Which ultrasound lesions contribute to dactylitis in psoriatic arthritis and their reliability in a clinical setting

Sara K. Felbo 1,2 · Mikkel Østergaard 1,2 · Inge J. Sørensen 1 · Lene Terslev 1,2

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Abstract

Objectives To explore the frequency 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 finger or toe was performed using greyscale and color Doppler mode. One examiner scanned all patients and a second examiner scanned 10 patients for inter-reader reliability. For each digit, 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 lesions, 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.

Key Points

- Dactylitis in psoriatic arthritis consists of multiple ultrasound lesions
- A dactylitis ultrasound sum-score gives an impression of severity by including all lesions
- Reliability of ultrasound scoring of dactylitis components is good

Introduction

Dactylitis is a key pathology in psoriatic arthritis (PsA) occurring in approximately half of patients [1]. It may be the first, occasionally the only, disease manifestation [2, 3] and its presence has been linked to erosive disease [4]. The importance of dactylitis in PsA is emphasized by the inclusion in the Classification Criteria for Psoriatic Arthritis (CASPAR) [2]. However, the pathogenesis and precise tissue involvement is still unclear. Early imaging studies using ultrasound and magnetic resonance imaging (MRI) concluded that tenosynovitis is the main component of dactylitis, accompanied by soft tissue edema and sometimes synovitis [5–7]. More recent studies have additionally shown potential relevance of enthesitis, extensor tendonitis, flexor tendon pulley inflammation, and bone marrow edema (only visible by MRI) [8–11]. The Outcome Measures in Rheumatology (OMERACT) ultrasound group has suggested potential ultrasound inflammatory lesions of dactylitis to be soft tissue thickening and edema, flexor tendon tenosynovitis, and joint synovitis [12].
Although a dactylitis ultrasound score was recently proposed [13], no OMERACT consensus has been reached on which ultrasound lesions constitute dactylitis. Therefore, we explored the frequency of different ultrasound lesions found in dactylitis in patients with PsA and reliability of scoring these lesions in a clinical setting.

**Patients and methods**

**Study design**

In this explorative, cross-sectional, single-center study, 31 consecutive patients with PsA according to CASPAR criteria [2] and clinical dactylitis of a finger or toe, defined as diffuse swelling of an entire digit, were included. The study complied with the Declaration of Helsinki, was approved by the local ethics committee (journal no. H-16035123), and informed consent was obtained from all participants prior to inclusion.

**Clinical and biochemical examination, patient-reported outcomes**

All patients underwent clinical evaluation including examination for tender and swollen joints (68/66 joints), tender entheses (Spondyloarthritis Research Consortium of Canada (SPARCC) enthesitis index [14]) 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 C-reactive protein (CRP) level was recorded. Patients reported their global assessment of disease activity and pain 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 machine (Milwaukee, Wisconsin, USA) with a 6–15 MHz linear transducer. Dactylitic digits were examined with grayscale (GS) and color Doppler (CD) modality. For CD, the frequency, pulse repetition frequency (PRF), and gain were set according to published guidelines [15]. Same settings were used for all patients. The dactylitic digit was examined from the dorsal and volar side, in longitudinal and transversal plane, and patients were positioned according to European League Against Rheumatism (EULAR) guidelines [16]. Following lesions were scored: subcutaneous edema, defined as hypo- or anechoic areas in the subcutaneous tissue (presence/absence, with/without hyperemia); soft tissue thickening as compared to a non-dactylitic digit, preferably the contralateral digit (presence/absence); synovitis of the metacarpophalangeal (MCP), proximal interphalangeal (PIP), distal interphalangeal (DIP), and interphalangeal (IP) joints (GS 0–3, CD 0–3, and combined score 0–3 [17]); tenosynovitis of the flexor tendon (GS 0–3, CD 0–3[18]); enthesitis at the attachment of the deep flexor tendon and the extensor tendon (medial and distal phalanx) (presence/absence of thickening, hypoechogenicity, calcifications/enthesophytes, erosions, and CD activity[19]); and paratenonitis of any level of the extensor tendon, defined as hypoechogenicity of peritenon and CD activity (presence/absence). All examinations were performed by one examiner (SKF, 5 years of musculoskeletal ultrasound experience) and 10 patients were also examined by a second examiner on the same day (LT, > 20 years of experience) for inter-reader agreement. Stored images were re-read by the first examiner after 3 weeks for intra-reader agreement.

