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Comparison of Hand Features in Systemic Sclerosis and Rheumatoid Arthritis Patients by Diagnostic Ultrasound and its Correlation to Disease Activity, Clinical and Radiological Findings

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ABSTRACT

Introduction and Aim: Imaging evaluation of the rheumatoid arthritis and systemic sclerosis represents a significant part in disease evaluation and follow up. However, it had many limitations and new tools are introduced continuously. The current work aimed to compare ultrasound characteristics of the hand involvement in systemic sclerosis (SSc) and rheumatoid arthritis (RA).

Patients and methods: The study included 30 SSc and 40 RA patients. All were evaluated by the full history taking, detailed clinical examination, disease activity scores and the health assessment questionnaires were completed. All necessary laboratory investigations were performed. Finally, radiological examination (plain X-rays and ultrasound for joints of hands and wrist) was performed.

Results: Patient age ranged from 22 to 58 years, and RA patients were significantly older, with female sex predominance. SSc was of diffuse (30%) and (70%) were of limited type. The disease activity of RA ranged from 2 to 9, while disease activity of SSc ranged between 1.3 to 3.5. In the SSc group, 56.7% had active disease compared to 40% in RA groups. Patients in the SSc group had a degree of disability, while 82.5% of patients in the RA group had mild- to- moderate disability. Ultrasound examination revealed that, synovitis was significantly increased in RA when compared to the SSc group (55.0% vs 23.3%). The sclerosing pattern of tenosynovitis was significantly increased in SSc than the RA group (92.3% vs 0.0% respectively). Results of ultrasound completely coincides with results of MRI. Finally, there was statistically significant, moderate, proportional correlation between ultrasound and each of erythrocyte sedimentation rate (ESR), and disease activity scores.

Conclusion: Ultrasound hand examination in scleroderma and RA is more accurate than separate clinical or X-ray examinations. However, it could not completely substitute clinical examination. But it is a suitable add on especially in detection of early disease activity.

Keywords: Hand; Ultrasound; Systemic Sclerosis; Rheumatoid Arthritis; Disease Activity.

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic multisystem disease of unknown etiology, characterized by inflammatory synovitis. Joint involvement in RA is usually a symmetric polyarthritis predominantly affecting the peripheral joints with a variable potential for deformation. It affects 1% of the general population, being three times more frequent in women than men. Its prevalence increases with age, and the difference between the genders becomes smaller. It usually begins between 35 and 50 years of age, and its onset relates to genetic predisposition and to the interaction of environmental agents [1].

Systemic sclerosis (SSc) is a multi-system connective tissue disease characterized by autoimmunity, microangiopathy and progressive interstitial and vascular fibrosis in the skin and internal organs [2]. The articular involvement, mainly in the feet and hands, is common in SSc [3], and is associated with a significant disability [4]. It is usually clinically and radiologically evaluated, resulting in an under-estimation of the manifestations such as synovitis and erosions [5]. In SSc, symptoms of joint involvement are reported by 24–97% of patients during the course of the disease [6]. Features of the hand SSc are ranging from arthralgias to frank arthritis, contractures, and tendon friction rubs [7]. Clinical assessment is limited by concomitant skin disease.

Musculoskeletal ultrasound (MSUS) at present time plays a crucial role in the diagnosis and treatment of the rheumatic diseases [8]. The presence of synovitis detected by MSUS is helpful in the diagnosis of undifferentiated arthritis (UA) and in inflammatory arthritis it is predictive of persistent disease, joint damage, and acute disease flare [9]. It has dramatically improved joint and tendon evaluation in rheumatoid arthritis (RA) and other inflammatory diseases. However, MSUS also has its shortages as it is operator dependent, and consuming a long time when there is a need to examine many joints [10]. MSUS is more sensitive than the clinical examination for detection of tenosynovitis in RA [11]. In addition, it is able to predict future radiographic progression [12]. Consequently, MSUS suggested to be included in the definition and characterization of remission. Additionally, its ability to assess disease activity utilized to guide therapeutic decisions [13]. Radiographic studies in SSc and RA have shown that joints, soft tissues, and bones of the hands are the commonly affected areas. However, radiographs had limited sensitivity for detection of early inflammatory changes (e.g., effusion, synovitis) and cannot evaluate tendon damage. Thus, radiographic and clinical assessments are considered imperfect evaluators of the whole spectrum of joint involvement in SSc and RA [10]. Over the last years, many researches have confirmed the role of US in detection of the subclinical synovitis, where X-ray did not detect erosions in RA. Conversely, limited studies had investigated the value of the US in joints assessment in SSc, in particular of distal interphalangeal joints [14].

