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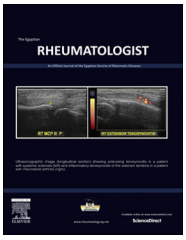

ORIGINAL ARTICLE

A comparative study between ultrasonographic hand features in systemic sclerosis and rheumatoid arthritis patients: Relation to disease activity, clinical and radiological findings

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Calcinosis

Abstract *Aim of the work:* To compare ultrasonographic (US) hand features in systemic sclerosis (SSc) and rheumatoid arthritis (RA) patients and to investigate their relationship with disease activity, clinical and radiographic data.

Patients and methods: Forty SSc and 30 RA patients were consecutively included. All patients underwent clinical examination, X-ray and US on the hand and wrist joints to detect synovitis, tenosynovitis, and calcinosis. Disease activity score-28 (DAS28) and European Scleroderma Activity index were used for RA and SSc patients respectively. Health Assessment Questionnaire-Disability Index (HAQ-DI) was used in all patients.

Results: The frequency of synovitis and tenosynovitis detected by US was found to be higher than that found by clinical examination in both RA and SSc patients ($p = 0.01$, $p = 0.02$, respectively). US synovitis was detected in 10 SSc (25%) and in 17 RA patients (56%). US tenosynovitis was found in 18 SSc (45%) versus 11 RA patients (36.6%). US synovitis and tenosynovitis in RA patients showed a statistically significant correlation with the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor, HAQ-DI and DAS28. Positive intrasynovial power Doppler signal was significantly frequent in RA than SSc patients ($p < 0.001$). Sclerosing tenosynovitis appeared to be specific to SSc patients. Calcifications were observed in both SSc and RA patients, but with no statistically significant difference ($p = 0.69$).

Conclusion: US provided valuable disease activity information in both RA and SSc patients more than clinical examination. US articular involvement in SSc is less frequent compared to that in RA, with specific appearance of sclerosing tenosynovitis in SSc patients.

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1. Introduction

Musculoskeletal ultrasound (MSUS) nowadays plays an important role in diagnosing and treating rheumatic diseases [1]. The presence of synovitis detected by MSUS is useful in the diagnosis of undifferentiated arthritis (UA) [2] and in inflammatory arthritis it is predictive of persistent disease [3], joint damage [4], and acute disease flare [5]. It has dramatically improved joint and tendon evaluation in rheumatoid arthritis (RA) and other inflammatory diseases [6]. However, MSUS also has its limitations as the technique is operator dependant, and assessments are time consuming if a large number of joints are examined.

In RA, MSUS is more sensitive than clinical examination for detecting synovitis [7,8] and the presence of MSUS synovitis correlates with future radiographic progression [9]. Consequently, it has been suggested that MSUS should be included in the definition of remission [10] and that MSUS assessment of disease activity could be utilized to inform therapeutic decisions as part of a treating to target strategy [11].

Regarding systemic sclerosis (SSc), joint symptoms are reported by 24–97% of SSc patients during the course of their disease, and are frequently disabling [12–16]. Manifestations of SSc hand are ranging from arthralgias to frank arthritis, contractures, and tendon friction rubs [12]. Clinical assessment is limited by concomitant skin disease.

Radiographic studies in SSc and RA have shown that the commonly affected areas are the joints, soft tissue, and bones of the hands [13,14,17–19]. However, radiographs exhibit some limitations regarding their sensitivity to detect early inflammatory changes, such as effusion or synovitis, and they cannot assess tendon damage. Therefore, radiographic and clinical evaluations are imperfect for assessing the whole spectrum of articular involvement in SSc and RA [6].

The objectives of our study were to compare the characteristics of US hand involvement in SSc and RA patients and to determine the correlations between US findings with disease activity, clinical and radiological parameters.

2. Patients and methods

2.1. Study design

The work was conducted as a comparative study between ultrasonographic hand features in SSc and RA patients and to study their relation to clinical and radiological findings. All subjects were recruited from Rheumatology departments, Cairo and Fayoum University hospitals and were all informed about the study and a written informed consent was obtained from each patient and healthy controls in accordance with the ethical principles for human investigations, as outlined in the 2nd Helsinki Declaration.

