The ultrasound 7 score in the assessment of synovitis in rheumatoid arthritis: correlation with clinical disease activity indices

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Objective
The aim of the paper was to assess value of ultrasound 7 score (US7) in the detection of synovitis in rheumatoid arthritis (RA) and its correlation with clinical disease activity indices.
Patients and methods
A total of 50 patients with RA were included. Disease activity was assessed by clinical disease activity indices. Erythrocyte sedimentation rate was measured, and simple erosion narrowing score was used for radiography scoring. Musculoskeletal US7 score was done which combines each joint score for synovial proliferation (gray-scale ultrasound 'GSUS7') and vascularization (power Doppler ultrasound 'PDUS7').
Results
Detailed joint region examination by US7 score was done. Dorsomedian aspect of wrist (94%), palmar aspect of metacarpophalangeal joint (MCP) II (96%), and palmar aspect of phalangeal interproximal (PIP) II and III (92%) were the most affected joint regions with synovitis by GSUS. However, for detection of synovitis by PDUS, dorsomedian aspect of wrist and dorsal aspect of MCP, PIP II, and PIP III were involved. Erosions were found most in radial aspect of MCP II (70%), lateral aspect of metatarsophalangeal joint V (72%), and dorsal aspect of PIP II (54%) and PIP III (44%). All clinical disease activity indices were correlated with GSUS7 and PDUS7 synovitis.
Conclusion
US7 was simple and practical sum scoring system for use in the detection of synovitis in patients with RA. The correlations between the clinical disease activity indices, erythrocyte sedimentation rate, duration of illness, radiographic score, and components of the US7 score reflects the value of US7 score in assessment of disease activity and severity.

Keywords:
clinical disease activity indices, rheumatoid arthritis, ultrasound 7 score

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Introduction

Rheumatoid arthritis (RA) is a common, systemic autoimmune disease affecting 0.5–1% of the population [1]. The diagnosis of RA is based essentially on clinical and biological parameters, although the new American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria include MRI and ultrasound (US) as additional tools to assess objectively joint involvement [2].

During the course of RA, disease activity may fluctuate widely. Measurement of disease activity has become an important component of RA management. Quantitative measurement of RA disease activity is recommended by the ACR [3], the EULAR [4], and the treat-to-target task force [5].

Several disease activity indices based on different clinical, laboratory, and physical measures have been introduced. Most of these, including the Disease Activity Score (DAS) [6], the modified DAS in 28 joints (DAS28) [7], the Simplified Disease Activity Index [8], the Clinical Disease Activity Index (CDAI) [9], and the Routine Assessment of Patient Index Data 3 (RAPID 3) [10], rely on either quantitative joint counts, patient-reported outcomes, or both.

Radiographs and other imaging modalities such as US and MRI may all be appropriate to measure disease

activity [11–13]. However, the sensitivity of US is greater than that of other imaging techniques in the early detection of aggressive arthritis and surveillance of disease activity [14]. The semiquantitative US scoring system, ultrasound 7 score (US7 score), has been proposed to assess established RA. It was developed to standardize the US examination in daily rheumatologic practice and in multicenter studies [15]. The validated seven-joint score (US7) combines each joint score for synovial proliferation (gray-scale ultrasound 'GSUS7') and vascularization (power Doppler ultrasound 'PDUS7') [16].

The aim of the study was to assess the value of US7 in the detection of synovitis in patients with RA and its correlation with the clinical disease activity indices.

Patients and methods

A total of 50 consecutive patients (46 female and four male) who fulfilled the 1987 ACR classification criteria for RA [17] were included in the present study. All patients were attending the Outpatient Rheumatology Clinic, Minia University Hospital. Informed consent was taken from all participants in the study. The study was approved by the ethics committee of the Faculty of Medicine.

