness (0-4, mean (SD)*	1.8 (1.1)
AUSCAN function (0-36), mean (SD)*	14.8 (7.5)
SF-36 PCS (0-100), mean (SD)*	44.6 (8.6)

* 52 completed AUSCAN scores and 49 completed SF-36 were available.
SD=standard deviation, BMI=body mass index, VAS=visual analogue scale, AUSCAN=Australian/Canadian Osteoarthritis Index, SF-36=Short-Form 36, PCS=Physical component summary score.

Prevalence of US features

Nearly all (96%) patients with OA had GS synovitis in at least one hand joint; the median number of affected joints per patient was six (table 2). Effusion, synovial thickening and PDS were less commonly seen (91%, 73% and 85%, respectively). Twenty per cent of all hand joints showed GS synovitis, consisting mainly of effusion.

US features were equally distributed between left and right hands, and were predominantly found in 1st CMCJ, 2nd and 3rd PIPJ and DIPJ (see supplementary file

Table 2: Prevalence of ultrasound (US) features in 55 patients with hand osteoarthritis (HOA).

US features	HOA patients (n=55)
Gray scale synovitis*	
Patients (n (%))	53 (96.4)
Affected joints (median (range))	6.0 (0-13)
Total score (median (range))	8.0 (0-24)
Effusion*	
Patients (n (%))	50 (90.9)
Affected joints (median (range))	6.0 (0-13)
Total score (median (range))	7.0 (0-24)
Synovial thickening*	
Patients (n (%))	40 (72.7)
Affected joints (median (range))	2.0 (0-9)
Total score (median (range))	2.0 (0-14)
Power Doppler signal*	
Patients (n (%))	47 (85.5)
Affected joints (median (range)))	2.0 (0-8)
Total score (median (range))	3.0 (0-11)

* Maximum score per patient for affected joints is 30, and the maximum total score is 90.

S1). Twenty-five per cent of all hand joints showed at least one inflammatory US feature. In 5.2% two features were present and in 2.3% three US features were present.

Association of US features and pain upon palpation in hand joints

All US features showed a dose-dependent association with pain after adjustment for age, gender and BMI: OR (95% CI) for GS synovitis 4.5 (2.2 to 9.0), effusion 4.4 (2.0 to 9.4), synovial thickening 4.9 (2.2 to 11.0) and PDS 4.1 (2.2 to 7.9). Further adjustment for US features revealed that GS synovitis was associated with pain independently of PDS (OR 4.0 (1.9 to 8.2)), and that effusion and synovial thickening were associated with pain independently of each other and PDS (OR 3.7 (1.8 to 7.6) and 2.5 (1.1 to 6.3), respectively). PDS was no longer associated with pain after further adjustments (table 3).

Table 3: Association of ultrasound (US) features and pain upon palpation in 55 patients with hand osteoarthritis (HOA).

US feature score	N	Adjusted OR * (95% CI)	Adjusted OR ** (95% CI)
GS synovitis			
0	1289	1	1
1	244	2.2 (1.6 to 3.0)	2.1 (1.5 to 2.8)
2	84	5.4 (3.2 to 8.8)	4.7 (2.8 to 7.8)
3	33	4.5 (2.2 to 9.0)	4.0 (1.9 to 8.2)
Effusion			
0	1337	1	1
1	227	2.3 (1.6 to 3.0)	2.0 (1.5 to 2.6)
2	61	4.9 (3.0 to 7.9)	3.8 (2.3 to 6.1)
3	25	4.4 (2.0 to 9.4)	3.7 (1.8 to 7.6)
Synovial thickening			
0	1529	1	1
1	76	2.3 (1.4 to 3.8)	1.3 (0.7 to 2.4)
2+3	37+8	4.9 (2.2 to 11.0)	2.6 (1.1 to 6.3)
PDS			
0	1511	1	1
1	107	1.9 (1.3 to 2.7)	1.4 (1.0 to 2.1)
2+3	30+2	4.1 (2.2 to 7.9)	2.0 (0.8 to 4.9)

*Adjustment made for age, gender, BMI;
**In addition the following adjustments were made: GS synovitis for PDS, effusion for synovial thickening and PDS, synovial thickening for effusion and PDS, PDS for synovial thickening and effusion.
PDS, power Doppler signal; GS, gray scale; BMI, body mass index.

Association of US features and self-reported pain, function or HRQoL

A statistically significant association was demonstrated for GS synovitis with AUSCAN pain, stiffness and SF-36 PCS. Of the other features, only effusion showed an association with AUSCAN pain. (see supplementary file S2).

DISCUSSION

The majority of patients with HOA show inflammation on US. In individual joints, we showed a dose-dependent association between inflammatory features and pain. In addition, GS synovitis, effusion and synovial thickening were independently associated; PDS was not. GS synovitis was also associated with AUSCAN pain and stiffness and with SF-36 PCS, as was effusion with AUSCAN pain.

Few studies have investigated the relationship between US features and pain in HOA. Keen *et al*. showed no association between self-reported pain and US features[4]. However, patient effects were not taken into account. In the present study, after adjustments for patient effects and confounders, associations between pain and inflammatory features were revealed.

