

Ultrasonographic Evidence of Predominance of Acute Extracapsular and Chronic Intrasynovial Patterns in 100 Cases of Psoriatic Hand Dactylitis

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ABSTRACT. Objective. To use ultrasonography to study whether the duration of psoriatic dactylitis was associated with different patterns of extracapsular and synovial-based involvement.

Methods. One hundred cases of hand dactylitis from 85 patients with psoriatic arthritis (PsA) were consecutively enrolled in a multicenter cross-sectional study and divided into 2 groups according to dactylitis duration (shorter or longer than the median: 20 weeks). All dactylitis fingers were investigated using high-frequency ultrasound both in greyscale (GS) and power Doppler (PD), evaluating the presence of flexor tenosynovitis, soft tissue edema, subcutaneous PD signal (PDS), extensor tendon involvement, and joint synovitis.

Results. Cases with a shorter dactylitis duration (< 20 weeks) had a significantly higher prevalence of GS flexor tenosynovitis of grade > 2, PD flexor tenosynovitis, soft tissue edema, and subcutaneous PDS ($p = 0.001$, $p < 0.001$, $p < 0.05$, and $p = 0.001$, respectively). However, the presence of synovitis in GS and PD mode (in both cases at proximal interphalangeal level) was more frequent in patients with longer dactylitis duration ($p < 0.001$). When detected in the chronic form, flexor tenosynovitis was grade 2 or lower.

Conclusion. In a large cohort of PsA hand dactylitis, we found a predominant extracapsular inflammation (flexor tenosynovitis and soft tissue edema) in early cases and a high prevalence of joint synovitis at proximal interphalangeal level in the chronic form. However, longitudinal imaging studies are needed to clarify these aspects. (First Release November 1 2019; J Rheumatol 2020;47:227–33; doi:10.3899/jrheum.190046)

Key Indexing Terms:
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Dactylitis is a common feature of psoriatic arthritis (PsA), occurring in 16% to 49% of patients with PsA, mostly in early disease^{1,2,3}. As the most specific PsA manifestation it has been included in the CLASSification for Psoriatic ARthritis (CASPAR) criteria^{4,5}, although it has been observed in all forms of spondyloarthritis⁶, including the enteropathic form⁷. Dactylitis is defined as diffuse and uniform swelling of the entire digit and it is considered a clinical marker of disease severity^{8,9}. Clinically, it can present as a tender, painful, warm, and erythematous digit (acute form). It can also present as a swollen paucisymptomatic

digit, not associated with inflammatory modifications (chronic form)¹⁰, which remains poorly understood^{11,12}.

Dactylitis was long considered to be the result of the association of the metacarpophalangeal (MCP), proximal interphalangeal (PIP), and distal interphalangeal (DIP) joints with flexor tenosynovitis^{13,14}. In the 1990s, early ultrasound (US) studies reported a predominant flexor tenosynovitis, while the frequency of coexisting joint synovitis varied from 16% to 62%^{15,16,17}, and these data were confirmed by subsequent magnetic resonance imaging (MRI) studies^{18,19,20}. These results led the authors to conclude that flexor tenosynovitis was a major contributor to the clinical appearance of dactylitis, and joint synovitis was a variable coexisting feature. Fournié, *et al*²¹ used US to show diffuse digital soft tissue inflammation in dactylitic patients (reported as subcutaneous and extratendinous) and termed this lesion *pseudo-tenosynovitis*. A recent study independently reported that this lesion was useful in the differentiation of PsA from rheumatoid arthritis²².

Only a recent US study of 48 cases of PsA dactylitis evaluated the correlation between sonographic features and duration of dactylitis. That study highlighted a significantly higher prevalence of flexor tenosynovitis and peritendinous soft tissue edema in acute form (< 24 weeks) and joint synovitis in the chronic form (> 24 weeks)²³. We tested the hypothesis that earlier disease may be associated with a greater degree of extracapsular pathology, in line with prominent accessory pulley involvement in early disease. This multicenter observational cross-sectional study was designed to confirm in a greater number of patients the association between US patterns of disease compartmentalization in dactylitis and its duration.

MATERIALS AND METHODS

Patients. We performed a cross-sectional multicenter study on consecutively enrolled PsA patients with finger dactylitis who were in 3 Italian rheumatology centers (Naples, Reggio Emilia, and Negrar) with a recognized expertise in PsA and US imaging, between August 2017 and September 2018. The study was approved by the local ethics committees of the participating centers and was conducted in conformity with The Declaration of Helsinki (Ethical committee approval number: 5/12). Written informed consent was obtained from all participants.