The aim of the work was to compare the characteristics of US hand involvement in systemic sclerosis (SSc) and rheumatoid arthritis (RA) patients and to determine the correlations between US findings with disease activity, clinical and radiological findings.

PATIENTS AND METHODS

The study included 30 SSc patients who fulfill ACR criteria [15] together with 40 RA patients who fulfill the 2010 ACR/EULAR criteria [16]. Patients were recruited from the Rheumatology outpatient Clinic, Al-Azhar University Hospitals and Outpatient Clinics of General Hospitals in Damietta Governorate. All patients were evaluated by the full history taking regarding patient demographics, disease duration and medications. In addition, a detailed clinical examination (systemic and local for different joints) was performed and disease activity scores and health assessment questionnaires were accomplished. For joint examination, the number of affected joints and signs of inflammation were recorded. Joint instability and deformities were also noted and documented. Specifically, for SSc patients, tenderness, swelling, tendon friction rubs and contractures of the meta-carpo-phalangeal (MCP), proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints of the hands and wrists were recorded.

For disease activity in RA patients, the disease activity score-28 [17] was used. If greater than 5.1, it indicates active disease, if less than 3.2 indicated low disease activity and less than 2.6 indicated remission. For SSc patients, the European Scleroderma Study Group activity index was used [18]. It is a 10-point scale with increased scale indicate more disease activity. After that, the Health Assessment Questionnaire (HAQ) was applied for both SSc and RA patients. The eight categories assessed by the Disability Index are 1) dressing and grooming, 2) arising, 3) eating, 4) walking, 5) hygiene, 6) reach, 7) grip, and 8) common daily activities. For each of these categories, patients report the amount of difficulty they have in performing two or three specific activities. Patents usually find the HAQ Disability Index entirely self-explanatory, and clarifications are seldom required. The Health Assessment Questionnaire Disability Index (HAQ-DI) is currently the most widely used measure of functioning and disability across rheumatic diseases, particularly in RA. The HAQ has 20 questions and is widely validated. The score goes from 0 (no incapacity) to 3 (full incapacity); a score below 0.5 is considered normal whereas a score above 1.5 indicates severe disability [19]. All necessary laboratory investigations were performed. These included erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP), rheumatoid factor (RF), complete blood count (CBC), anti-cyclic citrullinated antibody (anti-CCP), anticentromere antibodies, anti-nuclear antibodies (ANA) by immunofluorescent, anti-Scl70. Finally, radiological examination in the form of plain X-rays and ultrasound for joints especially of hands and wrist were performed. The US examination of joints of both hands and fingers (MCP, PIP, and DIP joints) and the wrists (radiocarpal

[RC], ulnarcarpal [UC] and intercarpal [IC] joints), was performed by Toshiba xario 200 ultrasound machine using a near focused linear array transducer with a center frequency of 10–14 MHz for the detection of synovitis, tenosynovitis and calcinosis.

Ethical considerations: the study protocol was reviewed and accepted by the local research and ethics committee of Damietta Faculty of Medicine institutional review board. All patients signed informed consent after full explanation of the study and assurance of patient's privacy. The study completed according research ethics code of Helsinki declaration.

Statistical analysis: Data were collected, anonymized and fed to the statistical package for social sciences (SPSS) software package in a standard format. The 16 version of the package was used (SPSS Inc., Chicago, USA). Numerical data were expressed by their arithmetic means for central tendency and standard deviation for dispersion. Minimal and Maximal values were also included. On the other side, categorical variables were expressed by their relative frequency and percentages from each group. Groups compared by appropriate statistical tests to examine the significance. For example, two means were compared by independent samples student "t" test. However, categorical distributions were compared by Chi-square test or appropriate equivalents. P value < 0.05 was considered significant to interpret our results.