Clinical and laboratory assessment

Disease activity was assessed in each patient based on CDAI, global arthritis score (GAS), and RAPID 3. The CDAI ranges from 0 to 76, and patients can be divided into those at low (CDAI≤10), moderate (CDAI≤22), and high disease activity (CDAI>22). A CDAI less than or equal to 2.8 corresponds to remission [9]. The GAS ranges from 0 to 62 (with remission defined as ≤3 and near remission ≤7) [18]. RAPID 3 includes the 3 MDHAQ (Multidimensional Health Assessment Questionnaire) patient self-report RA Core Data Set measures for physical function, pain, and patient global estimate. Proposed RAPID 3 (range: 0–10) severity categories (rather than activity) are as follows: high (>4), moderate (2.01–4), low (1.01–2), and near remission (≤1) [10]. Erythrocyte sedimentation rate (ESR; normal level<20 mm/h) level was measured for all patients.

Radiographic assessment

Standard anteroposterior views of the hands, wrists, and foot were obtained from patients with RA. Simple erosion narrowing score (SENS) was used for radiography scoring [19].

Ultrasound assessment

Musculoskeletal ultrasonography of wrist, hands, and forefoot was performed with a 10–18 MHz linear scanner and middle class to high-end machine US device. All patients were assessed and examined by one medical staff. US7 includes the joints most likely to be affected by RA: wrist, metacarpophalangeal joint (MCP) II and III, phalangeal interproximal (PIP) II and III, and metatarsophalangeal joint (MTP) II and V joints of the clinically most affected hand and forefoot. These joints were evaluated for synovitis and tenosynovitis/paratenonitis and superficial bone erosions according to EULAR criteria [17] and Outcome Measures in Rheumatology definition [20] including GSUS and PDUS (Table 1) [16]. Synovitis and synovial/tenosynovial vascularity were scored semiquantitatively (grades 0–3) by PDUS according to Szkudlarek *et al* [21].

Table 1 Ultrasound 7 score components

	Wrist	MCP/PIP second and third	MTP second and fifth	Joint regions (range)
US7 synovitis sum score in GSUS (grade 0–3)	DorsomedianUlnar Palmomedian	Palmar	Dorsal	9 (0–27)
US7 synovitis sum score in PDUS (grade 0–3)	DorsomedianUlnar Palmomedian	Dorsal and palmar	Dorsal	13 (0–39)
US7 tenosynovitis/paratenonitis sum score in GSUS (absent=0, present=1)	Dorsomedian Ulnar Palmomedian	Dorsal and palmar (in level of MCP second and third)		7 (0–7)
US7 tenosynovitis/ paratenonitis sum score in PDUS (grade 0–3)	Dorsomedian Ulnar Palmomedian	Dorsal and palmar (in level of MCP second and third)		7 (0–21)
US7 erosion sum score in GSUS (absent=0, present=1)	Dorsomedian Ulnar Palmomedian	Dorsal and palmar (only radial at MCP second)	Dorsal and palmar (only lateral at MTP fifth)	17 (0–17) or14 (0–14) if wrist not included

GSUS, gray-scale ultrasound; MCP, metacarpophalangeal; MTP, metatarsophalangeal; PDUS, power Doppler ultrasound; PIP, proximal interphalangeal; US7, ultrasound 7.

Synovitis (effusion and synovial hypertrophy) in GSUS was classified semiquantitatively as described by Scheel *et al*. [22]. Tenosynovitis/paratenonitis as well as erosions in GSUS were registered as being absent (0) or present (1).

The US7 score includes a combination of semiquantitative GS and PD findings obtained by a formula that includes the sum of different parameters. Its score ranges from 0 to 27 for GS and from 0 to 39 for PD [16].

GS_synovitis (GSUS-score 7)=GS_D_wrist+GS_P_wrist+GS_U_wrist+GS_P_MCP2+GS_P_MCP3+GS_P_PIP2+GS_P_PIP3+GS_D_MTP2+GS_D_MTP5=9 (scanning)×3 (highest GS score 0–3)=27.

PD_synovitis (PDUS-score **7)**=PD_D_wrist+PD_P_wrist+PD_U_wrist+PD_D_MCP2+PD_P_MCP2+PD_D_MCP3+PD_P_MCP3+PD_D_PIP2+PD_P_PIP2+PD_D_PIP3+PD_P_PIP3+PD_D_MTP2+PD_D_MTP5=13 (scanning)×3 (highest PD score 0–3)=39.

