Original Article

Study on the Correlation between 7-joint Ultrasound Score and Disease Activity in Patients with Rheumatoid Arthritis

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Abstract

Background: The objective of this study was to investigate the correlation between the 7-joint ultrasound score (US7) and disease activity in patients with rheumatoid arthritis (RA). **Methods:** Forty-four patients with active RA were assessed, and the correlation between US7 and disease activity indicators such as the disease activity score (DAS28), rheumatoid factor (RF), the erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) was analyzed. In addition, the proportions of US7 points accounted for by different joint regions and joint surfaces were analyzed. **Results:** RF, CRP, and ESR were significantly increased in the RA group compared with the control group ($P < 0.05$). In the RA group, DAS28 ($r = 0.0.561$, $P < 0.01$), RF ($r = 0.635$, $P < 0.01$), ESR ($r = 0.585$, $P < 0.01$), and CRP ($r = 0.492$, $P < 0.01$) were positively correlated with US7. In terms of contributions to US7, the most susceptible joint surface is the dorsal surface, and the most susceptible joint area is the dorsal wrist. **Conclusion:** US7 is positively correlated with disease activity indicators of RA, which can objectively reflect disease activity in RA patients and provide a reference for clinical diagnosis and efficacy evaluation.

Keywords: 7-joint ultrasound score, correlation, disease activity, disease activity score 28, rheumatoid arthritis, ultrasound

Introduction

Rheumatoid arthritis (RA) is an autoimmune disease. In severe cases, this disorder can cause joint deformities and loss of function,[1] affecting patients' quality of life.[2] There is no cure for RA, and clinical treatment is mainly driven by symptom-based standards. Assessment of disease activity is the key to determining the clinical efficacy of treatment and identifying endpoints. The disease activity score (DAS28), rheumatoid factor (RF), the erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are important indicators of traditional RA disease activity. However, some subclinical synovitis cannot be detected only by clinical symptoms and laboratory tests.[3] The 7-joint ultrasound score (US7) is currently the only comprehensive scoring system that includes all typical RA pathological changes (synovitis, tenosynovitis, and bone erosion).[4] The purpose of this study was to analyze the correlation between US7 and disease activity indicators in RA patients.

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Materials and Methods

Research subjects

RA patients who had complete data and were diagnosed and treated in Wujin Hospital Affiliated with Jiangsu University from 2016 to 2019 were selected. All patients met the RA classification criteria developed by the American College of Rheumatology and the European League Against Rheumatism in 2010. The patients were in the clinically active phase and had completed laboratory and ultrasound examinations before treatment. The exclusion criteria were as follows: (1) people

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with congenital abnormalities of the hand or with deformities caused by trauma, (2) people with other connective tissue diseases or joint swelling and pain with unknown causes, (3) people with allergies, (4) pregnant and lactating women, and (5) patients with comorbid malignant tumors or other serious primary or secondary diseases.

Clinical and laboratory examinations

Laboratory tests were completed before treatment, and inflammatory markers, including RF, CRP, and ESR, were recorded. DAS28 scoring method was used to score the patients' clinical activity, and the clinical evaluation of RA patients was completed by rheumatologists with the title of attending or above.

Seven-joint ultrasound score inspection and scoring standards

The clinical evaluation of RA patients was completed by a rheumatologist with an attending title or above, and each patient received an ultrasound examination within 1 day after the evaluation. All ultrasound examinations and image assessments were performed by an ultrasound physician with more than 3 years of experience in musculoskeletal and joint ultrasound examinations. The examinations were performed with a Toshiba Aplio 500 ultrasonic diagnostic instrument and a linear array probe (dynamic range 60 dB, DiffII14, frequency 5–14 MHz). The wrist joint; the metacarpophalangeal joints (MCPs) of fingers 2 and 3 (designated MCP II and MCP III), the proximal interphalangeal joints (PIPs) of fingers 2 and 3 (designated PIP II and PIP III), and the plantar sides of the metatarsophalangeal joints (MTPs) of toes 2 and 5 (designated MTP II and MTP V) were assessed on the more symptomatic side of the body. Gray-scale ultrasound (GSUS) and power Doppler (PD) were performed. GSUS synovitis [Figure 1a; including traditional joint fluid and synovial hyperplasia], PD ultrasound (PDUS) synovitis [Figure 1b], GSUS tenosynovitis [Figure 1c], PDUS tenosynovitis [Figure 1d], and bone erosion [Erosion (ES), Figure 1e] were observed in each joint. Binary scores were used to evaluate GSUS tenosynovitis and bone erosion, with "No" being 0 points and "Yes" being 1 point. GSUS was used to evaluate synovitis (hyperplasia) on a semiquantitative scale: 0 point for no synovial hyperplasia, 1 point for a hypertrophic synovium that does not exceed the highest point of the bone surface, 2 points if the joint capsule is parallel to the joint, and 3 points if the joint capsule extended further. PDUS was used to evaluate the blood flow signal in the synovium and tendon sheath on a semiquantitative scale: 0 score, there was no obvious blood flow signal in the synovium. 1 point, 1-2 spot blood flow signals can be detected in the synovial membrane. 2 points, Dot or linear blood flow signals can be detected at ≥3 places in the synovial membrane, but the area does not exceed 50% of the thickened synovial membrane. 3 points, dendritic or reticular blood flow signals can be seen in the synovial membrane, and the area exceeds 50% of the thickened synovial membrane. For each joint, the synovitis, tenosynovitis, and ES scores were summed to calculate the total score for the joint; the total scores of the seven selected joints were summed to calculate the final US7 score.[5]