The inclusion criteria were the fulfillment of CASPAR criteria in patients older than 18 years¹ having an acute or chronic dactylitis² with a duration of more than a month. The exclusion criteria were the following: (1) current engagement in heavy manual work, (2) recent history of hand trauma, (3) treatment with biologic synthetic disease-modifying antirheumatic drugs (DMARD), and (4) a previous corticosteroid injection in the involved finger.

Before US examination, a clinical assessment was performed by clinicians (AM, CS, RS) with longstanding expertise in the field of PsA who diagnosed the dactylitis using the dactylometer and the Leeds Dactylitis Index (LDI)²⁴. The LDI measures the ratio of the circumference of the involved digit to the circumference of the contralateral digit; a minimum difference of 10% is necessary to define a dactylitic digit. The ratio of circumference is multiplied by a tenderness score (0 = no tenderness, 1 = tender, 2 = tender and winces, 3 = tender and withdraws).

The rheumatologic evaluation included tenderness of the involved finger, tender joint count (TJC), and swollen joint count (SJC). Erythrocyte

sedimentation rate (ESR), C-reactive protein (CRP), and rheumatoid factor were collected. The duration of dactylitis was defined from the onset of reported diffuse digital swelling and pain.

For the purposes of analysis, we divided all cases of dactylitis into 2 groups according to its duration (shorter or longer than the median: 20 weeks). Moreover, all the cases were split into quartiles based on dactylitis duration.

US protocol. US examination of the dactylitis finger was performed by 3 rheumatologists (NG, PM, IT), expert in musculoskeletal US examination and blinded to clinical and laboratory data. All US scans were performed using a MyLab 70XVG machine equipped with a 6–18 MHz linear transducer (Esaote SpA). The US greyscale (GS) imaging measurements were optimized for maximal image resolution. Power Doppler (PD) settings were standardized at the following values: 500 Hz for pulse repetition frequency, 3 for wall filter, 4 for persistence, and color gain 45–55%. The window of the color box was restricted to the areas studied.

Flexor and extensor tendons, MCP, PIP, and DIP joints of the affected fingers were assessed by GS and PD US evaluation in longitudinal and transverse scanning views, in accordance with current guidelines and publications^{25,26}. Joints were examined from both dorsal and volar sides. The following dactylitis-related sonographic lesions were investigated: flexor tenosynovitis (both in GS and in PD mode), soft tissue edema, subcutaneous PD signal (PDS), extensor tendon involvement (including paratenonitis and enthesitis of extensor tendon at proximal-interphalangeal joint), and synovitis (both in GS and in PD mode).

Tenosynovitis was defined in GS according to the Outcome Measures in Rheumatology (OMERACT) definitions²⁷. Soft tissue edema was defined as a diffuse hypo/isoechoic thickening of the extratendinous soft tissues around the flexor tendon (pseudotenosynovitis) with positive PDS in the subcutaneous tissue, in long axis view²¹. We defined paratenonitis as a hypoechoic area surrounding a tendon without synovial sheath, with or without peritendinous PDS^{28,29}. Enthesitis of extensor tendon at PIP joint was defined by the presence of hypoechoic and increased thickness of the tendon insertion into the bone, as compared to the body of the tendon and to the contralateral^{30,31}.

Synovitis was defined according to the recent European League Against Rheumatism–OMERACT definition as hypoechoic synovial hypertrophy regardless of the presence of effusion and any grade of PD signal³². Tenosynovitis was assessed using the 4-grade semiquantitative scoring scale in GS and Doppler mode, as proposed by the OMERACT US group²⁷. Synovitis was scored using a semiquantitative score (0–3) both for GS and Doppler mode, according to studies^{32,33}.

Statistical analysis. The statistical analysis was performed using SPSS, version 23. All quantitative variables were expressed as mean $\pm$ SD or median and range in case of strong violation of normality, while qualitative variables were expressed as percentages.

Intraobserver and interobserver reliabilities were obtained in 2 measurements (basal and at 3 months from the first US evaluation) using 20 static images of 20 patients. We used the Cohen's κ coefficient for each sonographic lesion, and values > 0.8 were considered excellent. Continuous variables were compared using T test or nonparametric tests when appropriate. Noncontinuous variables were compared using chi-square test. Statistical tests were performed at a significance level of $\alpha = 0.05$.