RESULTS

In the present study, patient age ranged from 22 to 58 years, and there was a significant increase in the age in the RA than the SSc group (44.57±7.91 vs 36.20±6.51). There was a female sex predominance in both groups with no significant difference between groups. The disease duration ranged from 2 to 14 years, and there was a significant decrease of disease duration in SSc when compared to the RA group (5.90±1.66 vs 8.20±2.74). Finally, the type of systemic sclerosis was of diffuse type in 9 patients (30%) and 21 (70%) were of limited type (Table 1).

Regarding medical treatment in the SSc group, 30% had DMARDs, 40% use steroids and 30% cyclophosphamide, while in the RA group, DMARDs was used by 90%, steroids by 77.5% and none of them use cyclophosphamide with a significant increase of DMARDs and steroids in the RA group. The disease activity of RA measured by DAS28 and the score ranged from 2 to 9 and the mean value was 4.56±0.65; while disease activity of SSc measured by European activity index ranged between 1.3 to 3.5 with a mean value of 2.42±0.65. The disease activity in the SSc group was as the following: 17 patients (56.7%) had active disease and 13 cases (43.3%) had remission; while in the RA group, 40% had active disease, 25% had low active disease and 35% had remission, with a significant difference between RA and SCs groups. Patients in the SSc group had a degree of disability, while 82.5% of patients in the RA group had mild- to- moderate disability, and there was a significant difference between both groups. In addition, HAQ ranged from 0.3 to 1.5 and there was a significant increase in the SSc group when compared to the RA group (1.00±0.26 vs 0.79±0.28 respectively) (Table 1). There was a significant increase in the number of patients with tender joints in the RA when compared to the SSc group (65.0% vs 40.0% respectively). In addition, there was a significant increase of number of tender joints in the RA when compared to the SSc group (5.53±1.92 vs 1.75±0.75 respectively). Tender joints were wrist, MCP, PIP and DIP in 25.0%, 83.3%, 58.3% and 0.0% successively in the SSc group, compared to 73.1%, 73.1%, 57.7% and 7.7% successively in the RA group. In addition, there was a significant increase in patients with swollen joints in RA when compared to the SSc group (52.5% vs 20.0% respectively). Similarly, there was a significant increase of the number of swollen joints in RA when compared to the SSc group (6.80±1.77 vs 1.66±0.81 respectively). On the other side, the tendon friction rub was significantly increased in the SSc versus RA group (30.0% vs 1.5% respectively) (Table 2). There was no significant difference between studied groups, as regard to pulse, blood pressure, temperature and respiratory rate.

Regarding ESR, it ranged from 14 to 52, with a significant decrease in SSc when compared to the RA group (21.93±3.98 vs 31.05±7.06 respectively). Additionally, there was a statistically significant decrease of CRP in SSc than the RA group (5.60±2.94 vs 7.65±2.16 respectively). Finally, RF factor was positive in 56.7% in the SSc group compared to 90.0% of patients in the RA group. There was no significant difference between the SSc and the RA groups as regard to RBCs, hemoglobin, hematocrit and platelets. However, WBCs were significantly increased in the RA when compared to the SSc group (9.82±1.13 vs 8.47±1.07 thousands/ml respectably). In addition, there was a statistically significant decrease of Anti-CCP in SSc than the RA group (6.7% vs 35.0% respectively). On the other side, there was a significant increase of Anti-centromere, ANA, and anti-Sc70 in the SSc group than the RA group (56.7%, 56.7%, 26.7% vs 27.5%, 40.0% and 0.0% respectively) (Table 3). In the SSc group, juxta-articular osteoporosis was reported in 36.7%, the joint space narrowing was reported in wrist and MCP in 6.7% and 13.3%; and erosions of wrist was reported in 3.3% and deformity was reported in just one patient (3.3%). On the RA group, osteoporosis was reported in 65.0%, space narrowing of wrist, MCP and PIP in 25.0%, 47.5% and 30.0%; erosion was of wrist, MCP and PI in 25.0%, 40.0% and 32.5% respectively, while deformity was reported in 62.5%. There was a significant increase of all abnormalities detected by radiology among RA when compared to the SSc group (Table 3).