GS, gray-scale; D, dorsal scan; P, palmar scan; U, ulnar scan; MCP, metacarpophalangeal joint; PIP, phalangeal interproximal; MTP, metatarsophalangeal joint; PD, power Doppler.

Statistical analysis

The statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics were done by number and percent as well as mean and SD. Correlations were calculated using Pearson's correlation coefficient. A backward/stepwise multiple linear regression model was used for detection of independent predictors of ultrasonographic erosions. The level of statistical significance was set at P less than 0.05.

Results

Characteristics of patients with rheumatoid arthritis

Characteristics of patients with RA are shown in Table 2. According to cut-off values of CDAI, four (8%) patients were in remission, six (12%) of low activity, 12 (24%) of moderate activity, and 28 (56%) of high activity. Concerning GAS, eight (16%) patients were near remission. According to RAPID 3, three (6%) patients were near remission, five (10%) of low activity, 12 (24%) of moderate activity, and 30 (60%) of high activity.

Table 2 Clinical characteristics of patients with rheumatoid arthritis

	Patients (*N*=50)
Age (years)	
Range	24–72
Mean±SD	43.90±10.78
Sex	
Male [*n* (%)]	4 (8)
Female [*n* (%)]	46 (92)
Duration of illness (years)	
Range	1–37
Mean±SD	8.70±6.11
CDAI	
Range	8–64
Mean±SD	39.3±15.2
GAS	
Range	5–38.7
Mean±SD	25.8±9.6
RAPID 3	
Range	0.7–8.3
Mean±SD	5±2.3
Conventional DMARD use [*n* (%)]	
Methotrexate	49 (98)
Antimalarial drugs	50 (100)
Leflunomide	10 (20)
Sulfasalazine	2 (4)
NSAID use [*n* (%)]	48 (96)
Corticosteroids use [*n* (%)]	16 (32)
ESR first (mm/h)	
Range	7–115
Mean±SD	45.8±22.3
SENS	
Range	3–68
Mean±SD	25.7±16.1
GSUS7 synovitis	
Range	9–27
Mean±SD	16.2±4.5
PDUS7 synovitis	
Range	4–28
Mean±SD	11.6±4.8
GSUS7 tenosynovitis	
Range	0–7
Mean±SD	6.02±2.1
PDUS7 tenosynovitis	
Range	0–13
Mean±SD	6.08±2.2
GSUS7 erosion	
With wrist	
Range	0–12
Mean±SD	5.9±2.5
Without wrist	
Range	0–9
Mean±SD	4.7±1.9

CDAI, clinical disease articular index; DMARD, disease-modifying antirheumatic drugs; ESR, erythrocyte sedimentation rate; GAS, global arthritis score; GSUS, gray-scale ultrasound; PDUS, power Doppler ultrasound; RAPID 3, routine assessment of patient index data; SENS, simple erosion narrowing score.

Detailed joint region analysis by ultrasound 7 score

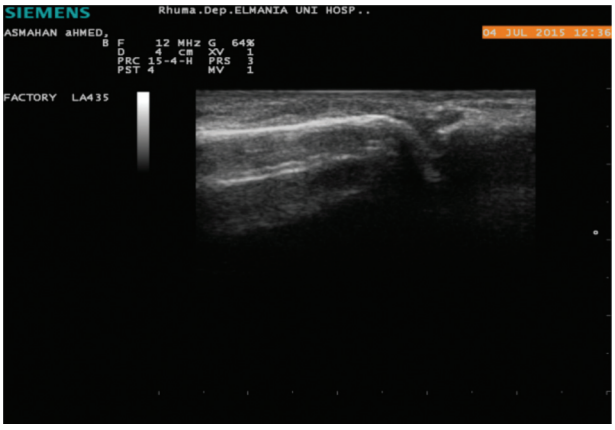
By GSUS, wrists synovitis was determined in 47 (94%) of 50 patients, MCP joint II and III synovitis was found in 48 (96%) (Fig. 3), PIP II and PIP III synovitis was found in 46 (92%), and

MTP II and V synovitis in 44 (88%) (Fig. 1). Different grades of synovitis are shown in Table 3.