RESULTS

Clinical features of the 2 dactylitis groups. The main demographic, clinical, and laboratory characteristics of the 2 groups (shorter or longer than 20 weeks) are reported in Table 1. Both groups were not significantly different for body mass index, PsA duration, TJC, SJC, ESR, CRP, and therapies. However, patients with longer dactylitis duration were predominantly male ($p < 0.05$) and older ($p = 0.01$). The

Table 1. Clinical and laboratory features according to dactylitis duration (shorter or longer than the median: 20 weeks).

Variables	< 20 Weeks	≥ 20 Weeks	p
Total cases	54	46	
Sex distribution (male/female)	26/28	32/14	0.031
Age in yrs, mean ± SD	43.7 ± 15.6	51.4 ± 13.9	0.01
BMI, kg/m ² , mean ± SD	25.3 ± 2.7	26.1 ± 3.6	ns
PsA duration disease, mos, mean ± SD	45.4 ± 47.1	52.5 ± 44.5	ns
Tenderness (%)	91	42	< 0.001
LDI, mean ± SD	35.4 ± 16.2	19.5 ± 19.5	< 0.001
Patient pain VAS score, mean ± SD	6.8 ± 2.7	4.9 ± 2.2	< 0.001
TJC, 68 joints, mean ± SD	6.6 ± 5.1	5.7 ± 4.1	ns
SJC, 66 joints, mean ± SD	3.2 ± 2.1	2.4 ± 1.9	ns
ESR, mm/h, mean ± SD	19.1 ± 14.4	17.2 ± 12.4	ns
CRP, mg/dl, mean ± SD	1.1 ± 1.9	0.8 ± 1.3	ns
No therapy, n (%)	18 (33.3)	18 (39.1)	ns
Actual therapy with only NSAID, n (%)	4 (7.4)	3 (6.5)	ns
Actual therapy with prednisolone, n (%)	3 (5.6)	6 (13.1)	ns
Actual therapy with csDMARD, n (%)	29 (53.7)	19 (41.3)	ns
Methotrexate, n (%)	16 (29.6)	9 (19.5)	ns
Sulfasalazine, n (%)	9 (16.7)	7 (15.2)	ns
Leflunomide, n (%)	4 (7.4)	3 (6.5)	ns

BMI: body mass index; CRP: C-reactive protein; csDMARD: conventional synthetic disease-modifying antirheumatic drugs; ESR: erythrocyte sedimentation rate; LDI: Leeds Dactylitis Index; NSAID: nonsteroidal antiinflammatory drugs; PsA: psoriatic arthritis; SJC: swollen joint count; TJC: tender joint count; VAS: visual analog scale; ns: not significant.

patients of the 2 groups were significantly different for the frequency of tenderness ($p < 0.001$). Moreover, the mean values of LDI score and patient pain visual analog scale (VAS) score were significantly higher in cases with shorter dactylitis duration ($p < 0.001$).

Sonographic intraobserver reliability. For the 3 sonographers (NG, PM, IT), the intraobserver reliability was excellent for all variables ($\kappa > 0.8$). The interobserver reliability depicted by κ coefficient was 0.87 (95% CI 0.81–0.93) for GS flexor tenosynovitis, 0.83 (95% CI 0.75–0.90) for PD flexor tenosynovitis, 0.89 (95% CI 0.85–0.93) for soft tissue edema, 0.86 (95% CI 0.74–0.97) for subcutaneous PDS, 0.88 (95% CI 0.84–0.92) for extensor tendon involvement, 0.84 (95% CI 0.76–0.93) for GS synovitis, and 0.91 (95% CI 0.85–0.96) for PD synovitis.

Sonographic findings. At least 1 US abnormality was found in all patients. Flexor tenosynovitis was seen in 88% of dactylitis (grade > 2 in 46% of cases), while related PD flexor tenosynovitis was observed in 72% of cases (grade > 2 in 57% of cases). Soft tissue edema was present in 91% of dactylitis and subcutaneous PDS was present in 85% of cases. Extensor tendon involvement was evident in 12% of dactylitic fingers (with associated PDS in 10% of cases). GS synovitis involving at least 1 joint was observed in 40% of cases; it was present more frequently at PIP level (28% of cases), while it was present at MCP and DIP level in 15% and 9% of cases, respectively. PD synovitis involving at least 1 joint was evident in 21% of cases; it was more frequently

detected at PIP level (17% of cases) and it was seen at the MCP and DIP levels in 7% and 4% of cases, respectively. Simultaneous synovitis of MCP, PIP, and DIP joints was not found in any patient.