2.2. Patients

We studied 40 SSc patients (30 females and 10 males) who fulfilled ACR criteria [20] with a mean age of 34.4 ± 8.5 years, together with 30 RA patients (22 females and 8 males) who satisfied the 2010 ACR/EULAR criteria [21] with a mean age of 44.0 ± 9.4 years. The SSc patients were further subdivided into diffuse (dSSc) and limited (lSSc) according to the criteria proposed by Le Roy and his colleagues [22]. All patients were assessed for sex, age, disease duration and medications taken. For the disease activity measures, we used the disease activity score-28 (DAS 28) for RA patients [23] and the European Scleroderma Study Group activity index was used for SSc patients [24]. The Health Assessment Questionnaire and Disability Index (HAQ-DI) was used for both SSc and RA patients [25].

2.3. Laboratory data

The ESR was measured by the Westergren method; serum CRP by nephelometry; Rheumatoid factor (RF) by latex test; anti-cyclic citrullinated antibody (anti-CCP) by ELISA; and Anticentromere antibodies and Anti nuclear antibodies (ANA) by immunofluorescent while anti-Scl70 by ELISA.

2.4. Clinical assessment

Clinical evaluation on each patient was performed by 2 rheumatologists, blinded to the X-ray and US characteristics. Tender and swollen joint counts, together with the presence of tendon friction rubs and contractures were recorded [26].

2.5. X-ray evaluation

Standard antero-posterior views of the hands and wrists were obtained from SSc and RA patients. The following features were noticed for each joint: juxta-articular osteoporosis, space narrowing, marginal and central erosions and deformity. X-rays were evaluated by a radiologist blinded to the identity of patients and to the clinical and ultrasonographic characteristics.

2.6. US examination

US was performed on the joints of both hands and fingers (metacarpophalangeal [MCP], proximal interphalangeal [PIP], and distal interphalangeal [DIP] joints) and the wrists (radiocarpal [RC], ulnarcarpal [UC] and intercarpal [IC] joints), with LOGIQ P5/A5/A5Pro ultrasound machine using a near focused linear array transducer with a center frequency of 10–14 MHz. US examination aimed at the detection of synovitis, tenosynovitis and calcinosis. PD was graded using a validated semiquantitative scoring system, which consists of a scale of 0–3, where (0) represented no PD signal, (1) one or two vessels in small joints or up to three single vessels in large joints, (2) less than half of the synovial area and (3) more than half of the synovial area [27].

Data analysis was performed through Statistical Package of Social Sciences (SPSS) software program for windows version 21. Data were expressed as number and percentage for qualitative variables or mean and standard deviation for quantitative ones. Comparison between groups was performed through the Chi square or Fisher's exact test for qualitative variables and independent sample *t*-test (if parametric) or the Mann Whitney test (if non-parametric) for quantitative ones. *p* values less than 0.05 were considered significant.

3. Results

The study included 40 SSc patients (30 females and 10 males), 25 had limited form and 15 had diffuse form with a mean age of 34.4 ± 8.5 years and a mean disease duration of 5.2 ± 2.6 years in addition to 30 RA patients (22 females and 8 males) with a mean age of 44.0 ± 9.4 years and a mean disease duration of 6.8 ± 5.1 years. ANA was detected in 15 SSc patients while 20 were anti-centromere positive and 10 anti-Scl 70 positive. Rheumatoid factor (RF) was detected in 52% of the SSc patients and 85% in the RA patients while anti-CCP was detected in 30% of RA patients and 2% in SSc patients. The mean ESR and CRP in SSc patients was 20.2 ± 8.0 mm/h and 3.9 ± 4.8 mg/dl respectively, while in RA patients the ESR and CRP were 30.2 ± 7.0 mm/h and 5.0 ± 6.8 mg/dl respectively. The mean DAS28 was 3.86 ± 2.17 and the HAQ-DI was 1.7 ± 0.8.