Ultrasound examination revealed that, synovitis was significantly increased in RA when compared to the SSc group (55.0% vs 23.3%). Synovitis was inflammatory, Doppler grade 1 and grade 2 or 3 among 28.6%, 71.4% and 0.0% of the SSc group and among 77.3%, 50.0% and 50.0% of the RA group successively, with a significant increase of inflammatory type and power Doppler 2 or 3 among the RA group. In addition,

tenosynovitis was reported in 43.3% and 45.0% of the SSc and RA groups, respectively. The sclerosing pattern was significantly increased in SSc than the RA group (92.3% vs 0.0% respectively). All tenosynovitis in the RA group were inflammatory, compared to 53.8% of the SSc group, and both patterns were significantly increased in SSc group. Extensor tendons were affected 53 compared to 7 patients in the SSc and RA groups, while flexor tendons were affected in 44 and 12 patients in the SSc and RA groups. Finally, calcinosis was reported in 13.3% and 5.0% of the SSc and RA groups. All calcinosis were intra-articular in both groups (Table 4).

Results of ultrasound completely coincides with results of MRI. Comparing ultrasound to X-ray in the scleroderma group, results revealed that, ultrasound confirms x-ray findings in 43.3% (23.3% confirm positive data and 20.0% confirms negative data), while ultrasound elicits a new change in 33.3% and disproves original findings in 23.3%. On the other side, when compared to clinical diagnosis, ultrasound confirms original data in 63.3% (confirms data in 40.0% and confirms negative data in 23.3%), elicits new changes in 16.7% and disprove original data in 20.0% (Table 5). In the RA group, ultrasound confirms data of X-ay among 50.0%, discover new changes in 17.5% and disprove original findings in 32.5%; and when compared to clinical diagnosis, it confirms original data among 60.0%, discover new data among 15.0% and disprove original findings among 25.0% (Table 5). These data revealed that, ultrasound coincides with clinical diagnosis than x-ray. The good diagnostic power of ultrasound compared to either clinical or X-ray findings in both groups could be attributed to better diagnosis of soft tissue changes.

In the present work, there was a significant increase of DAS28, European scleroderma score and ESR in patients with synovitis when compared to negative subjects. In the same way, the number of tender and swollen joints and CRP increased in synovitis subgroup, but the difference did not reach statistical significance. However, there was no significant difference between tenosynovitis and negative subjects as regards to compared variables. In addition, there was no significant difference between calcinosis and negative subjects as regards to compared variables (Table 6).

In the present study, there was statistically significant, moderate, proportional correlation between ultrasound and each of ESR, DAS28 and European scleroderma score (Table 7).

Table (1): Comparison between groups regarding patient characteristics

Variable		SSc group (n=30)	RA group (n=40)	Total (n=70)	Test	P
Age (years)		36.20±6.51; 22-51	44.57±7.91; 29-58	40.98±8.40; 22-58	4.71	<0.001*
Patient gender	Male	9(30.0%)	13(32.5%)	22(31.4%)	0.05	0.82 (ns)
	Female	21(70.0%)	27(67.5%)	48(68.6%)		
Disease duration (year)		5.90±1.66	8.20±2.74	7.21±2.59;2-14	4.05	<0.001*
SSc type	Diffuse	9(30.0%)				
	Limited	21(70.0%)				
Medications	DMARDs	9(30.0%)	36(90.0%)	45(64.3%)	26.88	<0.001*
	Steroids	12(40.0%)	31(77.5%)	43(61.4%)	10.17	0.001*
	Cyclophosphamide	9(30.0%)	0(0.0%)	9(12.9%)	13.77	<0.001*
DAS28 for RA activity			4.56±2.36;2-9			
European SSc activity index		2.42±0.65;1.3-3.5				
Disease activity	Active	17(56.7%)	16(40.0%)	32(46.4%)	8.81	0.012*
	Low active	0(0.0%)	10(25.0%)	10(14.5%)		
	Remission	13(43.3%)	14(35.0%)	27(39.1%)		
Disability	No disability	0	7(17.5%)	7(10.0%)	5.83	0.016*
	Mild to moderate	30(100.0%)	33(82.5%)	63(90.0%)		
HAQ		1.00±0.26	0.79±0.28	0.88±0.29	3.19	0.002*