Flexor tenosynovitis plus soft tissue edema were present in 79% of cases, while flexor tenosynovitis plus joint synovitis involving at least 1 joint were observed in 31% of cases. Soft tissue edema plus joint synovitis involving at least 1 joint were evident in 12% of dactylitic fingers.

Table 2 shows the frequency of US abnormalities in the 2 groups of patients. Cases with shorter dactylitis duration (< 20 weeks) had a significantly higher prevalence of GS flexor tenosynovitis of grade > 2 and PD flexor tenosynovitis (any grade; $p = 0.001$ and $p < 0.001$, respectively). Extracapsular soft tissue edema was more common in the shorter disease duration group ($p < 0.05$; Figure 1 and Figure 2). Likewise, subcutaneous PDS was more common in the shorter disease duration group ($p = 0.001$). On the other hand, the presence of synovitis in GS and PD mode (in both cases at PIP level) was more frequent in patients with a dactylitis duration ≥ 20 weeks ($p < 0.001$ and $p = 0.02$, respectively). Figure 3 reports the prevalence of selected US abnormalities after splitting cases into quartiles based on dactylitis duration.

We found no differences in the prevalence of the US abnormalities (in particular flexor tenosynovitis, soft tissue edema, and joint synovitis) comparing subjects treated versus not treated with conventional synthetic DMARD either in the general population or in the subgroups with dactylitis duration less than and > 20 weeks (Table 3).

Table 2. Prevalence of ultrasonographic abnormalities according to dactylitis duration (shorter or longer than the median: 20 weeks).

Variables	< 20 Weeks	≥ 20 Weeks	p
Total cases	54	46	
GS flexor tenosynovitis, all cases	93	83	ns
GS flexor tenosynovitis grade ≥ 2	65	24	0.001
PD flexor tenosynovitis, all cases	87	54	< 0.001
PD flexor tenosynovitis grade ≥ 2	74	37	0.001
Soft tissue edema	97	82	0.018
PDS	96	71	0.001
GS extensor tendon involvement	9	15	ns
PD extensor tendon involvement	9	11	ns
GS synovitis involving at least 1 joint	18	65	< 0.001
PD synovitis involving at least 1 joint	9	35	0.02
MCP GS synovitis, all cases	11	20	ns
MCP GS synovitis grade ≥ 2	0	4	ns
MCP PD synovitis, all cases	6	9	ns
MCP PD synovitis grade ≥ 2	2	6	ns
PIP GS synovitis, all cases	6	54	< 0.001
PIP GS synovitis grade ≥ 2	6	45	< 0.001
PIP PD synovitis, all cases	6	30	0.001
PIP PD synovitis grade ≥ 2	4	4	ns
DIP GS synovitis, all cases	9	8	ns
DIP GS synovitis grade ≥ 2	3	6	ns
DIP PD synovitis, all cases	3	4	ns
DIP PD synovitis grade ≥ 2	0	0	ns
GS flexor tenosynovitis plus soft tissue edema	91	65	0.002
GS flexor tenosynovitis plus GS synovitis involving at least 1 joint	18	48	0.001
Soft tissue edema plus GS synovitis involving at least 1 joint	19	50	0.001

Data are percentages. DIP: distal interphalangeal; GS: greyscale; MCP: metacarpophalangeal; PD: power Doppler; PDS: subcutaneous PD signal; PIP: proximal interphalangeal; ns: not significant.

DISCUSSION

This is the first multicenter study, to our knowledge, to evaluate the relationship between US lesions and dactylitis duration in a large PsA hand dactylitis cohort using high-frequency US. Our findings revealed that the prevalence of GS flexor tenosynovitis of grade > 2, PD flexor tenosynovitis, soft tissue edema, and subcutaneous PDS are higher in patients with shorter dactylitis duration. Moreover, the mean values of LDI score were significantly higher in cases with shorter dactylitis duration.