The treatment regimens for the RA patients were DMARDs (Methotrexate, Leflunomide and Hydroxychloroquine) in 28/30 patients and steroids in 22/30 patients (mean dosage 7.9 ± 5.9 mg/day). As for the SSc patients treatment regimen included a low dose of steroids ranging between 5 and 10 mg in 18/40 patients, DMARDs mostly methotrexate and azathioprine in 11/40 patients and cyclophosphamide in 5/40 patients.

3.1. Clinical features

Thirteen SSc patients (32.5%) had tender joints on palpation and 6 patients (15%) had swollen joints, in addition tendon friction rubs were present in 11 SSc patients (27.5%). Among RA patients, 19 (63.3%) had tender joints on palpation and 13 patients (43.3%) had swollen joints while tendon friction rub was present in 1 RA patient (3.3%). The clinical articular features of the SSc and RA patients are shown in (Table 1).

3.2. Radiographic findings

The main radiographic features of hand involvement in our study were as follows: among RA patients, bone erosions involving the wrist in 8 (26.7%) patients, MCPs in 12 (40%) of the patients and PIPs in 9 (30%) patients. Joint space narrowing involving the wrist in 6 (20%) of the patients, MCPs in 15 (50%) of the patients and PIPs in 10 (33.3%) patients, demineralization in 20 (66.7%), patients, calcinosis in 2 (6.6%) patients and osteophytes in 2 (6.6%). On the other hand SSc patients found to have bone erosions in 1 (2.5%) patient involving the wrist joint, joint space narrowing over the wrist in 1 (5%) patient, MCPs in 3 (7.5%) patients and PIPs in 1 (2.5%) patient. Demineralization in 15 (37.5%) patients, acro-osteolysis in 1 (2.5%) patient and calcinosis in 4 (10%) patients (Table 2).

Table 2 Radiologic articular involvement among systemic sclerosis (SSc) and rheumatoid arthritis (RA) patients.*

	SSc patients (n = 40)	RA patients (n = 30)
Radiologic demineralization	15 (37.5)	20 (66.7)
Joint space narrowing		
Wrists	2 (5)	6 (20)
MCP joints	3 (7.5)	15 (50)
PIP joints	1 (2.5)	10 (33.3)
Erosions		
Wrists	1 (2.5)	8 (26.7)
MCP joints	0 (0)	12 (40)
PIP joints	0 (0)	9 (30)
Calcinosis	4 (10)	2 (6.7)
Acro-osteolysis	1 (2.5)	0 (0)
Osteophytes	1 (2.5)	3 (10)

SSc = systemic sclerosis; RA = rheumatoid arthritis; MCP = metacarpophalangeal; PIP = proximal interphalangeal; DIP = distal interphalangeal.
* Values are the number (percentage) unless otherwise indicated.

Table 1 Clinical articular involvement and disability index among systemic sclerosis (SSc) and rheumatoid arthritis (RA) patients.*

	SSc patients (n = 40)	RA patients (n = 30)	p Value
Patients with tender joints	13 (32.5)	19 (63.3)	
Number of tender joints (mean ± SD)	1.9 ± 1.04	5.84 ± 3.96	0.015
Distribution of tender joints			
Wrist	2 (15.4)	14 (73.7)	
MCP	8 (61.5)	14 (73.7)	
PIP	8 (61.5)	11 (57.9)	
DIP	0 (0.0)	2 (10.5)	
Patients with ⩾1 swollen joint	10 (25)	16 (53.3)	
Number of swollen joints (mean ± SD)	1.4 ± 0.5	6.5 ± 3.4	0.024
Distribution of the swollen joints			
Wrist	1/10 (10)	6/16 (37.5)	
MCP	9/10 (90)	7/16 (43.8)	
PIP	4/10 (40)	3/16 (18.8)	
DIP	0/10 (0)	0/16 (0.0)	
Tendon friction rubs	11 (27.5)	1 (3.3)	
HAQ-DI score (mean ± SD)	0.9 ± 0.8	0.87 ± 0.88	0.009

SSc = systemic sclerosis; RA = rheumatoid arthritis; MCP = metacarpophalangeal; PIP = proximal interphalangeal; DIP = distal interphalangeal; HAQ-DI = Health Assessment Questionnaire-Disability index.
* Values are the number (percentage) unless otherwise indicated.