Table (2): Comparison between groups regarding tender and swollen joints detected by clinical examination

Variable		SSc group	RA group	Total	Test	P
Tender joints		12(40.0%)	26(65%)	38(54.3%)	**4.31**	**0.038***
Number of tender joints		1.75±0.75;1-3	5.53±1.92; 2-9	4.34±2.41; 1-9	**6.55**	**<0.001***
Tender joints	Writs	3(25.0%)	19(73.1%)	22(57.9%)	**7.78**	**0.005***
	MCP	10(83.3%)	19(73.1%)	29(76.3%)	0.74	0.48
	PIP	7(58.3%)	15(57.7%)	22(57.9%)	0.001	0.97
	DIP	0	2(7.7%)	2(5.3%)	0.97	0.32
Swollen joints		6(20.0%)	21(52.5%)	27(38.6%)	**7.64**	**0.006***
Number of swollen joints		1.66±0.81;1-3	6.80±1.77;2-10	5.66±2.70;1-10	**6.80**	**<0.001***
Swollen joints	Writs	5(83.3%)	17(81.0%)	22(81.5%)	0.02	0.89
	MCP	5(83.3%)	17(81.0%)	22(81.5%)	0.02	0.89
	PIP	4(66.7%)	11(55.0%)	15(57.7%)	0.25	0.61
	DIP	0	0	0	-	-
Tendon friction rubs		9(30.0%)	1(2.5%)	10(14.3%)	**10.58**	**<0.001***

Table (3): Comparison between groups regarding laboratory and X-ray investigations

Variable			SSc group	RA group	Total	Test	P value
Laboratory	ESR		21.93±3.98	31.05±7.06	27.14±7.44;14-52	**6.34**	**<0.001***
	CRP		5.60±2.94	7.65±2.16	6.77±2.70;2-14	**3.35**	**0.001***
	RF factor	Positive	17(56.7%)	36(90.0%)	53(75.7%)	**10.35**	**0.001***
		Negative	13(43.3%)	4(10.0%)	17(24.3%)		
	RBCs x 10^6		3.62±0.16	3.66±0.18	3.64±0.17;3.38-4.0	0.84	0.39
	WBcs x 10^3		8.47±1.07	9.82±1.13	9.24±1.29;5.90-13.20	**5.04**	**<0.001***
	Hemoglobin		11.26±0.49	11.35±0.56	11.31±0.53;10.50-12.50	0.74	0.45
	Hct%		36.27±1.57	36.56±1.79	36.43±1.69; 33.81-40.0	0.68	0.49
	Platelets x 10^3		206.97±38.46	211.10±40.22	209.33±39.25; 149-330	0.43	0.66
	Anti-CCP		2(6.7%)	14(35.0%)	16(22.9%)	**7.80**	**0.005***
	Anti-centromere		17(56.7%)	11(27.5%)	28(40.0%)	**6.07**	**0.014***
	ANA		17(56.7%)	16(40.0%)	33(47.1%)	1.91	0.16
	Anti-Scl70		8(26.7%)	0(0.0%)	8(11.4%)	**12.04**	**0.001***
X-ray	Juxta-articular osteoporosis		11(36.7%)	26(65.0%)	37(52.9%)	**5.52**	**0.019***
	Joint space narrowing	Wrist	2(6.7%)	10(25.0%)	12(17.1%)	**4.05**	**0.044***
		MCP	4(13.3%)	19(47.5%)	23(32.9%)	**9.07**	**0.003***
		PIP	0	12(30.0%)	12(17.1%)	**10.86**	**0.001***
	Erosions	Wrist	1(3.3%)	10(25.0%)	11(15.7%)	**6.07**	**0.014***
		MCP	0	16(40.0%)	16(22.9%)	**15.55**	**<0.001***
		PIP	0	13(32.5%)	13(18.6%)	**11.97**	**0.001***
	Deformity		1(3.3%)	25(62.5%)	26(37.1%)	**25.70**	**<0.001***

Table (4): Comparison between groups as regard to results of ultrasound of the hand