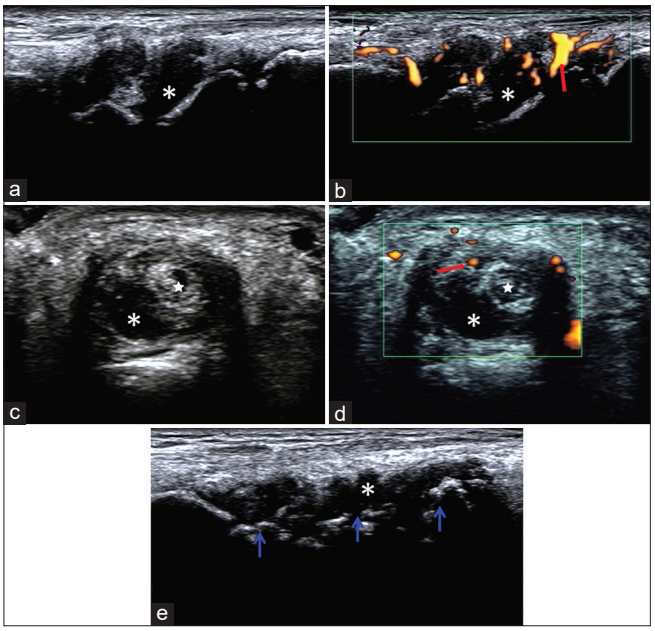

Figure 1: (a) Synovial hyperplasia of the left wrist joint (3 points), (b) Doppler checks left wrist energy (3 points), (c) Synovium hyperplasia of the 6th extensor tendon of the right wrist (1 point), (d) Energy Doppler flow diagram of the 6th extensor tendon sheath of the right wrist (1 point), and (e) Multiple bone erosion in the right wrist (1 point). *: Proliferating synovium, Red arrow: Energy Doppler blood flow signal, ★: Tendon, Blue arrow: Bone erosion

Statistical analysis

SPSS 17.0 (IBM, Armonk, NY, USA) statistical analysis software was used. Measurement data that conformed to the normal distribution were expressed as the mean ± standard deviation (X ± S), and Student's *t*-test was used to compare groups. Nonnormally distributed data were expressed as the median and quartiles, M (P25-P75). In these cases, groups were compared the Mann–Whitney *U*-test. Spearman correlation analysis was used to evaluate the correlation between disease activity indicators and US7 scores. $r \geq 0.6$ was considered a strong correlation, $0.4 \leq r < 0.6$ was a moderate correlation, and $r < 0.4$ was a weak correlation. Statistical significance was defined as $P < 0.05$.

Ethical approval

This study was approved by the Ethics Committee of Wujin Hospital Affiliated with Jiangsu University (approval no. 2015-05), and informed consent was obtained from the subjects or their legal guardians.

Results

Clinical data and test results

This study included 44 RA patients aged 20–83 years, with an average age of 57.9 ± 13.3 years. The duration of the disease ranged from 1 to 30 years, with an average of 9.1 ± 8.5 years. The patients comprised 11 males and 33 (75%) females. There was no significant difference between the RA group and the control group in terms of age or sex ratio, and

there were significant differences in US7, RF, CRP, and ESR [Table 1].