Table 3 Comparison of ultrasonography findings between systemic sclerosis (SSc) and rheumatoid arthritis (RA) patients.*

	SSc patients (n = 40)	RA patients (n = 30)	p-Value
Synovitis	10 (25)	17 (56)	0.044
Characteristics of synovitis			
Inflammatory activity	3 (20)	57 (95)	<0.001
Power Doppler grade 1	3 (20)	32 (53.3)	0.02
Power Doppler grade 2 or 3	0 (0)	25 (41.6)	0.002
Distribution of synovitis			
Ulnarcarpal joints	0 (0)	8 (13.3)	0.3
Radiocarpal joints	1 (6.6)	11 (18.3)	0.4
Intercarpal joints	0 (0)	11 (18.3)	0.1
MCP joints	9 (60)	35 (58.3)	1.0
PIP joints	4 (26.6)	15 (25)	1.0
DIP joints	0 (0)	0 (0)	1.0
Tenosynovitis	18 (45)	11 (36.6)	0.63
Characteristics of tenosynovitis			
Sclerosing pattern	81 (90)	0 (0)	<0.001
Inflammatory activity	45 (50)	14 (87.5)	0.006
Sclerosing and inflammatory pattern	34 (37.7)	0 (0)	0.002
Distribution of tenosynovitis			
No. of extensor tendons	44	6	
Sclerosing pattern	42 (95.5)	0 (0)	<0.001
Power Doppler	17 (38.6)	3 (50)	0.7
No. of flexor tendons	46	10	
Sclerosing pattern	39 (84.8)	0 (0)	<0.001
Power Doppler	25 (54.3)	9 (90)	0.07
Calcifications	4 (10)	2 (6.6)	0.7
In the tendon sheath	0 (0)	0 (0)	–
Intraarticular	4 (100)	2 (100)	–
In the soft tissue	0 (0)	0 (0)	–
Osteophytes	4 (10)	6 (20)	1.0
Erosions			
Wrists	1 (2.5)	10 (33)	0.003
MCPs	0	14 (46)	0.002
PIPs	0	10 (33)	0.001
Joint space narrowing			
Wrists	4 (10)	8 (26)	
MCPs	4 (10)	18 (60)	
PIPs	1 (2.5)	10 (33)	

SSc = systemic sclerosis; RA = rheumatoid arthritis; MCP = metacarpophalangeal; PIP = proximal interphalangeal; DIP = distal interphalangeal.

* Values are number (percentage) unless otherwise indicated.

3.3. Ultrasonographic findings in SSc and RA patients

The results of US findings in SSc versus RA patients are shown in (Table 3).

3.3.1. US synovitis in SSc and RA patients

Regarding synovitis (i.e. effusion and/or synovial proliferation) (Fig. 1), US detected synovitis in 10 (25%) of 40 SSc patients and in 17 (56%) patients with RA, synovitis was found in the wrists, MCP joints and PIP joints of SSc patients with a statistically significant difference when compared to the RA patients (p = 0.04). Power Doppler revealed inflammatory activity in 3 joints with synovitis in SSc patients, all of which were of grade 1. Positive intrasynovial power Doppler signal was significantly frequent in RA than SSc patients (57/60 joints [95%] versus 3/15 joints [20%], p < 0.001). A grade 2 or 3 power Doppler signal was more likely observed in RA than in SSc patients (25/60 joints [41.7%] versus 0/15 joints (p = 0.002).