On the other hand, the presence of GS synovitis and intraarticular PDS at PIP level was more frequently observed in patients with longer dactylitis duration. However, flexor tenosynovitis was also present in the chronic form but was of a lesser magnitude. These results confirm the association between US patterns of disease compartmentalization in dactylitis and its duration, as already shown in a previous study with a smaller sample of patients²³.

At present, the natural clinical course of dactylitis remains largely unknown and longitudinal studies on soft tissue changes in dactylitis have never been done. Previous

US^{15,16,17} and MRI^{18,20,34} studies have demonstrated that dactylitis is characterized by the variable association of inflammatory involvement of flexor tendons (tenosynovitis), adjacent soft tissue thickening/edema, and synovitis of MCP, PIP, and DIP joints. The main limits of previous US studies were the very small samples of patients (usually < 30 dactylitic digits), the low frequency of the probe used (7.5 or 10 MHz), and the absence of PD examination^{15,16,17}. In accord with our data, an MRI study by Olivieri, *et al* of dactylitic toes with a dactylitis duration shorter than 7 weeks showed flexor tenosynovitis and peritendinous soft tissue edema in all patients and a low prevalence of joint synovitis¹⁹.

In our study, patients were enrolled in a consecutive manner and they were not selected according to treatment. Although we cannot exclude an influence of treatment on presence and severity of US abnormalities, the comparison of the prevalence of any US alterations did not differ between the treated and the untreated patient groups.

Our present study has several limitations. The main one is its cross-sectional nature. The duration of symptoms is therefore obtained only through medical history. Another limitation of our study is the artificial definition of acute or chronic dactylitis based on the median of the duration of symptoms in the patients of our group. In addition, we cannot exclude that patients with dactylitis duration > 20 weeks could have had a less severe form of dactylitis; only longitudinal studies can clarify these aspects. Moreover, we have used a very general definition of edema because there is currently no agreement on a definition of soft tissue thickening/edema. However, the high intra- and interobserver reliability of US abnormalities supported the validity of this definition. For a more correct evaluation of soft tissue changes in relation to dactylitis duration, it would be useful to use a semiquantitative score. Similarly, there is no precise definition and grading for the subcutaneous PDS. Another possible limitation is that we have enrolled patients with different drug treatments. Currently there are no data about modification induced by treatment of US characteristics of dactylitis. Moreover, no significant differences were present comparing treatment in the 2 groups of patients. Further, we did not evaluate lesions of volar plate, pulley, and extensor tendons at distal phalanx insertion because of limitations of the US machine we used. The study of these structures should be performed with a higher frequency probe (22–24 MHz).

This is the first multicenter study, to our knowledge, that evaluated the relationship between US lesions and dactylitis duration in a large PsA hand dactylitis cohort. Despite limitations of our study, we found a predominance of flexor tenosynovitis, soft tissue edema, and subcutaneous PDS in early cases and a high prevalence of joint synovitis at PIP level in the chronic form. Our findings could suggest a possible change from a predominant extracapsular pattern in the early phase to an intrasynovial pattern in the chronic