Contributions of each score type to the total 7-joint ultrasound score in the rheumatoid arthritis group

The total US7 of 44 RA patients was 849 [Figure 2]. Synovitis scores accounted for a significantly higher proportion of US points than tenosynovitis or ES did. GSUS synovitis accounted for 391 (46%) points, PDUS synovitis accounted for 260 (30%) points, GSUS tenosynovitis accounted for 68 (8%) points, PDUS tenosynovitis accounted for 53 (6%) points, and ES accounted for 87 (10%) points.

Contributions of different joint areas and joint surfaces to the total 7-joint ultrasound score of the rheumatoid arthritis group

The joint area that made the largest contribution was the dorsal wrist joint (20.37%), followed by the dorsal MCP II (11.03%), and palmar wrist joint (10.87%) [Figure 3].

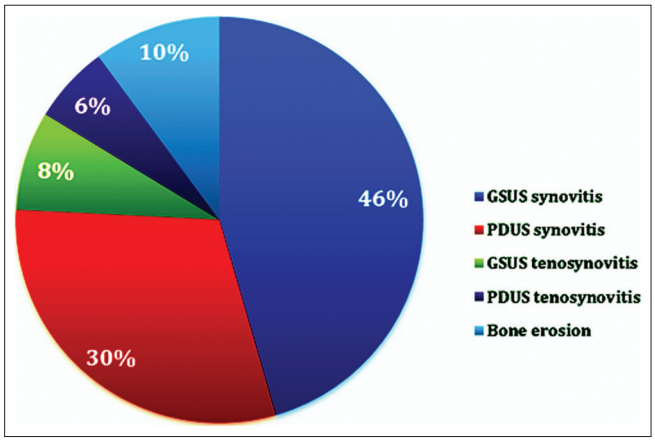

Figure 2: The proportion of each type in the total score of US7. US7: 7-joint ultrasound score, GSUS: Gray-scale ultrasound, PDUS: Power Doppler ultrasound

Through further statistical analysis, we found that the main articular surface contributing to the total US7 was the dorsal surface (58%), followed by palmar/plantar (35%) and lateral (7%) [Figure 4].

Correlation between 7-joint ultrasound score and nonspecific inflammatory indicators

Spearman correlation analysis was used to analyze the correlation between US7 and disease activity indices in the RA group, as shown in Table 2 and Figure 5. The results showed that DAS28 ($r = 0.0.561$, $P < 0.01$), RF ($r = 0.635$, $P < 0.01$), ESR ($r = 0.585$, $P < 0.01$), and CRP ($r = 0.492$, $P < 0.01$) were positively correlated with US7 in the RA group. PDUS synovitis, GSUS synovitis, and PDUS tenosynovitis were correlated with DAS28, RF, CRP, and ESR in the US7 score. GSUS tenosynovitis and bone erosion had no correlation with DAS28, RF, CRP, and ESR.

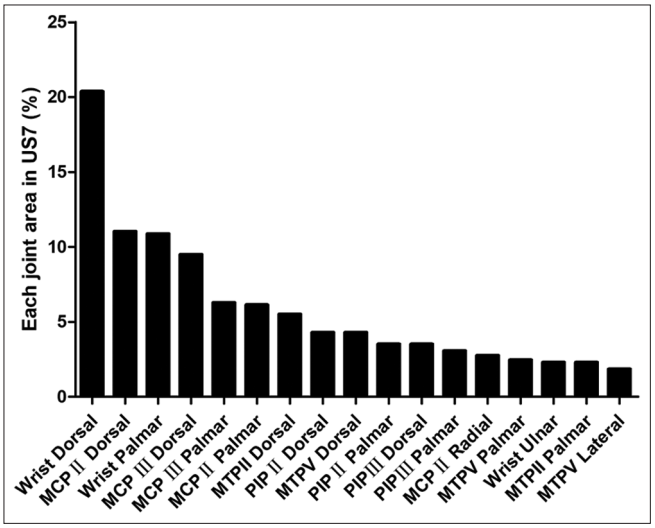

Figure 3: The proportion of each joint area in the total US7 score. US7: 7-joint ultrasound score