3.3.2. US tenosynovitis in SSc and RA patients

Regarding US of the tendons, tenosynovitis was found in 18 SSc patients (45%) and 11 (36%) among RA patients (Fig. 2). A total of 90 tendons with tenosynovitis were detected, among the tendons with tenosynovitis, 81 (90%) were characterized by a hyperechoic tendon sheath thickening, a pattern considered as sclerosing. Sclerosing tenosynovitis appeared to be specific to SSc patients (81/90 tendons in SSc patients versus 0/16 tendons in RA patients (p < 0.001) (Fig. 2). A power Doppler signal corresponding to an inflammatory pattern was detected in 45/90 tendons (50%) with tenosynovitis. In addition 34 (37.7%) of 90 tendons with tenosynovitis were both sclerosing and inflammatory. US tenosynovitis occurred in patients with concomitant synovitis in 4 (40%) of 10 cases.

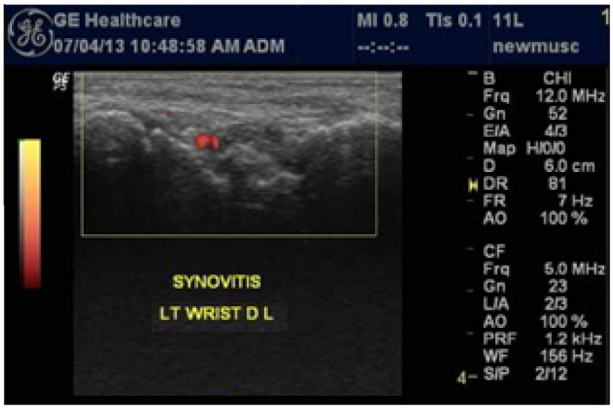

Figure 1 Ultrasonographic image of the left wrist showing synovitis with grade 1 PD signal.

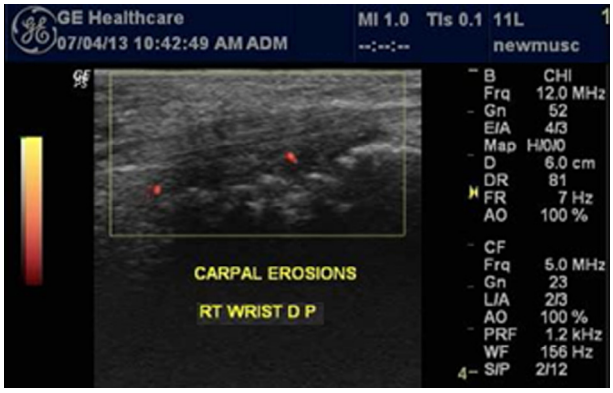

Figure 4 Ultrasonographic image showing carpal erosions in a patient with RA.

3.3.3. US calcifications, erosions and joint space narrowing in SSc and RA patients

Regarding US of the soft tissues, calcifications were detected in 4 (10%) SSc and 2 (6.6%) RA patients (Fig. 3) but with no statistically significant difference ($p = 0.69$). On the other hand there was a statistical significant difference between US hand erosions and joint space narrowing in RA and SSc patients ($p < 0.001$) (Fig. 4).

3.3.4. Relationship between ultrasonographic variables with disease activity, clinical and radiological findings

In SSc patients, the prevalence of synovitis, tenosynovitis detected by US was found to be higher than that found by clinical examination ($p = 0.01$, $p = 0.02$ respectively), while US tenosynovitis was more likely to occur in patients with tendon friction rubs on clinical examination ($p = 0.04$).

