

Dactylitis in psoriatic arthritis – prevalence and reliability of ultrasound lesions in a clinical setting

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Abstract

Objectives. To investigate the prevalence of ultrasound elementary lesions in dactylitis in psoriatic arthritis (PsA), and the reliability of scoring these lesions in a clinical setting.

Methods. In 31 patients with PsA and clinical dactylitis, ultrasound assessment of the affected digit was performed using grey-scale and color Doppler mode. One examiner scanned all patients and a 2nd examiner scanned 10 patients for inter-reader reliability. The following lesions were evaluated: subcutaneous edema; soft tissue thickening; synovitis of the digital joints; tenosynovitis of the flexor tendon; enthesitis at the deep flexor tendon and the extensor tendon entheses; and paratenonitis of the extensor tendon. A dactylitis sum-score was calculated. Findings in clinically tender and non-tender digits were compared.

Results. The most frequent lesions were soft tissue thickening (81%) and subcutaneous edema (74%) followed by synovitis (56–68%) and flexor tenosynovitis (52%). Color Doppler was most frequently found subcutaneously (55%) and around the flexor tendons (45%). All lesions were typically found in combinations, most commonly subcutaneous edema and synovitis (71%), subcutaneous edema and flexor tenosynovitis (52%), and all three in combination (52%). Tender digits had a higher dactylitis sum-score and numerically higher prevalence of most lesions than non-tender digits. Intra- and inter-reader agreements were moderate to excellent, though lower for few components of digital enthesitis, especially hypoechogenicity.

Conclusion. Dactylitis in PsA appears to encompass several pathologies, most often subcutaneous changes combined with synovitis and/or flexor tenosynovitis. Reliability of scoring established ultrasound lesions of dactylitis in a clinical setting is moderate-excellent.

Introduction

Dactylitis, the uniform swelling of an entire digit, is a key pathology in psoriatic arthritis (PsA). It occurs in approximately half of patients with PsA (1) and may be the first, and occasionally the only, disease manifestation (2, 3). The importance of dactylitis in PsA is emphasized by the inclusion in the Classification Criteria for Psoriatic Arthritis (CASPAR) (2) and its presence has been linked to erosive disease (4). However, the pathogenesis and precise tissue involvement in dactylitis is still unclear. Early imaging studies using ultrasound and magnetic resonance imaging (MRI) concluded tenosynovitis to be the main component of dactylitis (5), accompanied by soft tissue edema and sometimes synovitis (6–8). More recent studies have shown additional involvement of several other structures (9–11). The Outcome Measures in Rheumatology (OMERACT) ultrasound group have suggested potential components (elementary lesions) of dactylitis to be soft tissue thickening and edema, flexor tendon tenosynovitis, joint synovitis as well as structural changes of the bone such as extra- and intraarticular osteoproliferation, erosions, and sesamoid abnormalities (9). Enthesitis is another key element of spondyloarthritis which is suspected to be the main pathology of dactylitis (10).

Although a dactylitis ultrasound score was recently proposed (12), there is yet no OMERACT consensus on which ultrasound elementary lesions constitute dactylitis. Therefore, we investigated, by ultrasound, the prevalence of different elementary lesions found in dactylitis in patients with PsA, and the reliability of scoring these lesions in a clinical setting.

Patients And Methods

Study design

In this cross-sectional, single center study, 31 consecutive patients with PsA according to the classification criteria for psoriatic arthritis (CASPAR) (2) and clinical dactylitis, defined as diffuse swelling of a digit, as judged by a rheumatologist, were included. The study complied with the Declaration of Helsinki, the local ethics committee approved the research protocol (journal no. H-16035123) and informed consent was obtained from all subjects prior to inclusion.

Clinical and biochemical examination, patient reported outcomes

All patients underwent routine clinical evaluation including joint examinations for tender and swollen joints (68/66 joints), tender entheses count (SPARCC enthesitis index (13)) and evaluator's global assessment of disease activity on a visual analogue scale (VAS). The dactylitic digit was noted as tender/not tender on clinical examination. The level of C-reactive protein (CRP) was recorded. Patients reported their global assessment of disease activity and global pain evaluation on a VAS and filled out the Health Assessment Questionnaire – disability index (HAQ-DI).