In our study, 96% of patients showed GS synovitis, 91% effusion, 86% PDS and 73% synovial thickening. Vlychou *et al*. showed synovial thickening in 87% of all studied patients, although the presence of PDS was comparable[5]. However, that study was performed in patients with erosive HOA, which may account for the difference. Further studies to compare the presence of inflammatory signs in several HOA subsets are warranted.

On average, patients in this study had fewer joints showing GS synovitis than found by Keen *et al.* (6 versus 12)[4]. Whether this is due to a difference in HOA phenotype or difference in US technique is difficult to determine. Patients in the study of Keen *et al*. had a slightly higher VAS pain score. PDS scores were, however, similar in both studies.

In this study GS synovitis, as well as effusion and synovial thickening separately, were studied. In earlier studies of HOA, either GS synovitis was scored or effusion and synovial thickening. GS synovitis is often chosen because it is thought that separation of effusion and synovial thickening is not straightforward[10]. We showed that it is technically possible to study effusion and synovial thickening as separate entities.

This study has potential limitations. Firstly, symptoms such as pain and stiffness depend on personal factors that were not assessed. However, in this study design, painful joints were compared with non-painful joints in the same patient, thereby minimizing the confounding effect from personal factors. Secondly, only the dorsal sides of the joints were examined. This was done in accordance with a protocol formulated by experts in the field[10]. It is possible that GS synovitis is underestimated by scanning only the dorsal side.

In this study, strong dose-dependent associations were found between inflammatory US features and pain in separate hand joints. These findings are promising in elucidating the aetiology of pain in HOA. The association between US features and pain may give rise to further research for therapeutic strategies. However, repeat studies to confirm the association of US features and pain are needed.

Supplementary file S1: Distribution of ultrasound (US) features by joint in 55 patients.

	DIP				PIP					MCP					CMC	Total(%)
	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	(n=1540)
Left																
No. of joints with syn. thickening	2	4	2	1	3	8	10	6	5	2	1	1	0	0	11	56 (6.8)
No. of joints with effusion	18	19	16	18	19	9	16	8	14	4	3	1	0	1	18	164 (19.9)
No. of joints with PDS	4	2	2	3	9	10	9	4	0	4	4	1	0	1	12	65 (7.9)
No. of joints with 2 US features	2	4	1	2	6	4	5	2	4	1	0	1	0	0	7	39 (4.7)
No. of joints with 3 US features	1	0	0	0	0	3	5	1	0	1	3	0	0	0	5	19 (2.4)
Right																
No. of joints with synovitis	7	3	2	1	6	7	8	6	4	0	4	0	0	0	17	65 (7.9)
No. of joints with effusion	19	19	13	16	18	10	12	14	5	2	5	1	0	0	16	150 (18.2)
No. of joints with PDS	5	3	1	2	3	9	8	7	3	5	5	2	1	1	19	74 (9.0)
No. of joints with 2 US features	5	3	0	2	5	5	6	6	1	0	0	0	0	0	14	47 (5.7)
No. of joints with 3 US features	1	0	0	0	0	4	2	2	0	0	4	0	0	0	6	19 (2.4)

DIP, distal interphalangeal joint; PIP, proximal interphalangeal joint; MCP, metacarpalphalangeal joint; CMC, carpometacarpal joint; syn., synovial; PDS, power Doppler signal.

Supplementary file S2: Association, depicted as β-coefficients, between ultrasound (US) features and self-reported pain, function and quality of life in 55 patients with hand osteoarthritis (OA).

US features	β-coefficients (95% confidence intervals)*				
	VAS pain	AUSCAN pain	AUSCAN function	AUSCAN stiffness	SF-36 PCS
GS synovitis	0.3 (-0.1, 3.7)	0.5 (0.2, 0.9)	0.3 (-0.1, 1.2)	0.3 (0.003, 0.2)	-0.4 (-1.7, -0.3)
Effusion	0.2 (-1.0, 3.1)	0.5 (0.2, 0.9)	0.3 (-0.1, 1.3)	0.2 (-0.04, 0.2)	-0.3 (-1.5, 0.1)
Synovial thickening	0.3 (-0.6, 5.9)	0.1 (-0.4, 0.7)	0.1 (-0.6, 1.6)	0.3 (-0.02, 0.3)	-0.2 (-2.1, 0.4)
PDS	-0.1 (-5.3, 2.4)	-0.2 (-1.2, 0.2)	-0.1 (-1.6, 1.1)	-0.2 (-0.3, 0.1)	0.1 (-0.9, 2.1)

*Adjusted for age, gender, BMI, and in addition adjustments were made for other US features: GS synovitis for PDS, effusion for synovial thickening and PDS, synovial thickening for effusion and PDS, PDS for effusion and synovial thickening.
US, ultrasound; VAS, visual analogue scale; AUSCAN, Australian/ Canadian Osteoarthritis Index; SF-36, Short-Form 36; PCS, physical componens summary score; GS, gray scale; PDS, power Doppler signal; BMI, body mass index.

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