Enthesitis was defined as inflammatory if thickening, hypoechogenicity, and/or CD activity was present and as structural if calcifications/enthesophytes and/or erosions were present [20]. We calculated a dactylitis inflammatory sum-score (0–21) by adding scores for subcutaneous edema (GS 0–1, CD 0–1), synovitis (EULAR-OMERACT combined score 0–9 [17]), flexor tenosynovitis (GS 0–3, CD 0–3), presence of inflammatory signs of enthesitis for the three sites (0–3), and presence of paratenonitis (0–1).

**Statistical analyses**

We investigated inter- and intra-reader agreement using Cohen’s kappa and prevalence- and bias-adjusted Kappa (PABAK) [21] for binary outcomes, weighted kappa (squared weights) for ordinal outcomes, and intraclass correlation coefficient (ICC) for sum-scores. 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 [22]. Findings of tender and non-tender dactylitis were compared by Fischer’s exact test or Mann-Whitney U 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**

Seventeen (55%) of included patients were male, with short disease duration (median (interquartile range (IQR)) 1 (0–6) year) and moderate disease activity (median (IQR) DAPSA 21 (14–39)). Twenty-three (74%) of the examined digits were tender, and 8 (26%) were non-tender. Twelve (45%) of all examined digits were fingers, and 17 (55%) were toes. See supplementary table 1.
Ultrasound findings

Ultrasound findings are presented in Table 1, including findings of tender and non-tender digits. The most common lesions were soft tissue thickening (25 (81%)) and GS subcutaneous edema (23 (74%)). Subcutaneous hyperemia was found in half of the digits (17 (55%)). GS signs of synovitis were common (15–21 (56–68%)) while synovial CD activity was less common (5–9 (16–33%)). GS flexor tenosynovitis was found in half of the digits (16 (52%)) and almost all had concomitant CD activity. Inflammatory signs of enthesitis were most common at the attachment of the extensor tendon at PIP-level (12 (44%)), followed by the deep flexor tendon (11 (36%)) and the extensor tendon at DIP/IP-level (8 (26%)). Structural lesions were most common at the attachment of the deep flexor tendon (12 (39%)) and less frequent at the extensor tendon (6 (22%)) at PIP- and 7 (23%) at DIP/IP-level. Paratenonitis was seen in 10 (32%) of the digits. See Figs. 1 and 2 for examples of lesions.

The lesions were often found in combination (supplementary table 2). With synovitis defined as GS score ≥ 1 (+/−CD), the most frequent combination was subcutaneous edema and synovitis (22 (71%)). With synovitis defined as GS score ≥ 2 (+/−CD) the most frequent combination was subcutaneous edema and flexor tenosynovitis (16 (52%)). Flexor tenosynovitis and synovitis were found in combination in 16 (52%) for the first definition, and in 10 (33%) for the latter. Flexor tenosynovitis was found without synovitis (GS ≥ 2) in 5 (17%) of the cases (0 (0%) when synovitis GS ≥ 1). All three (subcutaneous edema, synovitis, and flexor tenosynovitis) were found in combination in 16 (52%) and 10 (33%), respectively, for the two synovitis definitions.

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

Inter- and intra-reader agreement

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 were generally lower than for the other lesions, 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, agreement on presence of CD activity at the entheses showed excellent agreement (kappa 0.86–1.00). The ICC (95% confidence interval) for sum-scores was 0.95 (0.89–0.97) for intra-reader and 0.95 (0.80–0.99) for inter-reader. Numbers are presented in supplementary table 3.

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 constituting dactylitis and the reliability of scoring established ultrasound components of dactylitis in a clinical setting was good-excellent.