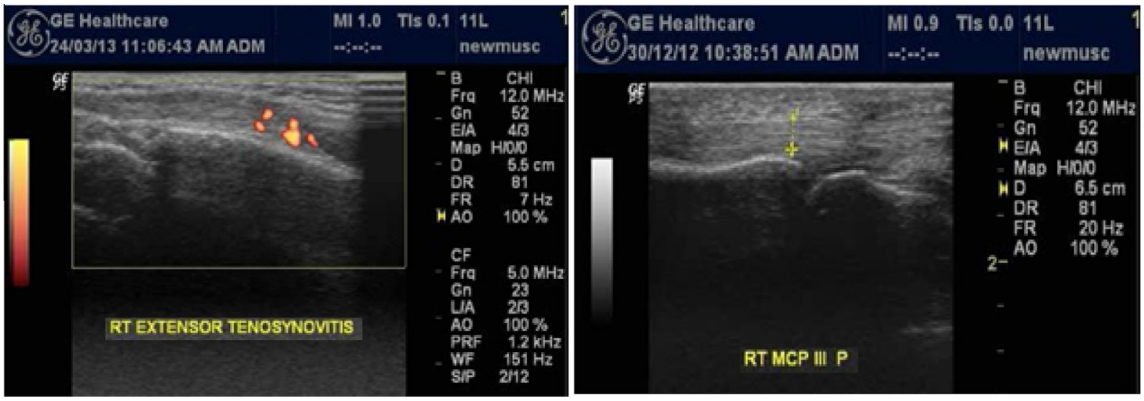

Figure 2 Ultrasonographic image (longitudinal section) showing inflammatory tenosynovitis of the extensor tendons in a patient with RA (left) and sclerosing tenosynovitis in a patient with SSc (right).

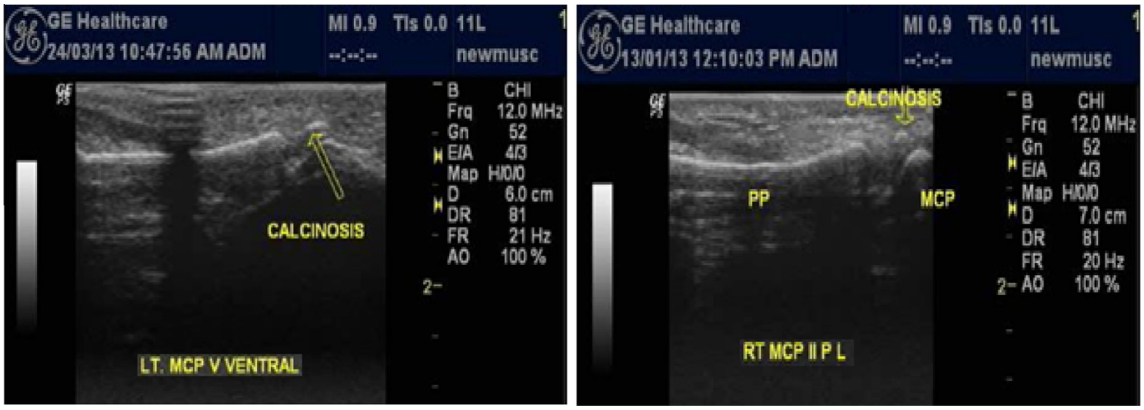

Figure 3 Ultrasonographic image showing intra-articular calcification within the MCP joint in a patient with RA (left) and in a patient with SSc (right).

US synovitis, tenosynovitis and calcinosis showed a non-statistically significant correlation with the patient's age ($p = 0.47$), gender ($p = 0.67$), disease duration ($p = 0.92$), Rheumatoid factor ($p = 0.28$), ESR ($p = 0.15$), CRP ($p = 0.36$) or HAQ-DI ($p = 0.14$).

US in SSc patients showed a significantly higher number of joints with osteophytes than X-ray ($p = 0.004$), while only one patient showing erosions detected by US and X-ray.

In RA patients, the prevalence of synovitis, tenosynovitis detected by US was found to be higher than that found by clinical examination ($p = 0.02$, $p = 0.03$, respectively).

US synovitis, tenosynovitis showed a statistically significant correlation with the ESR ($p < 0.001$, $p = 0.002$ respectively), CRP ($p < 0.001$, $p = 0.003$ respectively) rheumatoid factor ($p = 0.02$, $p = 0.03$ respectively), HAQ ($p < 0.001$ $p < 0.001$ respectively) and DAS28 ($p < 0.001$, $p < 0.002$ respectively). However, a non-statistically significant correlation was found with the patient's age ($p = 0.14$, $p = 0.12$), gender ($p = 0.33$, $p = 0.35$) and disease duration ($p = 0.76$, $p = 0.53$).

On the other hand, US calcinosis showed a statistically significant correlation with the patient's age ($p < 0.001$) and DAS28 ($p = 0.003$). However, a non-statistically significant correlation was found with the patient's gender ($p = 1.0$), disease duration ($p = 0.37$), HAQ ($p = 0.44$), ESR, CRP ($p = 0.18$, $p = 0.43$ respectively), and rheumatoid factor ($p = 1.0$).