Table 1: Clinical data and laboratory results

Item	RA group	Control group	*P*
n	44	16	/
Disease duration (years)[a]	9.1±8.5 (1–30)	/	/
Age (years), mean±SD (range)[a]	57.9±13.3	51.2±18.5	>0.05
Gender (female/male)	11/33	4/12	>0.05
Morning stiff time (min)[b]	5 (0–13)	None	/
RF (IU/mL)[b]	160 (64.2–376.7)	11.2 (4.7–19.2)	<0.05
CRP (mg/L)[b]	17.4 (4.9–63.7)	2.8 (1.4–5.7)	<0.05
ESR (mm/H)[a]	64.6±36.5	6.1±3.0	<0.05
DAS-28	4.63±1.12	/	/
GSUS synovitis[b]	8 (4–14)	0 (0–2)	<0.05
PDUS synovitis[b]	4 (1–9)	None	/
GSUS tenosynovitis[b]	1 (0–3)	None	/
PDUS tenosynovitis[b]	0 (0–2)	None	/
Bone erosion[b]	2 (1–3)	None	/
US7[b]	16 (11–25)	0 (0–2)	<0.05

[a]Mean±SD, [b]Median (quartile). SD: Standard deviation, RA: Rheumatoid arthritis, RF: Rheumatoid factor, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, DAS: Disease activity score, GSUS: Gray-scale ultrasound, US7: 7-joint ultrasound score, PDUS: Power doppler ultrasound

Discussion

Synovial inflammation is the main pathological change associated with RA, and the inflammatory response promotes angiogenesis in the joints, which is the main cause of joint destruction.[6] RA diagnosis and treatment guidelines emphasize its "erosive" characteristics.[7] A previous study found that the main reason for the continued progress of joint bone destruction in some patients in clinical remission was the persistence of synovial inflammation;[3] therefore, it is extremely important to accurately assess the degree of inflammation and control the progress of the disease.

The DAS28 score is the main index for the clinical evaluation of the disease activity of RA patients.[8] RF is an antibody against human or animal IgG molecule Fc fragment antigen-determining cluster. It is a continuous and highly potent RF, which often indicates the disease activity of RA.[9] CRP is an acute phase protein; ESR can reflect the accumulation of fibrinogen and immunoglobulins; RF is one of the important serum markers of RA; all three of these variables are acute inflammation indicators in the body.[10] However, the clinical symptoms of some RA patients are not typical, and the detection of laboratory indicators is often near the critical value, which makes the clinical diagnosis and differential diagnosis difficult. This study showed that US7 was positively correlated with RF, ESR, and CRP in RA patients, indicating that US7 can be used to assess the degree of inflammation in RA. This finding is consistent with previous reports.[11]

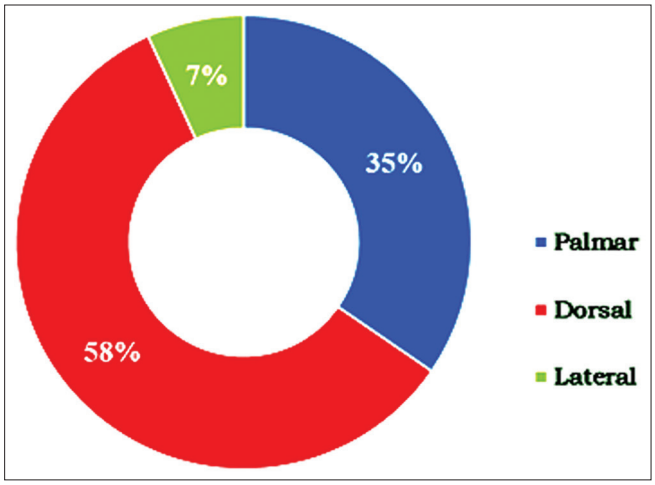

Figure 4: The proportion of each articular surface in the total US7 score. US7: 7-joint ultrasound score

This study found that in US7, GSUS synovitis, and PDUS synovitis were stronger than GSUS tenosynovitis, PDUS tenosynovitis, or ES with DAS28, RF, CRP, and ESR. A previous analysis showed that the main pathological change in RA was synovial inflammation, which consisted mainly of synovial hyperplasia of the joints, accompanied by microangiogenesis. This finding was confirmed in our study. In the total US7 of 44 selected RA patients, we found that joint synovitis (76%) accounted for a significantly higher proportion of points than tendon sheath synovitis (14%) or bone destruction (10%).