By PDUS, wrist activity was found in 41 (82%) patients (Fig. 2), MCP joint II and III activity was found in 44 (88%) and more frequently observed in the dorsal aspect than in the palmar aspect, PIP II and PIP III activity was found in 37 (74%) and more frequently seen in the dorsal than in the palmar aspect, and MTP II and V activity was found in 33 (66%) as shown in Table 4.

Tenosynovitis in GS mode was detected in 45 (90%) patients in the wrist joint with PD activity in 47 (94%). Tenosynovitis of the extensor carpi ulnaris tendon detected by GSUS was found in at least 20 (40%) of the joints examined, with PD activity of 14 (28%). Tenosynovitis of MCP joint II and III was found in 44 (88%) with PD activity in 43 (86%) as shown in Table 5.

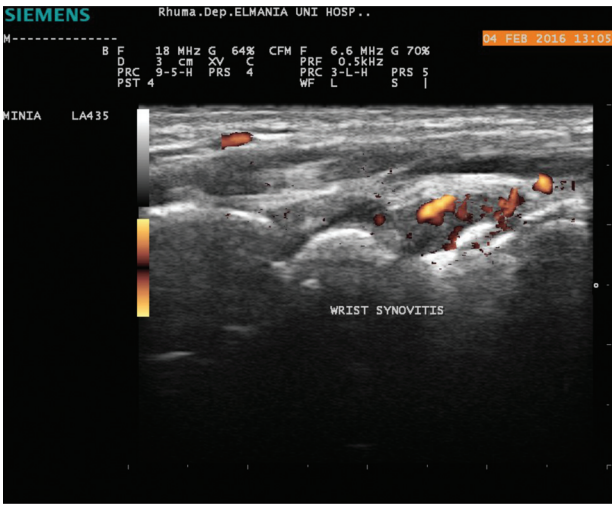
Figure 1



Grade 2 synovitis of metatarsophalangeal joint II – longitudinal scan.

By GSUS, wrist erosions were seen in 33 (66%) joints (Fig. 3) (dorsomedian aspect) and in 27 (54%) joints. Most erosions in MCP II were detected in the medial (radial) aspect in 35 (70%) joints, followed by the dorsal aspect in 29 (58%) and the palmar aspect 22 (44%). In MCP III, erosions were seen in 21 (42%) of the joints in the dorsal aspect and in 17 (34%) in the palmar aspect. Furthermore, erosions were detected more often in the dorsal aspect than in the palmar aspect (Fig. 4) [PIP II 27 (54%) vs. 21 (42%); PIP III 22(44%) vs. 16 (32%)]. Erosions in this joint were more often detected in the dorsal aspect [24 (48%)] than in the planter [22 (44%)]. Erosions in MTP V were most frequently detected in the lateral aspect in 36 (72%), followed by the dorsal in 29 (58%) and planter aspects in 19 (38%).

Figure 2



Dorsal longitudinal scan of wrist joint showing grade 2 synovitis with moderate amount of effusion and positive Doppler signals.