Ultrasound examination and scoring

Ultrasound was performed with a GE Logiq® E9, version R5 (Milwaukee, Wisconsin, USA) machine with a 6–15 MHz linear transducer. Dactylitic digits were examined with grey-scale (GS) and color Doppler (CD) modality. For CD, the frequency, pulse repetition frequency (PRF) and gain were set according to published guidelines (14). Same settings were used for all patients. The dactylitic digit and contralateral digit were examined from the dorsal and volar side, in longitudinal and transversal plane according to EULAR guidelines (14). Following pathologies were scored (15): subcutaneous edema, defined as hypo- or anechoic areas in the subcutaneous tissue (presence/absence, with/without hyperemia); soft tissue thickening (presence/absence, not necessarily with edema); synovitis of the metacarpophalangeal (MCP), proximal interphalangeal (PIP), distal interphalangeal (DIP) and interphalangeal (IP) joints (scored as GS 0–3, CD 0–3 and combined score 0–3 (16)); tenosynovitis of the flexor tendon (scored as GS 0–3, CD 0–3(17)); and enthesitis of the deep flexor tendon attachment and the extensor tendon at the attachment to the medial and the distal phalanx (presence/absence of thickening, hypoechogenicity/loss of fibrillary structure, calcifications/enthesophytes, erosions and CD activity(18)). The presence/absence and joint level of paratenonitis of the extensor tendon (defined as hypoechogenicity of peritenon and CD activity) was also noted. Examinations were performed by the same examiner for all 31 patients (SKF, 5 years of musculoskeletal ultrasound experience) and 10 patients were also examined by a second examiner (LT, >

20 years of experience) for inter-reader agreement. Stored images were re-read by the first examiner after approximately 3 weeks for intra-reader agreement.

Enthesitis was interpreted as inflammatory if presence of thickening, hypoechogenicity and/or CD Doppler activity, and as structural if presence of calcifications/enthesophytes and/or erosions (15). We calculated a simple dactylitis inflammatory sum-score (0–21) by adding scores for subcutaneous edema (GS 0–1, CD 0–1), synovitis of all joints (EULAR-OMERACT combined synovitis score 0–9 (16)), flexor tenosynovitis (GS 0–3, CD 0–3), presence of any inflammatory signs of enthesitis for each of the three sites (0–3) and presence of paratenonitis (0–1).

Statistical analyses

We investigated inter- and intra-reader agreement using Cohens Kappa and prevalence and bias adjusted Kappa (PABAK)(19) for binary outcomes, and weighted Kappa (squared weights) for ordinal outcomes. We considered Kappa values of 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as good and 0.81–1.00 as excellent (20). We also calculated the percentage exact agreement. Findings of tender and non-tender dactylitis were compared by two-sample t-test or Fischer's exact test, as appropriate (post-hoc analyses). Significance level was set to $p < 0.05$. Statistical analyses were performed with R, version 3.5.2.

Results

Population

Patients were 55% males, with short disease duration (median (interquartile range (IQR)) 1(0–6) year) and moderate disease activity (median (IQR) DAS28-CRP 3.2(2.4–4.5)). 74% of the examined digits were tender, 26% were non-tender. 45% of all examined digits were fingers, 55% were toes. See supplementary table 1.

Ultrasound findings

Ultrasound findings are presented in Table 1, including findings in tender and non-tender digits. The most common lesions were soft tissue thickening (81%) and GS subcutaneous edema (74%). Subcutaneous edema with CD activity was found in half of the patients (55%). GS signs of synovitis were also common (56–68%), while CD activity in the joints was less common (16–33%) – and mostly grade 2 when present. Flexor tenosynovitis was found in half of the digits (52%) and here almost all digits that were GS positive had concomitant CD activity, mostly grade 2. Inflammatory signs of enthesitis was most common at the extensor tendon attachment at PIP-level (44%), followed by the deep flexor tendon attachment (36%) and the extensor tendon attachment at DIP/IP-level (26%). Structural lesions were most common at the attachment of the deep flexor tendon (39%) and less frequent in the extensor tendon attachments (22% at PIP- and 23% at DIP/IP-level). Paratenonitis was seen in 1/3rd of the digits, on

several levels (10% at MCP, 22% at PIP and 3% at the DIP/IP level). See Figs. 1 and 2 for examples of lesions.