US in RA patients showed a significantly higher number of joints with joint space narrowing and erosions than X-rays ($p = 0.004$, $p = 0.003$ respectively).

4. Discussion

Our study enrolled 40 SSc and 30 RA patients. Our data showed that US synovitis was found in 56% of the RA patients in comparison to 43% with clinically detected articular manifestations and 25% of SSc patients in comparison to 15% of clinical synovitis which states clearly that US is more sensitive than clinical examination in detecting joint swelling in both RA and SSc patients. In keeping with our results, other studies showed that US detects subclinical synovitis and pathological findings which are not detected clinically [28–32]. In our study, US in SSc patients showed a significantly higher number of joints with osteophytes than X-rays ($p = 0.004$) with only one patient showing erosions by US, while in RA US showed a higher number of joints with joint space narrowing and erosions than X-rays. These results are consistent with published data [19,6]. In another Egyptian study on SSc patients, hand disability was mainly related to impaired hand mobility and also diminished strength. The use of US in adjunct to clinical examination refines the evaluation of hand impairment in these patients [33]. The reduced sensitivity of US in detecting erosions in SSc patients is probably due to limited number of SSc patients with erosive disease and whether an erosive arthritis is a part of the spectrum of scleroderma or just an overlapping RA is still a matter of debate [34].

Power Doppler US has demonstrated a high sensitivity (88.8%) and specificity (97.9%) for the assessment of inflammatory activity in the joints of patients compared with the dynamic contrast enhanced MRI [35]. In the same way our study showed inflammatory activity revealed by power Doppler in 3 joints with synovitis in scleroderma patients. Positive intra-synovial power Doppler signal was significantly frequent in RA than SSc patients. A grade 2 or 3 power Doppler signal was more likely observed in RA patients compared to grade 1 in SSc patients which indicates the articular difference between the two groups. This coincides with the results of studies carried out by other authors [36–38]. In RA patients we found a significant correlation between US detected synovitis and the DAS28, ESR and CRP. In contrast, other studies found that many RA patients who are regarded as having clinically inactive disease still exhibit evidence of persistent synovitis on US scanning [7] that appears predictive of worse outcomes [4]. However, other studies suggested that radiographic progression of patients in remission is largely restricted to those who continue to exhibit clinical evidence of joint inflammation (SJC $\geqslant 2$), since patients with an SJC $\leqslant 1$ or in sustained remission had minimal disease progression [39,40].

As regards tenosynovitis it was found in 18 SSc patients (45%), among the tendons with tenosynovitis (90%) of them were characterized by hyperechoic tendon sheath thickening a pattern characteristic of sclerosing tenosynovitis more observed in the extensor than flexor tendons. Sclerosing tenosynovitis appears to be specific for scleroderma patients compared to RA patients. Again, this coincides with the results of other authors [41] who stated that US tenosynovitis findings in scleroderma do not correlate with disability and they explained that by their patients having mildly severe tendon affection as suggested by the low prevalence of tendon friction rub. This unique pattern specific to scleroderma patients may be an important way to suspect scleroderma in cases of diffuse or uncertain articular manifestations where clinical examination may be insufficient in detecting articular involvement [36,38,42]. Regarding US of soft tissues, calcifications were detected in both scleroderma and RA patients (10% and 6.6%) respectively, with no statistically significant pattern, these data are in accordance with previous studies that showed calcifications in SSc patients in about 10–50% of the patients [43].

In conclusion, MSUS is not a substitute to history and physical examination, US hand involvement in SSC and RA can be more accurate than the single clinical examination. US articular involvement in SSc is less frequent and is characterized by mild inflammatory changes compared to that in RA, with specific appearance of sclerosing tenosynovitis in SSc patients more than RA. Further, larger prospective studies are warranted to evaluate the importance of using US in the follow up and assessment of SSc and RA patients.

Conflict of interest

None.

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