Table 3 Detailed joint region examination for synovitis in gray-scale ultrasound

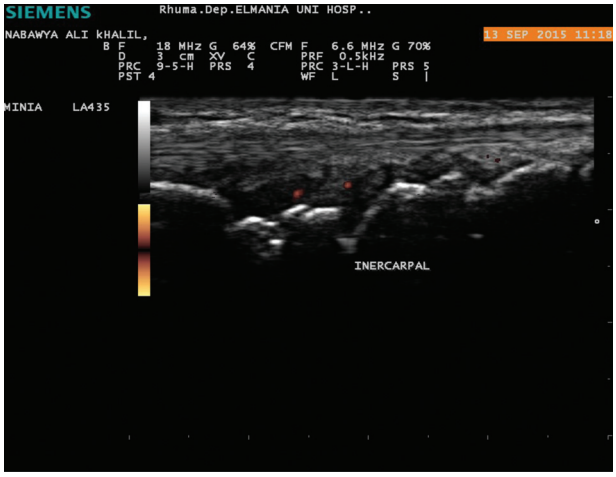
Affected joints in 50 patients with RA	Synovitis in GSUS [*n* (%)]			
	No synovitis	Grade 1	Grade 2	Grade 3
Wrist [47 (94%)]				
Dorsomedian	3 (6)	0	20 (40)	27 (54)
Palmomedian	3 (6)	1 (2)	34 (68)	12 (24)
Ulnar	3 (6)	34 (68)	11 (22)	2 (4)
MCPs [48 (96%)]				
Second MCP palmar	2 (4)	0	15 (30)	33 (66)
Third MCP palmar	2 (4)	8 (16)	28 (56)	12 (24)
PIPs [46 (92%)]				
Second PIP palmar	4 (8)	5 (10)	29 (58)	12 (24)
Third PIP palmar	4 (8)	26 (52)	11 (22)	9 (18)
MTPs [44 (88%)]				
Second MTP dorsal	6 (12)	27 (54)	14 (28)	3 (6)
Fifth MTP dorsal	6 (12)	33 (66)	9 (18)	2 (4)

GSUS, gray-scale ultrasound; MCP, metacarpophalangeal joint; MTP, metatarsophalangeal joint; PIP, proximal interphalangeal joint; RA, rheumatoid arthritis.

Correlations between the US7 score parameters and clinical data

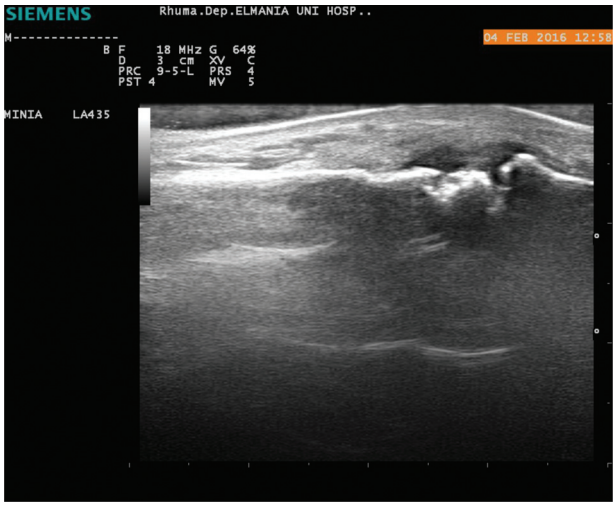
Table 6 showed significant positive correlations of duration of illness with GSUS7 and PDUS7 tenosynovitis and GSUS7 erosion (r=0.4, P=0.01; r=0.4, P=0.009; r=0.4, P=0.003, respectively). All clinical disease activity indices (CDAI, GAS, and RAPID 3) were significantly positively correlated with GSUS7 and PDUS7 synovitis, whereas RAPID 3 was the strongest variable that correlates with PDUS7 synovitis score (r=0.7, P<0.001) and CDAI was the only index that positively correlated with PDUS7 tenosynovitis (r=0.3, P=0.04). Moreover, there were significant positive correlations of ESR first with GSUS7 and PDUS7 synovitis, PDUS7 tenosynovitis, and GSUS7 erosion (r=0.5, P<0.001; r=0.7, P<0.001; r=0.3, P=0.03; r=0.3, P=0.04, respectively). Moreover, there were significant positive correlations between the radiographic score (SENS) and the all US7 score parameters (r=0.3, P=0.03 for GSUS7 synovitis; r=0.4, P=0.005 for PDUS7 synovitis; r=0.3, P=0.02 for GSUS7 tenosynovitis; r=0.4, P=0.005 for PDUS7 tenosynovitis; and r=0.6, P<0.001 for GSUS7 erosion), with more strong correlation with GSUS7 erosion score (r=0.6, P<0.001).

Figure 3



Dorsal longitudinal scan of the wrist joint showing active erosion of carpal bone.

Figure 4



Dorsal longitudinal scan of the phalangeal interproximal joint with an erosion with the synovitis in the other phalangeal interproximal joint in the left picture.