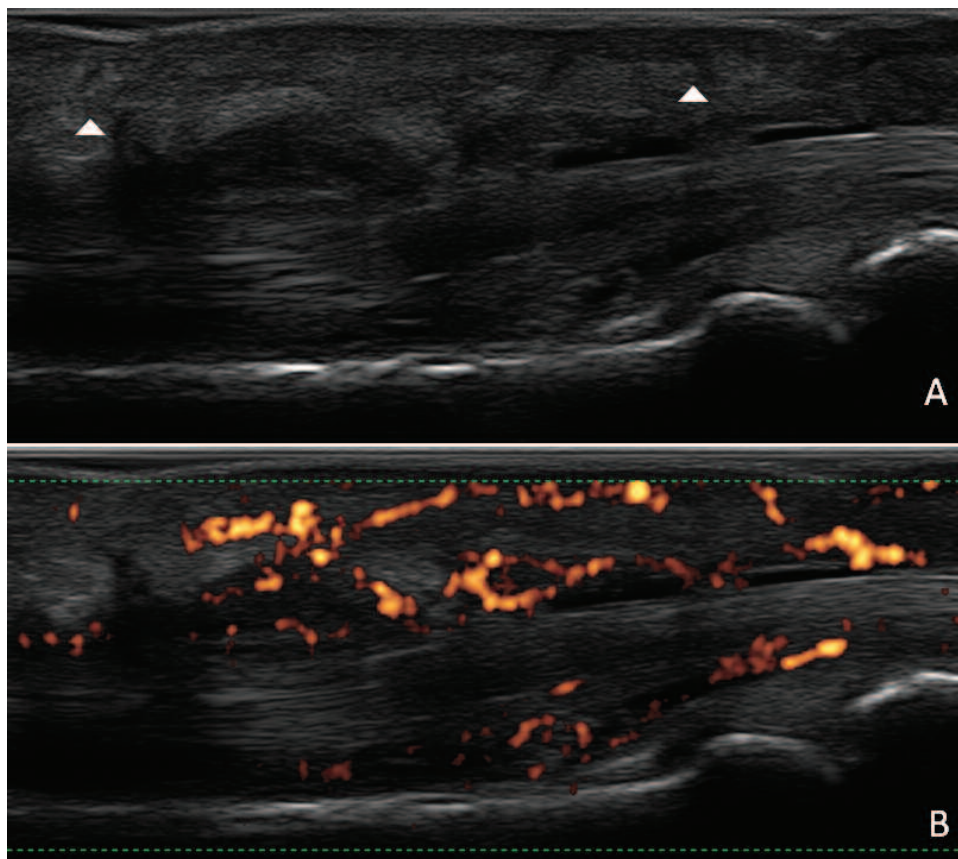


Figure 1. Longitudinal views of dactylitis belonging to the first group (dactylitis duration shorter than 20 weeks). A. Ultrasound shows flexor tenosynovitis of grade 2 with soft tissue edema (white arrowheads), whereas joint synovitis is absent. B. Power Doppler signal (PDS) is present around the tendon fibers and in subdermal tissue; intrarticular PDS is absent.

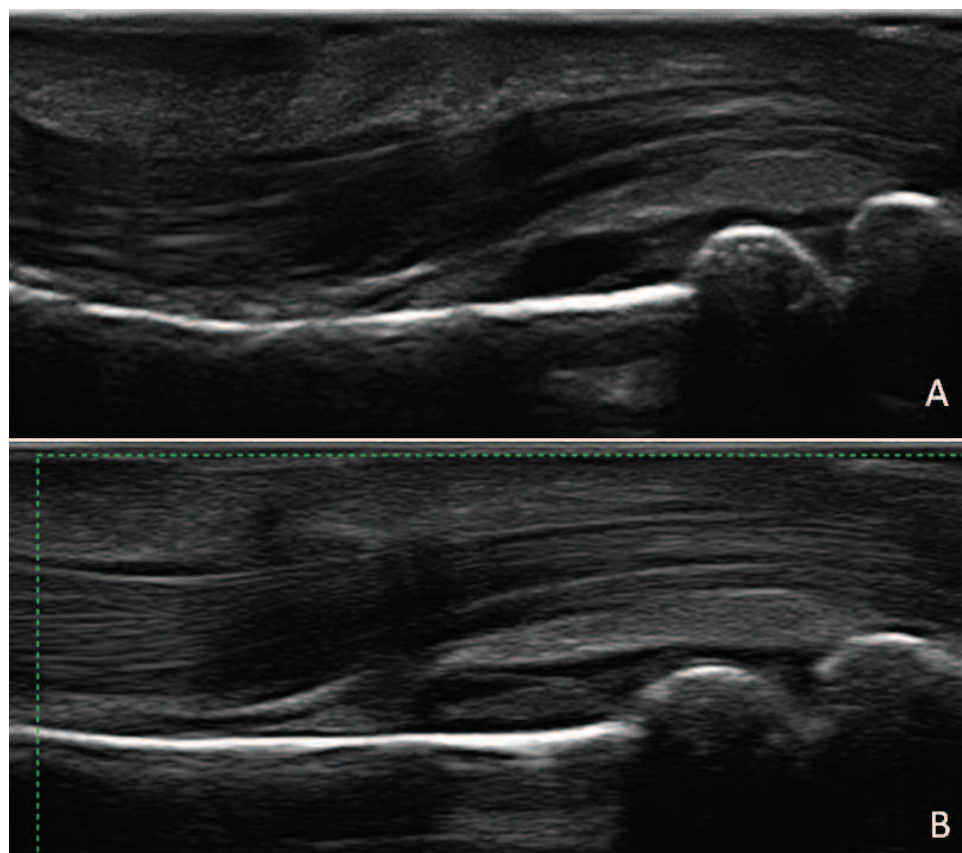


Figure 2. Longitudinal views of dactylitis belonging to the second group (dactylitis duration longer than 20 weeks). A. Ultrasound shows no peritendinous edema, distension of the flexor tendon sheath (grade 1), and of the capsule (grade 3) at proximal interphalangeal joint level. B. Power Doppler signal is absent in the articular, peritendinous, and subcutaneous areas.

