

Musculoskeletal ultrasound on the hand and wrist in systemic sclerosis

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Received 4 July 2015

Accepted 8 January 2016

Egyptian Rheumatology and Rehabilitation
2016, 43:95–101

Background

Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disorder. Musculoskeletal involvement represents a major cause of disability in SSc, which is localized especially at the level of the hands and feet. Musculoskeletal ultrasound (MSUS) had become a reference imaging tool in the evaluation of joint and soft-tissue abnormalities in rheumatic diseases.

Aim of the work

This study aimed to characterize ultrasonographic changes of the hand and wrist in patients with SSc as compared with patients with rheumatoid arthritis (RA), as well as determine the relation of these changes with clinical, laboratory, and radiographic findings in SSc.

Patients and methods

Twenty SSc patients and 20 control RA patients were included in this study. All patients underwent history taking, clinical examination, hand/wrist plain radiography, and MSUS performed on both hand and wrist joints.

Results

MSUS was more sensitive than radiographies in detecting soft-tissue calcifications in SSc patients and also in detecting erosions with no statistically significant difference ($P > 0.05$). In SSc patients, the prevalence of synovitis and tenosynovitis detected by ultrasound was found to be statistically significantly higher than that found by clinical examination ($P = 0.025$ and 0.011 , respectively). Patients with higher values of erythrocyte sedimentation rate and C-reactive protein were more likely to have synovitis and/or tenosynovitis and inflammatory activity on power Doppler assessment.

Conclusion

Ultrasound was more accurate than clinical examination and conventional radiography in the detection of subclinical synovitis, tenosynovitis, and the underlying fibrotic changes of tendon friction rub. In SSc patients, on using MSUS, articular involvement was found to be less frequent compared with that in RA patients, with specific appearance of sclerosing tenosynovitis in SSc patients.

Keywords:

rheumatoid arthritis, systemic sclerosis, ultrasound

Egypt Rheumatol Rehabil 43:95–101

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1110-161X

Introduction

Systemic sclerosis (SSc) is an autoimmune inflammatory disorder of unknown etiology, characterized by pronounced fibroproliferative alterations in the microvasculature and frequent cellular and humoral abnormalities, resulting in a severe and progressive fibrotic process [1].

Scleroderma is a rare disorder but its symptoms occur frequently in the general population, such as Raynaud's phenomenon, gastroesophageal reflux, fatigue, and joint symptoms, which are reported by 24–97% of SSc patients during the course of their disease. These symptoms are frequently disabling and can range from mild arthralgia to frank erosive arthritis with synovitis resembling rheumatoid arthritis (RA), contractures, and tendon friction rubs. Clinical assessment is usually limited by the concomitant

skin disease. Therefore, it is important to have a diagnostic method that allows early and rapid disease recognition [2].

The role of ultrasound (US) is becoming more and more relevant in the assessment of rheumatic diseases with wide availability and recent improvement in technology coupled with portability, low cost, and safety, which makes it the first-choice imaging investigation for the evaluation of musculoskeletal diseases [3]. However, US skills with its prerequisite of sufficient anatomical knowledge make the clinical

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diagnosis more precise and reduce uncertainty in the choice of therapy [4].

The hand is one of the anatomical regions that is frequently explored by US in rheumatology, because of the fact that this area is a common target in several rheumatic diseases [5].

The last generation of US systems equipped with high-frequency probes allows for a quick and accurate assessment of even minimal early pathological changes in patients with rheumatic conditions affecting the small joints and the soft tissues of the hand and wrist [6].

Musculoskeletal ultrasound (MSUS) can detect subclinical joint synovitis, effusion, and tenosynovitis, in addition to its ability to detect bone erosions and soft-tissue calcinosis earlier than plain radiography [7].

This study aims to characterize ultrasonographic changes of the hand and wrist in patients with SSc as compared with patients with RA, as well as determine the relation of these changes with clinical, laboratory, and radiographic findings in SSc.

Patients and methods

Study approval

This study was approved by the ethical committee of our institution. All patients gave their written informed consent before participation in the study.

Patients

Twenty patients with SSc, who fulfilled the American College of Rheumatology (1980) criteria, were enrolled into this study. An additional 20 age- and sex-matched RA patients who met the new classification criteria of the American College of Rheumatology/European League against Rheumatism for RA classification (2010) [8] were included as the control group.

Both RA and SSc patients were chosen with hand or wrist pain and/or swelling with or without limitation of movements.