A combination of the lesions was often found (supplementary table 2). When synovitis was defined as GS score ≥ 1 (+/- CD) the most frequent combination was subcutaneous edema and synovitis (of any joint) (71%). When synovitis was defined as GS score ≥ 2 (+/- CD) the most frequent combination was subcutaneous edema and flexor tenosynovitis (52%). Flexor tenosynovitis and synovitis were found in combination in 52% for the first definition, and in 33% for the latter. Flexor tenosynovitis was found without synovitis (GS ≥ 2) in 17% of the cases (0% when synovitis = GS ≥ 1). All three (subcutaneous edema, synovitis (of any joint) and flexor tenosynovitis) were found in combination in 52% and 33%, respectively for the two synovitis definitions. Subcutaneous edema without signs of synovitis (GS ≥ 1) or tenosynovitis was only found in one case (3%).

We found significantly higher values of the dactylitis sum-score and numerically higher values of individual pathologies in the tender dactylitic digits compared to the non-tender (except for GS synovitis of the MCP-joint and some lesions in the digital entheses), see Table 1.

Inter- and intra-reader agreement

Intra- and inter-reader agreement for ultrasound lesions are presented in supplementary table 3. Intra-reader agreement was good-excellent for subcutaneous edema (Kappa 0.80-1.00), soft tissue thickening (Kappa 1.00), flexor tenosynovitis (Kappa 0.93–0.96) and synovitis (Kappa 0.92–0.96), both for GS and CD scores. Inter-reader agreements for these lesions were good-excellent (Kappa 0.74-1.00). Paratenonitis had good intra- and inter-reader reliability (Kappa 0.73 and 0.62, respectively). Kappa values for elementary components of enthesitis in the digital entheses were generally worse than for the other pathologies, ranging from Kappa 0.66–0.86 (PABAK 0.79-1.00) for intra-reader and Kappa 0.00–1.00 (PABAK 0.38-1.00) for inter-reader. However, the agreement on presence of CD activity at the entheses showed an excellent agreement (Kappa 0.86-1.00). The intraclass correlation coefficient (ICC) for sum-scores was 0.95 (0.89–0.97) for intra-reader, and 0.95 (0.78–0.99) for inter-reader.

Table 1
 Ultrasound findings in dactylitic digits, for all and for tender vs non-tender digits

	All (n = 31)	Tender (n = 23)	Non-tender (n = 8)	OR/mean.diff (95% CI)	p-value
	No/mean (%/IQR)	No/mean (%/IQR)	No/mean (%/IQR)		
Subcutaneous oedema					
GS changes	23 (74)	17 (74)	6 (75)	1.1 (0.1–13.5)	1.00
CD activity	17 (55)	13 (57)	4 (50)	0.9 (0.1–5.3)	1.00
Soft tissue thickening	25 (81)	19 (83)	6 (75)	0.6 (0.07–8.8)	0.63
Flexor tenosynovitis					
GS positive	16 (52)	13 (57)	3 (38)	0.5 (0.06–3.1)	0.43
GS grade*	2 (2–2)	2 (2–2)	2 (1–2)	0.4 (-0.7-1.6)	0.35
CD activity	14 (45)	12 (52)	2 (25)	0.3 (0.03–2.3)	0.24
CD grade*	2 (2–3)	2 (2–3)	2 (2–2)	0.08 (-0.4-0.6)	0.72
Synovitis MCP/MTP					
GS positive	21(68)	15 (65)	6 (75)	1.6 (0.2–19.5)	1.00
GS grade*	2 (1–2)	2 (1–2)	2 (1–2)	0.0 (-0.9-0.8)	0.93
CD activity	5(16)	4 (17)	1 (13)	0.7 (0.01–8.3)	1.00
CD grade*	2 (2–2)	2 (2–2)	2 (2–2)	NA	NA
Synovitis PIP					
	n = 27	n = 20	n = 7		
GS positive	15 (56)	13 (65)	2 (29)	0.2 (0.0-1.9)	0.19
GS grade*	2 (1–3)	2 (1–3)	2 (1–2)	0.7 (-2.6-3.9)	0.40
CD activity	9 (33)	8 (40)	1 (14)	0.3 (0.0-2.9)	0.40
CD grade*	2 (2–2)	2 (2–2)	2 (2–2)	NA	NA
Synovitis DIP/IP					
GS positive	19 (61)	16 (70)	3 (38)	0.3 (0.0-1.9)	0.20