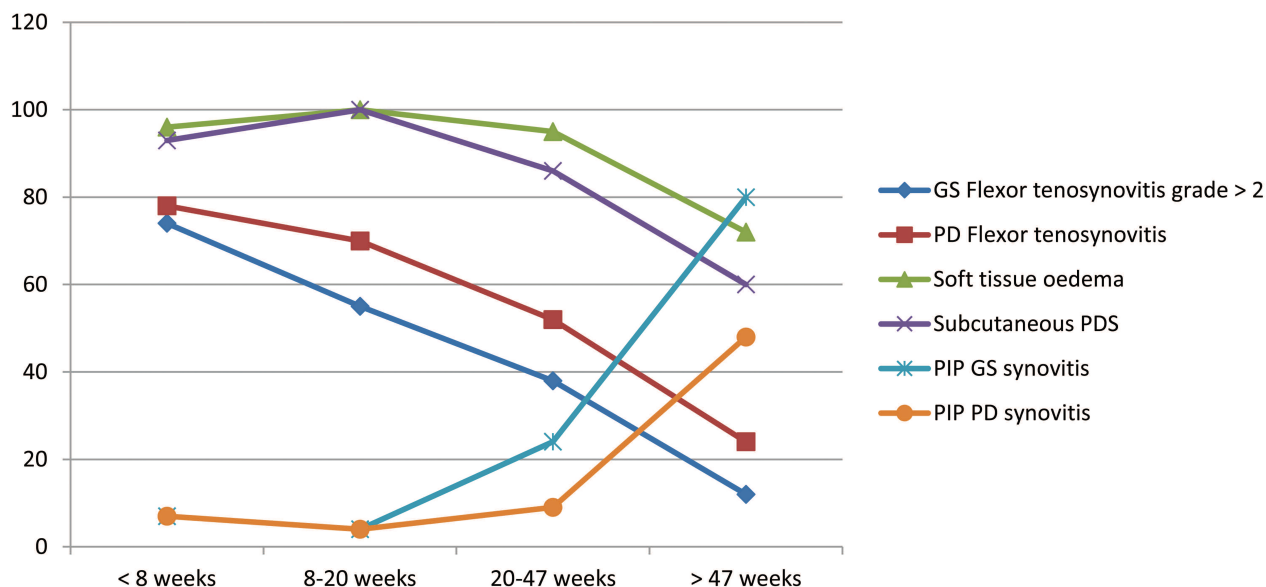


Figure 3. Prevalence of selected US abnormalities after splitting cases into quartiles based on dactylitis duration. US: ultrasound; GS: greyscale; PD: power Doppler; PDS: subcutaneous PD signal; PIP: proximal interphalangeal.

Table 3. Prevalence of ultrasonographic abnormalities according to therapy.

Variables	CsDMARD-treated Patients	CsDMARD-naive Patients
Total cases, n	48	52
GS flexor tenosynovitis	87	88
PD flexor tenosynovitis	75	69
Soft tissue edema	96	85
PDS	85	85
GS synovitis involving at least 1 joint	33	46
PD synovitis involving at least 1 joint	23	19
Cases with dactylitis duration < 20 weeks, n	29	25
GS flexor tenosynovitis	97	88
PD flexor tenosynovitis	86	88
Soft tissue edema	97	96
Subcutaneous PDS	93	100
GS synovitis involving at least 1 joint	14	24
PD synovitis involving at least 1 joint	10	8
Cases with dactylitis duration > 20 weeks, n	19	27
GS flexor tenosynovitis	74	89
PD flexor tenosynovitis	58	52
Soft tissue edema	95	74
Subcutaneous PDS	74	70
GS synovitis involving at least 1 joint	63	67
PD synovitis involving at least 1 joint	42	30

Data are percentages, except where noted. No p values were significant. csDMARD: conventional synthetic disease-modifying antirheumatic drugs; GS: greyscale; PD: power Doppler; PDS: subcutaneous PD signal.

evolution. However, longitudinal imaging studies are needed to clarify these aspects.

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