These patients were selected from among the inpatients and the outpatients at the Rheumatology and Rehabilitation and Internal Medicine Departments of Benha and Tanta University Hospitals between January 2014 and January 2015.

Every patient underwent clinical assessment and the results were recorded before radiographic and MSUS examination.

Skin involvement in SSc patients was evaluated using the modified Rodnan skin score [9].

All scleroderma patients and the control group were subjected to full history taking, thorough clinical examination, and routine laboratory studies [a complete blood count, evaluation of the erythrocyte sedimentation rate (ESR) by the Westergren method, and evaluation of serum C-reactive protein (CRP) by quantitative nephelometry]. They also underwent an enzyme linked immunosorbant assay for evaluation of antinuclear antibodies, anticentromere antibodies, and anti-Scl-70 antibodies.

Standard anteroposterior views of the hands and wrists were obtained for SSc and RA patients.

Musculoskeletal ultrasound examination

Grayscale ultrasound

MSUS examination was done just after clinical examination on the same day. In all SSc patients and the control group, MSUS examination was performed using a General Electric Logiq5 PRO (GE Healthcare, Milwaukee, Wisconsin, USA) with a 7–12 MHz linear array transducer. B-mode examination was conducted by setting the machine in order to obtain the widest spectrum of gray tones. Each joint of both hands (metacarpophalangeals, proximal interphalangeals, and distal interphalangeals) and both wrist joints were assessed for the presence of synovitis, joint effusion, bone erosion, soft-tissue calcification, and tenosynovitis [10].

Power doppler ultrasound examination

Power Doppler ultrasound examination (PDUS) was performed with a high-resolution equipment (Voluson Pro v; General Electric, U.S.A.) using 5–9 MHz multifrequency matrix array linear transducers. The pulse repetition frequency was kept low, and the region examined was also kept as small as possible to maximize the detection of abnormal blood flow within the synovium [11].

The regional blood flow was visualized by PDUS at a gain level without background noise. Vessels with maximal color activity were selected for a signal in the synovium that was graded as follows [12].

Grade 0: there is no flow signal in the synovium. Grade I: a mild flow signal indicates the presence of separate dot signals or short linear signals. Grade II: a moderate flow signal indicates the presence of clearly discernible vascularity with either many small vessels or several

long vessels with or without visible branching, though involving less than half the area of the synovium. Grade III: a severe flow signal indicates the presence of vessels involving more than half the area of the synovium.

In this way it was possible to obtain objective information on the quality of flow in the synovium as a supplement to the fraction of vascularization [13].

Statistical analysis

Statistical presentation and analysis of the present study was conducted using mean, SD, and the χ^2 -test by SPSS, version 20 (SPSS Inc., Chicago, Illinois, USA).

P-values greater than 0.05 were statistically insignificant, *P*-values less than or equal to 0.05 were considered statistically significant, and *P*-values less than or equal to 0.001 were considered highly significant.

Results

This study included 20 SSc patients, 17 women (85%) and three men (15%), whose ages ranged between 21 and 55 years (37.0 ± 10.6 years). Their disease duration ranged between 3 and 15 years (8.9 ± 3.9 years). Rheumatoid factor and anticyclic citrullinated peptide antibodies were detected in 30 and 4% of the SSc patients, respectively. The mean ESR and CRP levels were 27.9 ± 5.45 mm/h and 3.9 ± 2.5 mg/l, respectively.

The control group included 20 RA patients, 14 women (70%) and six men (30%), whose ages ranged between 30 and 60 years (43.4 ± 9.9 years). Their disease duration ranged between 5 and 20 years (9.5 ± 4.3).

SSc patients and the control group were matched for age and sex. SSc patients were divided into two groups: 13 patients (65%) had limited cutaneous SSc, whereas seven patients (35%) had diffuse cutaneous SSc (Tables 1–3).

In SSc, synovitis was detected in 60% of joints with grayscale and PDUS, whereas in RA patients synovitis was detected in 95% by grayscale and in 70% by PDUS. There was a statistically significant difference in the number of patients with synovitis and PDUS grades II and III, being higher in RA patients ($P < 0.05$).

There was a statistically significant difference ($P > 0.05$) regarding number of joints with effusion and a high statistically significant difference ($P > 0.001$) in the prevalence of erosions, being more in RA patients.