Table 4 Detailed joint region examination for synovitis in power Doppler ultrasound

Affected joints in 50 patients with RA	Synovitis in PDUS [*n* (%)]			
	No activity	Grade 1	Grade 2	Grade 3
Wrist [41 (82%)][a]				
Dorsomedian	9 (18)	7 (14)	29 (58)	5 (10)
Palmomedian	16 (32)	28 (56)	6 (12)	0
Ulnar	34 (68)	12 (24)	4 (8)	0
MCPs [44 (88%)][a]				
Second MCP palmar	16 (32)	26 (52)	8 (16)	0
Second MCP dorsal	6 (12)	28 (56)	14 (28)	2 (4)
Third MCP palmar	27 (54)	16 (32)	7 (14)	0
Third MCP dorsal	10 (20)	21 (42)	18 (36)	1 (2)
PIPs [37 (74%)][a]				
Second PIP palmar	22 (44)	19 (38)	9 (18)	0
Second PIP dorsal	13 (26)	23 (46)	13 (26)	1 (2)
Third PIP palmar	31 (62)	10 (20)	9 (18)	0
Third PIP dorsal	13 (26)	23 (46)	14 (28)	0
MTPs [33 (66%)][a]				
Second MTP dorsal	17 (34)	26 (52)	7 (14)	0
Fifth MTP dorsal	17 (34)	28 (56)	5 (10)	0

[a]Overall percentage in all joint aspects of both right and left sides. MCP, metacarpophalangeal joint; MTP, metatarsophalangeal joint; PDUS, power Doppler ultrasound; PIP, proximal interphalangeal joint; RA, rheumatoid arthritis.

Table 5 Detailed joint region examination for tenosynovitis in power Doppler ultrasound

Affected joints in 50 patients with RA	Tenosynovitis in PDUS [*n* (%)]			
	No activity	Grade 1	Grade 2	Grade 3
Wrist [47 (94%)][a]				
Dorsomedian	25 (50)	19 (38)	6 (12)	0
Palmomedian	19 (38)	27 (54)	4 (8)	0
Ulnar	36 (72)	4 (8)	10 (20)	0
MCPs [43 (86%)][a]				
Second MCP palmar	13 (26)	37 (74)	0	0
Second MCP dorsal	7 (14)	38 (76)	5 (10)	0
Third MCP palmar	13 (26)	37 (74)	0	0
Third MCP dorsal	8 (16)	35 (70)	7 (14)	0

[a]Overall percentage in all joint aspects of both right and left sides. MCP, metacarpophlangeal joint; PDUS, power Doppler ultrasound; RA, rheumatoid arthritis.

Table 6 Correlations between ultrasound 7 score parameters and clinical data

	GSUS7 synovitis		PDUS7 synovitis		GSUS7 tenosynovitis		PDUS7 tenosynovitis		GSUS7 erosion	
	r	*P* value	*r*	*P* value	*r*	*P* value	*r*	*P* value	*r*	*P* value
Duration of illness	0.1	0.5	0.02	0.9	0.4	0.01*	0.4	0.009*	0.4	0.003*
CDAI	0.5	<0.001*	0.6	<0.001*	0.3	0.1	0.3	0.04*	0.2	0.2
GAS	0.4	<0.001*	0.6	<0.001*	0.3	0.1	0.3	0.1	0.2	0.1
RAPID 3	0.5	<0.001*	0.7	<0.001*	0.2	0.1	0.3	0.06	0.2	0.09
ESR first	0.5	<0.001*	0.7	<0.001*	0.2	0.08	0.3	0.03*	0.3	0.04*
SENS	0.3	0.03*	0.4	0.005*	0.3	0.02*	0.4	0.005*	0.6	<0.001*

CDAI, clinical disease activity index; ESR, erythrocyte sedimentation rate; GAS, global arthritis score; GSUS, gray-scale ultrasound; PDUS, power Doppler ultrasound; RAPID 3, routine assessment patient index data 3; SENS, simple erosion narrowing score. *$P<0.05$, significant.