Variable		SSc group	RA group	Total	Test	P value
Synovitis		7(23.3%)	22(55.0%)	29(41.4%)	***7.08***	***0.008****
Characteristics of synovitis	Inflammatory	2(28.6%)	17(77.3%)	19(65.5%)	***5.57***	***0.018****
	Power Doppler grade 1	5(71.4%)	11(50.0%)	16(55.2%)	0.98	0.32
	Power Doppler grade 2 or 3	0	11(50.0%)	11(37.9%)	5.63	0.018
Tenosynovitis		13(43.3%)	18(45.0%)	31(44.3%)	0.02	0.89
Characteristics Of tenosynovitis	Sclerosing pattern	12(92.3%)	0	12(38.7%)	***27.10***	***<0.001****
	Inflammatory activity	7(53.8%)	18(100.0%)	25(80.6%)	***10.30***	***0.001****
	Both patterns	6(46.2%)	0	6(19.4%)	***10.30***	***0.001****
Distribution of tenosynovitis	Extensor tendons (ET)	53	7	60		
	ET Sclerosing pattern	49(92.5%)	0	49(81.7%)	***35.30***	***<0.001****
	ET power Doppler	20(37.7%)	4 (57.1%)	24(40)	0.97	0.32
	Flexor tendons (FT)	44	12	58		
	FT sclerosing pattern	36 (81.8%)	0	36(62.1%)	***27.49***	***<0.001****
	FT power Doppler	23(52.3%)	11 (91.7%)	34(58.6%)	***6.13***	***0.013****
Calcinosis	Total	4(13.3%)	2(5.0%)	6(8.6%)	1.15	0.21
	In tendon sheath	0	0	0		
	Intra-articular	4(13.3%)	2(5.0%)	6(8.6%)	1.15	0.21
	Soft tissue	0	0	0	0	

Table (5): Relation between ultrasound and each of clinical and radiological diagnosis in the scleroderma group

		SSc group		RA group	
		n	%	n	%
Ultrasound versus x ray	Confirm findings	7	23.3	20	50.0
	Confirm negative data	6	20.0	0	0
	Discover new changes	10	33.3	7	17.5
	Disprove original findings	7	23.3	13	32.5
Ultrasound versus clinical diagnosis	Confirm findings	12	40.0	21	52.5
	Confirm negative data	7	23.3	3	7.5
	Discover new changes	5	16.7	6	15.0
	Disprove original findings	6	20.0	10	25.0

Table (6): Relation between ultrasound findings and disease activity

		Positive		Negative		P value
		Mean	S. D	Mean	S. D	
Synovitis	DAS28	5.69	2.33	3.18	1.55	<0.001*
	ESSc	2.89	0.59	2.29	.62	0.032*
	HAQ	0.82	0.31	0.92	.32	0.202
	Number of tender joints	4.95	2.35	3.67	2.38	0.103
	Swollen joint number	6.21	2.52	5.08	2.87	0.283
	ESR	29.59	8.22	25.41	6.41	0.020*
	CRP	7.10	2.96	6.54	2.53	0.392
Tenosynovitis	DAS28	4.91	2.63	4.28	2.13	0.409
	ESSc	2.26	0.62	2.55	0.67	0.235
	HAQ	0.91	0.25	0.86	0.36	0.556
	Number of tender joints	4.00	2.75	4.68	2.06	0.391
	Swollen joint number	5.45	2.50	5.81	2.90	0.742
	ESR	26.84	7.91	27.38	7.15	0.763
	CRP	7.42	2.98	6.26	2.39	0.074
Calcinosis	DAS28	5.20	3.95	4.52	2.32	0.699
	ESSc	2.45	0.51	2.42	0.68	0.941
	HAQ	.98	0.24	0.87	0.31	0.410
	Number of tender joints	2.75	1.70	4.52	2.44	0.167
	Swollen joint number	3.00	2.82	5.88	2.63	0.151
	ESR	26.00	6.06	27.25	7.59	0.697
	CRP	6.66	2.42	6.78	2.75	0.922

Able (7): Correlation between Ultrasound score and disease activity indices, clinical and Lab values

	Ultrasound Score	
	r	p
ESR	0.340	0.004*
CRP	0.010	0.932
HAQ	-0.223	0.064
DAS28	0.449	0.004*
ESSc	0.459	0.011*