There was a statistically significant increase ($P > 0.05$) in synovitis in metacarpophalangeal joints in RA

Table 1 Clinical articular findings in scleroderma (SSc) patients

Clinical articular findings	SSc [<i>n</i> (%)]
Painful joints (palpation)	9 (45)
Wrist joints	4 (20)
MCP joints	3 (15)
PIP joints	3 (15)
DIP joints	4 (20)
Swollen joints	5 (25)
Wrist joints	2 (10)
MCP joints	1 (5)
PIP joints	1 (5)
DIP joints	3 (15)
Tendon friction rub	5 (25)

DIP, distal interphalangeal joint; MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint; SSc, systemic sclerosis.

Table 2 Plain radiographic findings in scleroderma (SSc) patients

Radiographic findings	SSc [<i>n</i> (%)]
Radiologic demineralization	9 (45)
Joint space narrowing	
Wrists	1 (5)
MCP joints	1 (5)
PIP joints	0 (0)
DIP	1 (5)
Erosions	
Wrists	1 (5)
MCP	1 (5)
PIP	0 (0)
DIP	1 (5)
Osteophytes	1 (5)
Resorption of distal ulna	0 (0)
Calcinosis	5 (25)
Acro-osteolysis	6 (30)

DIP, distal interphalangeal joint; MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint; SSc, systemic sclerosis.

patients, as detected by US, whereas the distal interphalangeals were significantly more affected in SSc patients ($P = 0.007$).

On US examination, tenosynovitis was found to affect 65% of SSc patients, being more in the extensor tendons (55%) than in the flexor tendons (20%), with a sclerosing pattern characterized by a hyperechoic tendon sheath thickening. This occurred more than the inflammatory PDUS pattern in both the extensor and flexor tendons (45 vs. 30% and 15 vs. 10%, respectively).

In RA patients, tenosynovitis also affected the extensor tendons (35%) more than it did the flexor tendons

Table 3 Comparison of MSUS findings between scleroderma (SSc) and rheumatoid arthritis (RA) patients

MSUS findings	Scleroderma [n (%)]	Rheumatoid arthritis [n (%)]	P-value
Synovitis grayscale	12 (60)	19 (95)	0.028*
PDUS			
PDUS grade I	9 (45)	4 (20)	0.091
PDUS grades II or III	3 (15)	10 (50)	0.018*
Distribution of synovitis			
Wrist joints	7 (35)	13 (45)	0.113
MCP joints	4 (20)	13 (45)	0.008*
PIP joints	5 (25)	14 (70)	0.114
DIP joints	7 (35)	0 (0)	0.007*
Joint effusion	10 (50)	16 (80)	0.046*
Erosion	3 (15)	15 (75)	0.001**
Tenosynovitis	13 (65)	9 (45)	0.204
Distribution of tenosynovitis			
Extensor tendons	11 (55)	7 (35)	0.527
Sclerosing pattern	9 (45)	0 (0)	0.001**
PDUS	6 (30)	7 (35)	0.518
Sclerosing and inflammatory pattern	5 (25)	0 (0)	
Flexor tendons	4 (20)	2 (10)	0.376
Sclerosing pattern	3 (15)	0 (0)	0.001**
PDUS	2 (10)	2 (10)	0.376
Sclerosing and inflammatory pattern	1 (5)	0 (0)	
Osteophytes	2 (10)	4 (20)	0.236
Soft-tissue calcification	8 (40)	0 (0)	0.001**

DIP, distal interphalangeal joint; MCP, metacarpophalangeal joint; MSUS, musculoskeletal ultrasound; PDUS, power Doppler ultrasound examination; PIP, proximal interphalangeal joint; SSc, systemic sclerosis.

Table 4 Comparison between clinical articular findings and MSUS findings in SSc patients

	Clinical articular manifestation (swollen joints) [n (%)]	MSUS findings (synovitis grayscale) [n (%)]	P-value
Scleroderma	5 (25)	12 (60)	0.025*
Wrist joints	2 (10)	7 (35)	
MCP joints	1 (5)	4 (20)	
PIP joints	1 (5)	5 (25)	
DIP joints	3 (15)	7 (35)	
	Tendon friction rub	Tenosynovitis	
	5 (25)	13 (65)	0.011*

DIP, distal interphalangeal joint; MCP, metacarpophalangeal joint; MSUS, musculoskeletal ultrasound; PIP, proximal interphalangeal joint; SSc, systemic sclerosis..

*Significant difference if $P < 0.05$.

(10%) with the inflammatory pattern. Sclerosing tenosynovitis was specific for SSc, remaining undetected in any RA patient, whereas inflammatory tenosynovitis occurred in both groups. Regarding soft-tissue calcifications on US examination, they were specifically found in 40% of SSc patients versus none in RA patients.