The contribution of different lesions in dactylitis is mostly in line with other recent imaging studies [10, 23] where subcutaneous changes were also found to be the most frequent component (90–92%). We found synovitis and flexor tenosynovitis occurring with similar rates, where other studies have reported flexor tenosynovitis to be more frequent than synovitis [6, 10, 23]. Our findings of more tenosynovial than synovial Doppler activity are in line with previous studies [23]. Involvement of entheses of the flexor and extensor tendons has been debated but no recent ultrasound dactylitis studies have reported numbers on these changes. We found lesions in both flexor and extensor tendon entheses, where previous MRI studies did not find involvement of flexor tendon entheses [7, 10] and varying involvement of extensor tendon entheses, ranging from 0% in earlier studies [7] to 50% in more recent studies [10].

Tender digits had higher sum-scores and numerically higher prevalence of most lesions than non-tender digits. In contrast, larger studies [23] 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 establish a difference. We calculated a dactylitis sum-score in order to evaluate the inflammatory burden of each digit and found that it was higher in tender than in non-tender dactylitis, in line with the perception that non-tender dactylitis is less inflammatory active [9]. We incorporated all possible sites, since each of them was involved in at least one of our patients. We weighted all components equally, but it could be argued that subcutaneous edema as the most frequent pathology should be scored semiquantitatively [24], which would increase its importance in a sum-score. However, no such scoring system currently exists and the applicability of such a score has been questioned as subcutaneous findings seem to be highly variable also in a non-psoriatic population [25]. Recently, a dactylitis score for psoriatic arthritis was published [13] including the same lesion as found in our study, apart from entheses. However, entheses, flexor tendon pulleys, and collateral ligaments have been reported.
involved in dactylitis [10, 11] and their relevance for a scoring system should be established in the future.

Reliability of scoring individual dactylitis components was overall good to excellent in our study 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 low inter-reader agreement, even when low frequency of lesions was considered. Especially evaluation of hypoechogenicity of entheses proved challenging questioning the relevance in a

### Table 1 Ultrasound findings in dactylitic digits, for all digits, and for tender compared to non-tender digits

|                      | All (n = 31) | Tender (n = 23) | Non-tender (n = 8) | OR/med. diff (95% CI) | p value |
|----------------------|-------------|----------------|-------------------|-----------------------|---------|
| **Subcutaneous edema** |             |                |                   |                       |         |
| 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^a           | 2 (2–2)     | 2 (2–2)        | 2 (1–2)           | 0.0 (0.0–1.0)        | 0.35    |
| CD activity          | 14 (45)     | 12 (52)        | 2 (25)            | 0.3 (0.03–2.3)       | 0.24    |
| CD grade^a           | 2 (2–3)     | 2 (2–3)        | 2 (2–2)           | 0.0 (−1.0–0.0)       | 0.92    |
| **Synovitis MCP/MTP** |           |                |                   |                       |         |
| GS positive          | 21 (68)     | 15 (65)        | 6 (75)            | 1.6 (0.2–19.5)       | 1.00    |
| GS grade^a           | 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^a           | 2 (2–2)     | 2 (2–2)        | 2 (2–2)           | 0.0 (−1.0–0.0)       | 1.00    |
| **Synovitis PIP**    |             |                |                   |                       |         |
| GS positive          | 15 (56)     | 13 (65)        | 2 (29)            | 0.2 (0.0–1.9)        | 0.19    |
| GS grade^a           | 2 (1–3)     | 2 (1–3)        | 2 (1–2)           | 1.0 (−1.0–2.0)       | 0.27    |
| CD activity          | 9 (33)      | 8 (40)         | 1 (14)            | 0.3 (0.0–2.9)        | 0.36    |
| CD grade^a           | 2 (2–2)     | 2 (2–2)        | 2 (2–2)           | 0 (−1.0–0.0)         | 0.79    |
| **Synovitis DIP/IP** |             |                |                   |                       |         |
| GS positive          | 19 (61)     | 16 (70)        | 3 (38)            | 0.3 (0.0–1.9)        | 0.21    |
| GS grade^a           | 2 (2–3)     | 2 (2–3)        | 2 (2–3)           | 0.0 (−1.0–1.0)       | 0.63    |
| CD activity          | 9 (29)      | 8 (35)         | 1 (13)            | 0.3 (0.0–2.9)        | 0.38    |
| CD grade^a           | 2 (2–2)     | 2 (2–2)        | 2 (2–2)           | 0.0 (−1.0–1.0)       | 1.00    |
| **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** | 12 (44) | 10 (50) | 2 (29) | 0.0 (0–1.9) | 0.07 |
| Structural           | 6 (22)      | 4 (20)         | 2 (29)            | 1.5 (0.1–28.6)       | 1.00    |
| **Extensor enthesitis DIP/IP** | 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)           | 3.0 (0.0–7.0)        | 0.04    |