DISCUSSION

The aim of the work is to compare the features of US hand involvement in SSc and RA and to determine the correlations between US findings with disease activity, clinical and radiological findings. RA Patient's data in the present work were comparable to those reported by Hetta *et al*. [20] who included 41 females (82%) and 9 males (18%). Their ages ranged from 20 to 66 years with a mean age of 43 ±10.5 years. The disease duration ranged from 1 to 18 years with a mean of 6.20 ± 4.2 years. Of their patients, 38 (76%) were seropositive and 12 (24%) were seronegative. Thirty-one patients were positive for CRP (60%). Iagnocco *et al*. [21] also investigated 46 patients (42 women and 4 men; median age 62 years, range 38–77) with SSc; 28 patients had a limited form and 18 had a diffuse form of disease. Treatment included low dose of prednisone, DMARDS, antiplatelet and NSAID drugs. Clinical evaluation of hand and wrist joint revealed the following findings: painful joints in 29 out of 92 (31.5%) wrists, 12% MCP, 14.7% PIP, 12.5% DIP and 4.3% CMC joints. Swollen joints were detected in 8.7% wrists, 5% MCP, 13.2% PIP and in 12.2% DIP joints. In addition, results of the present study are in agreement with that of Gohar *et al*. [22] who included 40 SSc patients (10 males and 30 females), 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. Mean DAS28 was 3.86±2.17 and the HAQ-DI was 1.7± 0.8

Regarding the good correlation between MRI and ultrasound, results of the present work are comparable to those reported by Hetta *et al*. [20] who reported that, in RA patients, ultrasound detected synovial hypertrophy (pannus) in 42 wrist joints while MRI detected it in 46 wrist joints, both modalities agreed in 42 patients, and ultrasound missed synovial hypertrophy in 4 joints detected by MRI. Statistical analysis of these results showed no significant statistical difference and high significant agreement between the two modalities in the detection of synovial hypertrophy. In addition, Rowbotham and Grainger [23] reported that, ultrasonography (US) is an increasingly used technique by the clinicians for the evaluation of inflammatory joint diseases. It has been shown to be sensitive in the detection of synovitis and bone erosions in both small and large joints. Bhasin and Cheung (2015) reported that,

color and power Doppler has been used to identify hyperemia associated with inflammation by visualizing the vascularity in the inflamed synovial membrane.

The use of US is recommended to improve the diagnostic accuracy of RA when the diagnosis stays uncertain [24]. EULAR recommendations are supported by studies showing the superiority of US to clinical exam in up to 75% of patients, for RA diagnosis [25,26]. A study analyzing patients with early oligoarthritis had demonstrated that the proportion of patients with US-proven polyarthritis was higher than with clinical examination (as in the present work), leading to a better RA classification. Among patients with undetermined early arthritis population, US involvement of metacarpophalangeal (MCP) improved the sensitivity to diagnose RA compared with clinical variables, and power Doppler (PD) retained high specificity for RA [27]. Bone erosions are commonly considered as the hallmark of RA and US is more sensitive than conventional radiography for the detection of bone erosions. The US of MCPs is able to detect 6.5 times more erosions among 7.5 times more patients than radiographies [28]. Forien and Ottaviani [29] concluded that, the US appears to be more sensitive than clinical exam for RA diagnosis and the two main US features to research are bone erosions and PD+ synovitis

As US is more sensitive than clinical evaluation for detection of synovitis, it could be suggested that US is able to measure dis-ease activity. It is well known that tender joint count (TJC) and swollen joint count (SJC) do not entirely reflect active inflammation [30]. In contrast, PD could recognize pathological synovial flow that could represent an indicator of synovial inflammatory activity [31].