There are reports in the literature that ultrasound examination of the joints of the palm is also very important.[12] Vlad reported that compared to the dorsal interphalangeal joints of the hand, Palmar interphalangeal joint was more strongly associated with clinical disease activity indicators (clinical disease activity indicators and simplified disease activity index).[13] The US7 standard developed by Backhaus *et al*. focuses mostly on the palmar sides of joints, but our study found that the proportion of involvement on the dorsal side (58%) was much higher than that of the palmar side (35%). We speculate that this outcome is due to the different races of the subjects in the included studies; further research is needed. Further analysis revealed that the most vulnerable joint area was the dorsal wrist joint, which is consistent with previous studies. In this study, the second-most affected joint area was the dorsal MCP II, whereas Ohrndorf and Backhaus reported that the second-most affected joint area was the dorsal MTP II.[14] This inconsistency may be related to the small number of cases included in our study.

Conclusion

US7 is an economical, simple, and fast measure, i.e., positively correlated with disease activity indicators in RA, such as DAS28, RF, ESR, and CRP, objectively reflects disease activity in RA patients and can provide a reference for clinical diagnosis and efficacy evaluation.

The main limitation of this study is that it is a single-center retrospective study. The included sample size was small, which may cause a certain degree of statistical bias. Thus, the results of this study need to be verified by coordinated multicenter studies.

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Table 2: Correlation analysis between 7-joint ultrasound score and disease activity indicators

	GSUS synovitis	PDUS synovitis	GSUS tenosynovitis	PDUS tenosynovitis	Bone erosion	US7
RF	0.527**	0.545**	0.179	0.371*	0.067	0.635**
ESR	0.522**	0.543**	0.197	0.299*	−0.041	0.585**
CRP	0.436**	0.474**	0.203	0.335*	−0.039	0.492**
DAS-28	0.550**	0.606**	0.144	0.252	0.101	0.561**

*P<0.05, **P<0.01. GSUS: Gray-scale ultrasound, US7: 7-joint ultrasound score, RF: Rheumatoid factor, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, DAS: Disease activity score, PDUS: Power doppler ultrasound

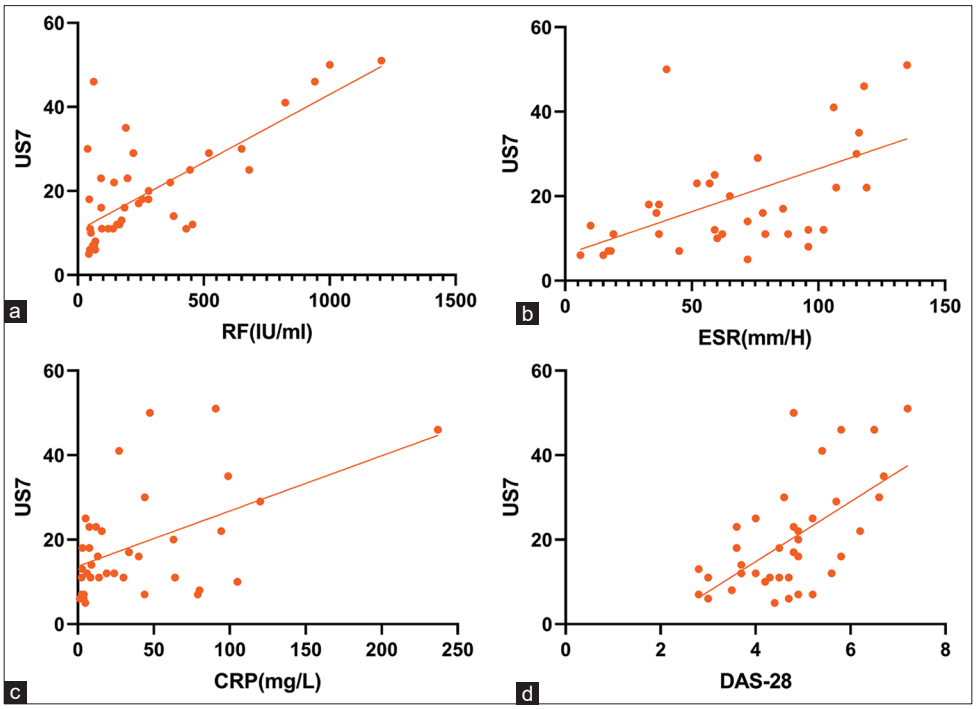

Figure 5: The correlation between US7 score and disease activity indicators RF (a), ESR (b), CRP (c), and DAS-28 (d). US7: 7-joint ultrasound score, DAS: Disease activity score, RF: Rheumatoid factor, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

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Conflicts of interest

There are no conflicts of interest.

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