Table 4 shows a comparison between clinical articular findings and MSUS findings in SSc patients: the prevalence of synovitis ($P=0.025$) and

tenosynovitis ($P=0.011$) detected by US was found to be statistically significantly higher than that found by clinical examination (60 vs. 25% and 65 vs. 25%, respectively).

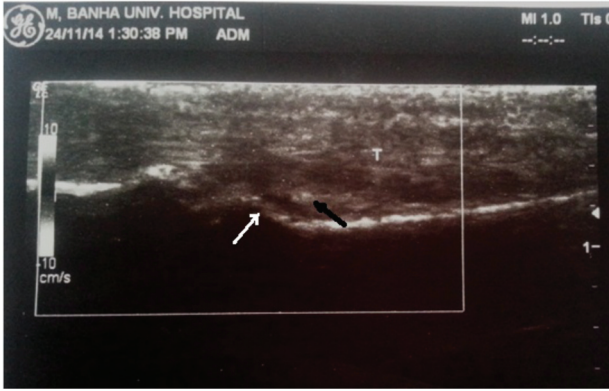
Table 5 shows a comparison between radiographic findings and MSUS findings in SSc patients: soft-tissue calcifications and erosions were more detectable by US than by radiography, with no statistically significant differences between them ($P > 0.05$ and > 0.05 , respectively).

Table 5 Comparison between radiographic findings and MSUS findings in SSc patients

	Radiography [n (%)]	MSUS [n (%)]	P-value
Soft-tissue calcification	5 (25)	8 (40)	0.076
Erosions	1 (5)	3 (15)	0.311

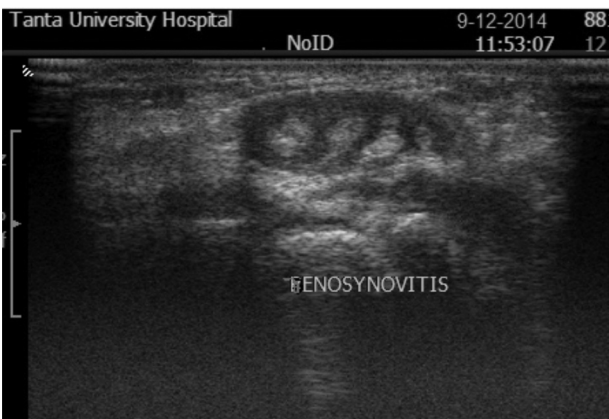
MSUS, musculoskeletal ultrasound; SSc, systemic sclerosis.

Figure 1



Ultrasonographic image of an systemic sclerosis patient showing fibrosing tenosynovitis (T) and soft-tissue calcification (black arrow).

Figure 2



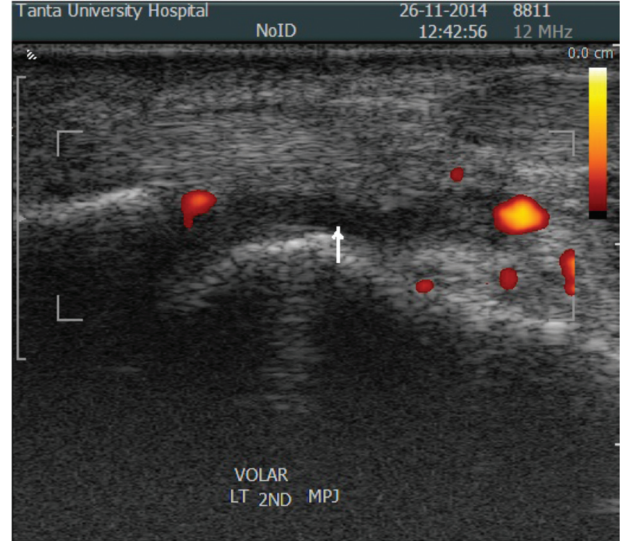
Ultrasonographic image (transverse section) of an systemic sclerosis patient showing tenosynovitis of the extensor tendons.

Association of joint and tendon findings with other characteristics of SSc:

The incidence of synovitis was found to be significantly higher on clinical examination and US in SSc patients with a disease duration of less than or equal to 3 years than in those whose disease duration was more than 3 years (three of seven patients vs. two of 13 patients; $P=0.03$) (60 vs. 17%; $P=0.02$).