	All (n = 31)	Tender (n = 23)	Non-tender (n = 8)		
GS grade*	2 (2-3)	2 (2-3)	2 (2-3)	-0.3 (-1.4-0.9)	0.53
CD activity	9 (29)	8 (35)	1 (13)	0.3 (0.0-2.7)	0.38
CD grade*	2 (2-2)	2 (2-2)	2 (2-2)	NA	NA
Flexor enthesitis					
inflammatory	11 (36)	10 (44)	1 (13)	0.4 (0.0-5.2)	0.60
structural	12 (39)	8 (89)	4 (50)	Inf (0.1-Inf)	1.00
Extensor enthesitis PIP	n = 27	n = 20	n = 7		
inflammatory	12 (44)	10 (50)	2 (29)	0 (0-1.9)	0.07
structural	6 (22)	4 (20)	2 (29)	1.5 (0.1-28.6)	1.00
Extensor enthesitis DIP/IP					
inflammatory	8 (26)	6 (26)	2 (25)	1.9 (0.1-137)	1.00
structural	7 (23)	4 (17)	3 (38)	Inf (0.1-Inf)	0.50
Paratenonitis	10 (32)	9 (39)	1 (13)	0.2 (0.0-2.3)	0.22
Dactylitis sum-score	7 (6-12)	8 (7-12)	4 (4-9)	3.3 (0.1-6.5)	0.05
Numbers based on 1st ex 1st read, presented as numbers (%) for binary variables and as median (interquartile range) for continuous variables. OR: Odds ratio, mean diff: difference of the mean in the two groups. 95% CI: 95% confidence intervals. P-value: p-values based on by Fischer's exact test or two-sample t-test as appropriate. *Grades: calculated for patients with positive (≥ 1) findings. GS: Grey-Scale, CD: Color Doppler, MCP: Metacarpophalangeal joint, MTP: Metatarsophalangeal joint, PIP: proximal interphalangeal joint, DIP: Distal interphalangeal joint IP: Interphalangeal joint.					

Discussion

In this single-center, cross-sectional ultrasound study of dactylitis in PsA, soft tissue thickening and subcutaneous edema in combination with synovitis and/or flexor tenosynovitis were the most common lesions, and the reliability of scoring established ultrasound components of dactylitis in a clinical setting was good-excellent.

The contribution of different pathologies in dactylitis are mostly in line with other recent imaging studies (10, 21) where subcutaneous changes were also found to be the most frequent component (90-92%). Next after subcutaneous changes we found synovitis and flexor tenosynovitis - both occurring with similar rates. Other studies though, have reported flexor tenosynovitis to be more frequent than synovitis

(8, 10, 21). We found more tenosynovial than synovial Doppler activity – in line with previous studies (21). We also found pathologies in both the flexor and extensor tendon entheses. Previous MRI studies have not found involvement of flexor tendon entheses (6, 10) and varying involvement of the extensor tendon entheses, ranging from 0% in earlier studies (6, 7) to 50% in more recent studies (10). No recent ultrasound dactylitis studies have reported numbers on these changes.

Tender digits had higher sum-scores and numerically higher prevalence of most pathologies than non-tender digits. In contrast, larger studies on this topic (21) found symptomatic dactylitis to have more extra-synovial features (flexor tenosynovitis, soft tissue edema and subcutaneous power Doppler) and asymptomatic dactylitis more synovitis (GS and power Doppler). Our numbers were probably too small to find this difference.

