Importance of baseline musculoskeletal ultrasound findings in the prognosis of rheumatoid arthritis

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Abstract
Objectives To investigate the prognostic value of baseline musculoskeletal ultrasound (MSUS) findings for rheumatoid arthritis (RA).

Method We retrospectively analyzed 138 patients with RA. Patients’ first MSUS record was considered as the baseline expression. The subsequent MSUS changes that showed alleviation or progression were regarded as the cutoff point. Gray-scale ultrasound (GSUS) synovitis, power Doppler ultrasound (PDUS) synovitis, PDUS tenosynovitis (TS), and bone erosion were scored using a semi-quantitative scale. According to the ultrasound (US) results of the cutoff point, patients were divided into the alleviation group and the progression group. Laboratory results (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], rheumatoid factor [RF], anticyclic citrullinated peptide [anti-CCP] antibody, and anti-keratin antibody [AKA]), disease activity score in 28 joints (DAS28)-ESR, and US scores were compared between the two groups to analyze the prognostic value of US findings in RA.

Results The alleviation group had higher levels of CRP, synovitis, TS, GSUS synovitis, PDUS synovitis, PDUS TS, and US total scores at baseline than the progression group \( (p < 0.05) \). The alleviation group received more aggressive treatment in their initial approach than the progression group \( (p < 0.05) \). The frequency of US examinations in the alleviation group was more than that in the progression group at follow-up \( (p < 0.05) \). Presence of baseline synovitis (OR 0.248, \( p = 0.006 \)) and a higher GSUS synovitis score (OR 0.521, \( p = 0.006 \)) were negatively correlated with RA progression.

Conclusions Presence of baseline synovitis and higher GSUS synovitis score do not always indicate worse prognosis of RA, which can be improved with aggressive treatment. Regular MSUS follow-up may have positive influences on prognosis.

Key Points
• The presence of synovitis at baseline and higher GSUS synovitis score do not necessarily imply poor prognosis of RA.
• Prompt and powerful therapy and regular ultrasound follow-up can slow down the progression of RA and improve its prognosis.
• Patients with slight and less arthritis at baseline might be ignored and get worse prognosis due to mild treatment strategies and irregular MSUS examination.

Keywords Grayscale · Musculoskeletal ultrasound · Prognosis · Rheumatoid arthritis · Synovitis

Introduction
Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that can cause joint deformity and affect the quality of life of patients. In the past years, the “treat to target” (T2T) strategy aimed at clinical remission has routinely been implemented in clinical practice [1, 2], and consequently, the prognosis of RA has been greatly improved. However, joint destruction continues to occur on some patients because of the worse radiographic progression. Subclinical synovitis is a common problem in the prognosis of RA, but because of the current stagnation of imaging, it is difficult to detect it by imaging methods, which leads to joint destruction in some patients [3].

Nowadays, musculoskeletal ultrasound (MSUS) has been widely used in arthritis assessment to identify changes in the joint, such as synovitis, tenosynovitis, and bone erosion [4, 5].
Through grayscale ultrasound (GSUS) and power Doppler ultrasound (PDUS) findings, individuals who are at high risk of RA [6] could be identified, and treatment efficacy could be assessed to determine the progression [7] and prognosis in RA [8–10]. In general, a patient with less involvement of the joint and low disease activity presumably easily achieves remission and has better prognosis than a patient with more involvement of the joint and high disease activity in RA. However, surprisingly, these patients sometimes have inconsistent outcomes. Ultrasound (US) characterization of these patients showed that some patients’ condition continued to improve, while others’ condition gradually deteriorated, and they even experienced bone erosion. This may be due to the heterogeneity in RA or unknown reasons. This retrospective cohort study aimed to investigate whether US characteristics such as synovitis, tenosynovitis, bone erosion, and US score at baseline could predict the future deterioration or alleviation in RA.

**Materials and method**

**Patients and clinical data**

We retrospectively analyzed 138 Chinese patients (age range from 18 to 75 years) who were diagnosed with RA from a single center (Department of Rheumatology and Immunology, the Second Hospital of Hebei Medical University, Shijiazhuang, China), from May 1, 2014, to September 1, 2020. All patients included in this study were required to fulfill the 1987 American College of Rheumatology (ACR) criteria for RA [11] or the 2010 ACR/European League Against Rheumatism (EULAR) criteria for RA [12]. Alternatively, the patient should have participated in at least two US examinations from baseline, and the minimum interval between two US examinations was 3 months. Exclusion criteria included the presence of other accompanying autoimmune diseases, infections, or tumors, finger disability and deformity, or those whose frequency of US examinations did not meet the requirements. This study was approved by the Ethics Committee of the Second Hospital of Hebei Medical University (approval No. 2018-R089). All participants provided written informed consent for participation.

Patients’ first US record was regarded as baseline expression. The subsequent US changes of those joints that showed Doppler alleviation or Doppler progression compared with baseline were regarded as the cutoff point. Data of the following parameters were collected at baseline and cutoff point: sex, age, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), anticyclic citrullinated peptide (anti-CCP) antibody, anti-keratin antibody (AKA), disease activity score in 28 joints (DAS28)-ESR, and treatment protocols. The patients received different therapies according to their disease condition at baseline, and the treatment protocols were adjusted during follow-up according to the “treat to target” strategy. The therapeutic schemes included conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biologic disease-modifying antirheumatic drugs (bDMARDs), Chinese patent medicine (CPM), and glucocorticoids (equivalent dose acetate prednisone).