Multivariate regression analysis of the clinical and laboratory parameters using erosion in gray-scale ultrasound as dependent variable

Using erosion in GSUS as dependent variable, GSUS7 synovitis, PDUS7 synovitis, ESR, and duration of illness were found to be the most significant independent predictive factors for ultrasonographic erosions (P=0.01, P=0.02, P=0.04, and P=0.04, respectively).

Discussion

Of the several validated US scores, including different joints, we used the US7. Despite including only small joints of one hand and one foot, the US7 fulfills the Outcome Measures in Rheumatology filter of truth, discrimination, and feasibility [16,23,24]. The US7 is as accurate as other validated US scores with a fairly small number of joints to be assessed, becoming an interesting global US scoring system of synovitis in RA at the patient level [24–27].

In the present study, detailed joint region examination by US7 score was done, and we found that the dorsomedian aspect of the wrist (94%), the palmar aspect of MCP II (96%), and the palmar aspect of PIP II and III (92%) were the most affected joint regions with synovitis by GSUS. In agreement with our results, Ohrndorf and Backhaus [26] reported that the most joints/joint regions affected by synovitis (detected by GSUS) were the wrist in the dorsal aspect, the MCP II in the palmar aspect, and PIP II in the palmar aspect. Moreover, Scheel *et al.* [22] detected synovitis in the finger joints, and it was most often presented in the palmar proximal side in 86% of patients. However, for the detection of synovitis by PDUS in this study, dorsomedian aspect of the wrist and dorsal aspect of the MCP, PIP II, and PIP III were involved, as PD activity was found more on the dorsal than palmar aspect of the joints as reported previously by Ohrndorf and Backhaus [26] and Vlad *et al.* [28].

Our results revealed that tenosynovitis of the extensor carpi ulnaris tendon detected by GSUS was found in at least 20 (40%) of the joints examined, with PD activity of 14 (28%). Erosions were found most in radial aspect of MCP II (70%), lateral aspect of MTP V (72%), and dorsal aspect of PIP II and PIP III. Similar results were reported by Ohrndorf and Backhaus [26], and this distribution of erosions was shown by a French–US working group before presenting new semiquantitative erosions score with good correlation to radiography.

This group also found erosions primarily in MTP V, followed by MCP II [29].

The positive correlations between clinical disease activity indices (CDAI, GAS, and RAPID 3), laboratory findings (ESR), radiographic score (SENS), and components of the US7 score showed the ability of US7 score to reflect disease activity and severity. Moreover, the significant correlations between duration of illness, CDAI, ESR, radiographic score, and GSUS7/PDUS7 tenosynovitis reflecting the value of tenosynovitis component in the US7 scoring system in contrary to results of Ohrndorf and Backhaus [26].

Our results proved the value of GSUS7 erosion component in the assessment of disease severity as it was correlated strongly with the radiographic score. The best predictors for ultrasonographic erosions in the present study were long duration of illness, high synovitis sum scores in GSUS and PDUS, and high ESR. In contrast to our study, Ohrndorf and Backhaus [26] reported that the synovitis score in GSUS was the only multivariately significant predictor.

In the current study, we noticed that patients in clinical remission 'according to cut-off values of CDAI' (four patients '8%') were found to have active synovitis by US in one or more joints for each patient as defined by Dougados *et al.* [30] 'according to both GSUS and PDUS in US7 score'. This can be explained as 'subclinical synovitis', which is defined as joint inflammation determined not by physical examination but by musculoskeletal US or MRI [31]. The importance of subclinical synovitis, especially as determined by PDUS, has been strengthened by several reports showing that its presence is predictive of further radiographic progression or clinical flare-ups [32,33].

In conclusion, the US7 was simple and practical sum scoring system for use in the detection of synovitis in patients with RA. The correlations between the clinical disease activity indices, ESR, duration of illness, radiographic score, and components of the US7 score reflected the value of US7 score in assessment of disease activity and severity. Follow-up studies are recommended to examine the role of the additive value of the US7 score compared with conventional clinical and serological parameters, especially regarding the outcome parameters, and evaluation of the treatment effect.

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Conflicts of interest
There are no conflicts of interest.

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