We calculated a simple dactylitis sum-score in order to evaluate the inflammatory burden of each digit and found that it was associated with tender more than non-tender dactylitis. We incorporated all possible sites, since each of them were involved in at least one of our patients. We weighted all components equally, but it could be argued that for example subcutaneous edema as the most frequent pathology should be scored semiquantitatively (22). This would increase its importance in a sum-score, and possibly enhance its sensitivity to change, although the applicability of such a score has been questioned, as subcutaneous findings seem to be highly variable also in a non-psoriatic population (23). Recently, a dactylitis score for psoriatic arthritis was published (12), including peritendon extensor inflammation, soft tissue edema, flexor tenosynovitis and synovitis. However, entheses, flexor tendon pulleys and collateral ligaments could potentially also be involved (10, 24) which could be evaluated in future studies.

Reliability of scoring individual dactylitis components was overall good to excellent both for established scores of synovitis and flexor tenosynovitis and for a simple present/absent score of subcutaneous edema with/without Doppler activity. Few enthesitis elementary lesions had poorer inter-reader agreement, even when low frequency of lesions was considered. Especially evaluation of hypoechogenicity of entheses proved challenging. Moderate -excellent agreement was found for all components of the published dactylitis score (12); however, this study did not include entheses. Reliability of scoring enthesitis of larger entheses in spondyloarthritis and PsA has been established(18); however, this is not validated for the small digital entheses and might not be directly transferrable, especially not for toes. The score of CD activity in entheses showed an excellent agreement, and the use of active enthesitis (requiring Doppler activity) could possibly be better option as sum-score component. The use of higher frequency probe could possibly improve agreement.

This study was performed using validated definitions present at the time of study initiation, in a clinical setting on consecutive patients, so results are readily applicable. The main inclusion criteria were PsA and dactylitis judged by a rheumatologist. Also, we included dactylitic fingers as well as toes and both tender and non-tender dactylitis. Inter-reader agreement was based on live scans and not stored images,

which also makes it more applicable in a clinical setting. The primary limitation is the relatively small number of subjects.

Further work is required to establish the relevance of individual ultrasound elementary components for diagnosis and monitoring of dactylitis and to validate an ultrasound dactylitis score in a clinical setting and on both fingers and toes, as such a score would be important in future clinical studies.

Conclusions

In conclusion, we found dactylitis in this cohort of PsA patients to consist of subcutaneous changes in combination with synovitis and/or flexor tenosynovitis. Signs of enthesitis were also present though less frequently. Scoring ultrasound lesions of dactylitis is currently of great interest, and while reliability of scoring established components in a clinical setting was good-excellent, scoring elementary lesions of small digital entheses was more challenging and needs to be explored further.

Abbreviations

CD

Color Doppler

CASPAR

Classification Criteria for Psoriatic Arthritis

DAS28-CRP

Disease Activity Score-28 joints with C-reactive protein (CRP)

EULAR

European League Against Rheumatism

GS

Grey scale

IQR

Interquartile range

OMERACT

Outcome Measures in Rheumatology

OR

Odds ratio

PABAK

Prevalence-adjusted and bias-adjusted kappa

Declarations

Ethics approval and consent

The study complied with the Declaration of Helsinki, the ethics committee of the capital region in Denmark approved the research protocol (journal no. H-16035123) and informed consent was obtained from all subjects prior to inclusion.

Consent for publication

Patients consent to publication.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests relevant to this article

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Authors' contributions

All authors designed the study and developed the study protocol. SKF and LT performed the ultrasound examinations and scoring as described. SKF performed analyses and wrote the first draft of the paper. All authors interpreted data, revised the manuscript, read, and approved the final manuscript.