Numbers based on 1st ex 1st read presented as numbers (%) for binary variables and as median (interquartile range) for continuous variables. OR, odds ratio; med. diff, median of the difference between the two groups; 95% CI, 95% confidence intervals; p value, p values based on by Fischer’s exact test or Mann-Whitney U test, as appropriate; GS, grayscale; CD, color Doppler; MCP, metacarpophalangeal joint; MTP, metatarsophalangeal joint; PIP, proximal interphalangeal joint; DIP, distal interphalangeal joint; IP, interphalangeal joint; Inf, infinity

^a Grades: calculated for patients with positive (≥ 1) findings
scoring system. Moderate-excellent agreement was found for all components of the published dactylitis score [13]; however, this study did not include entheses. Reliability of scoring enthesitis of larger entheses in spondyloarthritis and PsA has been established [19]; however, this is not validated for the small digital entheses and might not be directly transferrable.

**Fig. 1** Volar aspects of dactylitic finger (a, b) and toe (c, d). The dactylitic finger is visualized in a longitudinal and b transversal plane, with flexor tenosynovitis (open arrows) (grayscale grade 2, color Doppler grade 2) and subcutaneous edema (asterixis) with color Doppler activity (grayscale and color Doppler presence). Star indicates effusion of the proximal interphalangeal joint. The dactylitic toe shows c subcutaneous edema (asterixis) (grayscale presence) and thickened enthesis of the flexor tendon, hypoechogenicity, and calcifications (arrows) and d Doppler activity at the enthesis (bold arrow) (enthesitis presence) and subcutaneously (asterixis) (Doppler presence). ft, flexor tendon; PP, proximal phalanx; IP, intermediate phalanx; DP, distal phalanx.

**Fig. 2** Digital enthesial lesions of dactylitic digits showing a enthesis of the extensor tendon at the proximal interphalangeal finger joint with thickening, hypoechogenicity, and Doppler activity (stars), a, b paratenonitis of the extensor tendon with Doppler activity (stars), c thickening and enthesophyte (arrow) at the extensor tendon enthesis at the distal interphalangeal joint and d enthesophyte (arrow) of the deep flexor tendon enthesis. et, extensor tendon; ft, flexor tendon; PP, proximal phalanx; IP, intermediate phalanx; DP, distal phalanx.
especially not for toes. The score of entheseal CD activity had excellent agreement and the use of active enthesis (requiring Doppler activity) could be a better option as sum-score component. Use of a higher frequency probe might improve agreement.

This study has several strengths. It was performed using validated ultrasound definitions present at the time of study initiation, in a clinical setting on consecutive PsA patients with clinical dactylitis. We included both fingers and toes and both tender and non-tender dactylitis. Inter-reader agreement was based on live scans and not stored images. The primary limitation is the relatively small number of subjects, affecting the post hoc analyses of tender vs. non-tender dactylitis, another is the lack of a clinical dactylitis evaluation tool (e.g., Leeds Dactylitis Index). Furthermore, ultrasound cannot visualize bone marrow edema.

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 including both fingers and toes, as such a score would be important for future clinical studies.

Conclusions

We found dactylitis in this cohort of PsA patients to consist of subcutaneous changes in combination with synovitis and/or flexor tenosynovitis. Signs of enthesis were also present though less frequent. 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 digital enthesis was more challenging and needs to be explored further.

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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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Data availability

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

Compliance with ethical standards

Disclosures

None.

Ethics approval

The ethics committee of the capital region in Denmark approved the research protocol (journal no. H-16035123).

Consent to participate

Informed consent was obtained from all subjects prior to inclusion.

Consent for publication

Patients consent to publication.

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