Results of the present work go in agreement with a Swiss RA cohort, where a significant modest correlation was reported between US (grey scale (GS) and PD score) and DAS28 scoring. Interestingly, when RA patients were prospectively evaluated, the same authors observed a positive association between GS (r = 0.41) and/or PD changes (r = 0.54) and change in DAS28. Thus, disease activity determined by US was correlated with DAS28 with good sensitivity. However, the correlation is moderate and, at individual level, the variability stays important. Despite a correlation between US and clinical disease activity, 25–50% of RA patients in clinical remission had a persistent PD+ synovitis. As the absence of joint inflammation is the objective of RA treatment to avoid structural damage, the persistence of US joint inflammation might have an impact on prognosis [29]. In agreement with our results, a previous study showed that US detects subclinical synovitis and pathological findings which are not detected clinically [32]. In addition, our results are consistent with published data, regarding the ability of ultrasound to detect more synovitis and erosions than x-ray [33]. In another 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. The US reduced sensitivity in detecting erosions in SSc is possibly due to limited number of SSc patients with erosive changes and whether erosive arthritis is a part of the spectrum of scleroderma or just an overlapping RA is still debatable [34]. Power Doppler US has demonstrated a high sensitivity for the assessment of inflammatory activity in the joints of patients. Positive intra-synovial power Doppler signal was significantly frequent in the 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 agrees with the results of the study carried out by Allanore *et al*. [35].

In RA, we found a significant correlation between the US detected synovitis and the DAS28 and ESR but not CRP. Other studies found that many RA patients with clinically inactive disease still show US evidence of persistent synovitis [36].

Regarding tenosynovitis, a characteristic sclerosing teno-synovitis was restricted to the scleroderma group, and more observed in the extensor than flexor tendons. On the other hand, inflammatory pattern was more prevalent in the RA group. Sclerosing tenosynovitis appears to be specific for scleroderma patients compared to RA patients. Again, this coincides with the results of Elhai *et al*. [37] 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 SSc may be a significant way to suspect SSc in diffuse or uncertain articular manifestations where clinical examination may be inadequate in detection of the articular involvement [38].

Regarding the US of soft tissues, calcifications were detected in both scleroderma and RA (13.5 vs 5%) patients, with no statistically significant pattern, these data are in agreement with studies showed that calcifications in SSc patients in about 10–50% of patients [22]. Iagnocco *et al*. [21] in demonstrated a high prevalence of involvement at hand and wrist joints level, particularly regarding the presence of inflammatory findings and with evidence of synovial hypertrophy, PD signs of active local inflammation and joint effusion in scleroderma. These abnormalities represent the single components of synovitis and, therefore, their presence in the examined joints is consistent with the presence of diffuse inflammatory involvement. These results seem to be of interest, particularly when compared to clinical assessment: indeed, most of patients had no clinical signs of musculoskeletal involvement and few of them had physical findings of arthritis. Interestingly, the US findings of inflammation have been demonstrated both in the dcSSc and lcSSc forms, indicating that musculoskeletal involvement may be present in both subsets of the disease; indeed, no significant differences were revealed comparing the US findings in dcSSc to lcSSc. In addition, when the grade of local involvement was evaluated, they found that hand joints, besides being the site of mild effusion, were also characterized by mild synovial hypertrophy, which was accompanied by a severe PD signal. This last

finding, demonstrating the presence of a highly active inflammation, represents a novel aspect of hand joint involvement in SSc, which needs further evaluations. On the other hand, the presence of mild to moderate involvement for all the 3 findings that are consistent with joint synovitis was demonstrated at wrist level. Chitale *et al*. [38] found a high prevalence of B-mode tenosynovitis at the level of all local extensor and flexor tendons and, interestingly, active inflammation, as demonstrated by PD assessment, was detected in a great number of synovial tendon sites. Finally, Baffour *et al*. [39] reported that, in RA, limitations for ultrasound evaluation of inflammatory arthritis are few, predominantly being a relatively high learning curve for detailed evaluation, with the operator technique being paramount. Also, not all joint segments will be visualized on US, precluding assessment of the whole articular surface for erosions and chondromalacia. Additionally, US cannot visualize the edema of the bone marrow, which is considered an important indicator of the joint inflammatory changes, and also a predictor of erosive changes, with a significantly high negative predictive value (NPV) of 99%.

In conclusion, ultrasound examination of hand in scleroderma and RA patients is more accurate than each of separate clinical or x-ray examination. However, it could not completely substitute clinical examination. But it is a suitable add on especially in detection of early disease activity. It was able to detect abnormalities even in cases with remission. In addition, US articular involvement in scleroderma is less frequent and is characterized by mild inflammatory changes compared RA, with specific appearance of sclerosing tenosynovitis. Further, larger prospective studies are advocated to evaluate the importance of using US in the follow-up response to treatment in such conditions.

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