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Figures

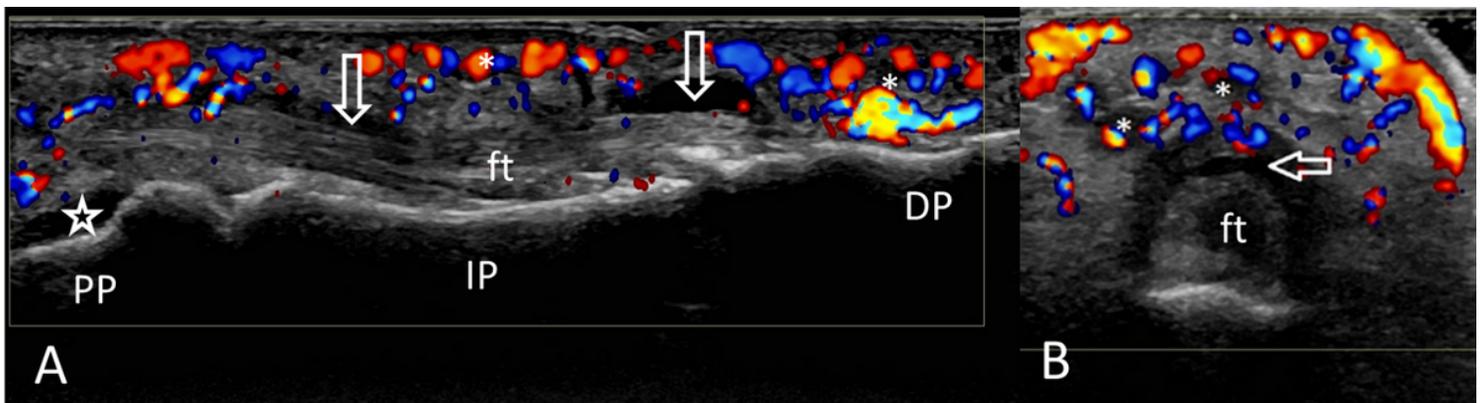


Figure 1

Volar aspect of dactylitic finger in (A) longitudinal and (B) transversal plane, showing flexor tenosynovitis (open arrows) and soft tissue edema (asterixis) with color Doppler activity. Star indicates effusion of the proximal interphalangeal joint. ft: flexor tendon, PP: proximal phalanx, IP: intermediate phalanx, DP: distal phalanx.

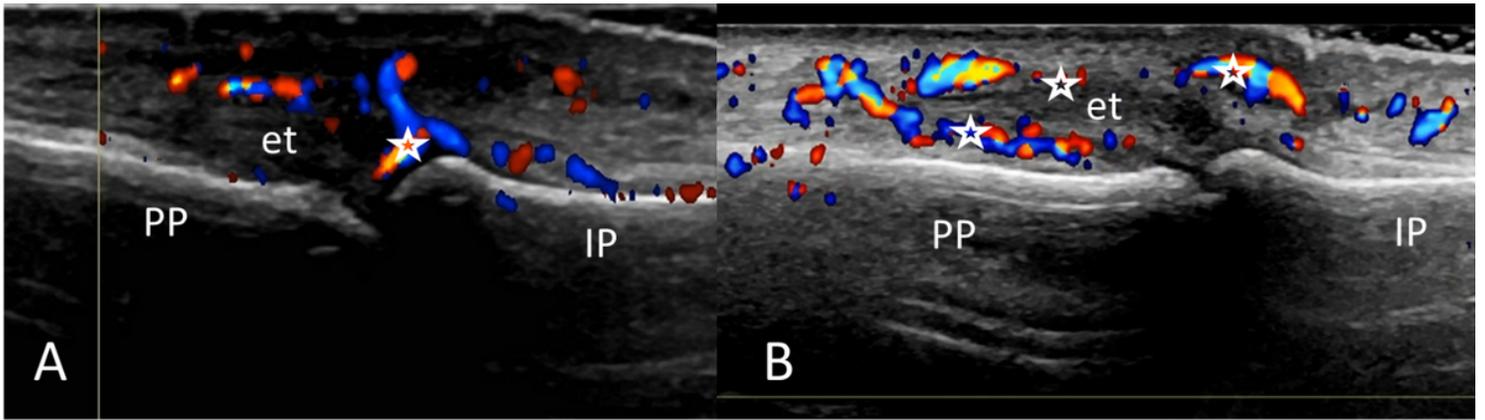


Figure 2

Dorsal aspect of two proximal interphalangeal finger joints, with (A) enthesitis of the extensor tendon enthesitis and (B) paratenonitis of the extensor tendon with Doppler activity (stars). et: extensor tendon, PP: proximal phalanx, IP: intermediate phalanx.

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