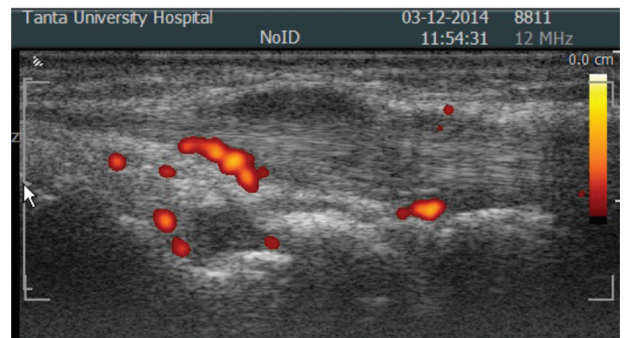
Sclectrosing tenosynovitis was associated with a higher modified Rodnan skin thickness score (15.9 ± 11.0 vs. 8.4 ± 5.5 ; $P=0.006$) as well as with the presence of

Figure 3



Power Doppler ultrasonographic image of an rheumatoid arthritis patient showing synovitis of the left second metacarpophalangeal joint with effusion (arrow).

Figure 4



Power Doppler ultrasonographic image (longitudinal scan) of an rheumatoid arthritis patient showing tenosynovitis of the extensor tendons.

anti-Scl-70 antibodies (33% of patients vs. 19% of patients; $P=0.02$) (Figs. 1–4).

Discussion

Radiographic studies in SSc and RA patients have shown that the commonly affected areas are the joints, soft tissues, and bones of the hands [14]. However, regarding their sensitivity, radiographs

exhibit some limitations in detecting 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 [15].

All our patients with clinical synovitis had US synovitis; however, synovitis was more frequently observed with US compared with clinical evaluation.

As regards clinical articular findings in scleroderma (SSc) patients, Elhai *et al.*[16] and Gohar *et al.* (17) reported lower results for tender joints (38 and 32.5%, respectively) and swollen joints (15 and 25%, respectively). The results for tendon friction rub were higher (27%) in the study by Gohar *et al.*[17] and lower (6%) in the study by Elhai *et al.*[16].

The results of Gohar *et al.*[17] regarding radiographic features of hand involvement in SSc patients were in agreement with our results, whereas the results reported by Cuomo *et al.*[18] and Elhai *et al.*[16] were different. In this study, bone erosions and synovitis detected by US (i.e. effusion and/or synovial proliferation), either by grayscale or by PD signals, were significantly higher in RA patients than in SSc patients. These results were similar to the results reported by Cuomo *et al.*[18] but different from those of Gohar *et al.*[17].

As regards tenosynovitis by MSUS we found that SSc patients had a higher incidence of tenosynovitis compared with RA patients with the sclerosing pattern being specific for SSc and not for RA, whereas inflammatory tenosynovitis occurred in both groups. These results were in agreement with those of Gohar *et al.*[17] and Elhai *et al.*[16].

Regarding US of soft tissues, calcifications were detected in SSc and not in RA patients, which was similar to the results reported by Cuomo *et al.*[18] and different from those of Elhai *et al.*[16] and Gohar *et al.*[17].

In this study osteophytes were detected by US in RA patients more than in SSc patients, which was similar to the results found by Gohar *et al.*[17] and different from those of Elhai *et al.*[16].

Our data showed that US synovitis and tenosynovitis were detected more than clinical synovitis and tenosynovitis in SSc patients, with a statistically significant difference ($P=0.025$ and 0.011 , respectively). Our results were similar to those of Cuomo *et al.*[18] (26/45 and 15/45 cases;

$P=0.03$), Elhai *et al.*[16] (46 vs. 15%; $P<0.01$), and Gohar *et al.*[17] ($P=0.01$ and 0.02 , respectively).

MSUS detected erosions and soft-tissue calcifications more frequently than did radiography, which was similar to the findings of Gohar *et al.*[17].

Patients with higher values for ESR and CRP were more likely to have synovitis and/or tenosynovitis and inflammatory activity with PD signals, whereas Cuomo *et al.*[18] found US-detected synovitis to be related only to the level of CRP.

As regards the relation between disease duration and synovitis, the results of Elhai *et al.*[16] were different from our study results, where the prevalence of US synovitis was not significantly different between SSc patients with a disease duration of less than or equal to 3 years and those with a disease duration more than 3 years. However, it was similar to our results as regards the relation between sclerosing tenosynovitis and modified Rodnan skin thickness score and the presence of anti-Scl-70 antibodies.

Conclusion

US was more accurate than clinical examination and conventional radiograph in the detection of subclinical synovitis, tenosynovitis, and the underlying fibrotic changes of tendon friction rub. In SSc patients by using MSUS, articular involvement was less frequent compared with RA patients, with specific appearance of sclerosing tenosynovitis in SSc patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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