**MSUS assessment**

All US examinations were performed by a rheumatologist with extensive experience in MSUS who was blinded to the clinical data. All patients were scanned on a MyLab 700 (ESAOTE) machine with a multifrequency linear transducer (LA 435 and IH 6–18). According to the standardized scanning method recommended by the EULAR [13, 14], the following 22 joints were evaluated: bilateral wrist joints, bilateral metacarpophalangeal joints 1–5, bilateral interphalangeal joints, and bilateral proximal interphalangeal joints 2–5. The GSUS and PDUS parameters were adjusted according to the device used. The GSUS frequency was 6–18 MHz, and the gain was 60%. The settings for PDUS were as follows: frequency, 9.1 MHz; gain, 50%; range of pulse repetition frequency, 750 Hz–1.0 kHz. There was a low wall filter, which had to be maintained throughout the study. The sonographic examination of each patient took approximately 10–20 min.

**US scoring**

Two MSUS doctors scored the US images of all RA patients according to the EULAR/Outcome Measures in Rheumatology Clinical Trials (OMERACT) scoring system [15, 16]. Then, the average score of the two doctors was calculated. GSUS synovitis, PDUS synovitis, PDUS tenosynovitis (TS), and bone erosion were scored using a semi-quantitative scale (grade 0–3). All scores were added up to the US total score. Higher scores indicated higher severity (damage). According to the results of the cutoff point US examination, the patients were divided into the alleviation group and the progression group. RA alleviation was defined as a US state without Doppler activity, or total PDUS score was lower than the baseline PDUS score of 22 joints. RA progression was defined as a total PDUS score was greater than the baseline PDUS score with/without an increase in the bone erosion score.
Statistical analysis

Statistical analysis was performed using SPSS, version 25.0 (IBM Corp., Armonk, NY, USA). Normally distributed continuous data are presented as the mean and standard deviation (SD). Non-normally distributed data are presented as median (minimum, maximum). Categorical variables are presented as absolute frequencies and percentages. Normally distributed variables were compared with Student t test, and non-normally distributed variables were compared with Mann–Whitney U test; categorical variables were compared with chi-square test or Fisher’s exact test. Intra-group comparisons were performed using the paired t test or Wilcoxon matched-pair signed-rank test. A multivariate binary logistic regression model was used to estimate the predictive value of US findings in RA. The parameter of p < 0.05 in the univariate analysis data was subjected to regression equation. p < 0.05 was considered to indicate statistical significance.

Results

Baseline characteristics of patients

In total, 138 patients with RA were included in the present study. Among them, 118 (85.5%) were female, and the mean age was 44.9 years (SD 11.9). At baseline, 115 (83.3%) patients were RF-positive and 113 (81.9%) patients were anti-CCP antibody-positive. The mean DAS28-ESR score was 3.97 (SD 1.18). Of the 138 RA patients, 118 (85.5%) showed abnormalities in US findings at baseline, while the remaining 20 (14.5%) had no abnormalities in the wrists and hands. Fifteen (10.9%) patients were treated with one csDMARD plus bDMARD, 54 (39.1%) patients were treated with one csDMARD plus CPM, 16 (11.6%) patients were treated with one csDMARD plus glucocorticoids, 50 (36.2%) patients were treated with two csDMARDs combined, and 3 (2.2%) patients were treated with three csDMARDs combined. Their baseline characteristics are described in Table 1.

Summary of patients’ cutoff point characteristics

According to the US manifestations at the cutoff point, the patients were divided into the alleviation group and the progression group (76 (55.1%) vs. 62 (44.9%)). In the alleviation group, 37 (48.7%) patients achieved complete remission (PDUS = 0) and 39 (51.3%) patients achieved partial remission (a decrease in PDUS score compared with baseline). In the progression group, 31 (50%) patients had increased PDUS synovitis with/without bone erosion, 11 (17.7%) patients presented with increased PDUS TS with/without bone erosion, and 20 (32.3%) patients concurrently presented with increased PDUS synovitis and TS with/without bone erosion. From baseline to the cutoff point, 46 (33.3%) patients underwent follow-up for 1 year, 62 (44.9%) patients had follow-up for 2–4 years, 22 (15.9%) patients had follow-up for 5 years, and 8 (5.8%) patients underwent follow-up for 6 years. Compared with baseline, ESR, CRP, RF, anti-CCP, DAS28-ESR, GSUS synovitis, PDUS synovitis, PDUS TS, and US total scores were found to be significantly decreased in the alleviation group. However, bone erosion increased (Fig. 1). In the progression group, only the anti-CCP level decreased, whereas the GSUS synovitis, PDUS synovitis, erosion, and US total score significantly increased (Fig. 2).

Table 1 Baseline characteristics of all patients (n = 138)

| Baseline characteristic | Value |
|-------------------------|-------|
| Age, years (mean ± SD)  | 44.9 ± 11.9 |
| Gender                  |       |
| Female, n (%)           | 118 (85.5) |
| Male, n (%)             | 20 (14.5)  |
| RF                      |       |
| Negative, n (%)         | 23 (16.7)  |
| Positive, n (%)         | 115 (83.3) |
| Anti-CCP                |       |
| Negative, n (%)         | 25 (18.1)  |
| Positive, n (%)         | 113 (81.9) |
| AKA                     |       |
| Negative, n (%)         | 103 (74.6) |
| Positive, n (%)         | 35 (25.4)  |
| DAS28-ESR, (mean ± SD)  | 3.97 ± 1.18 |
| Ultrasonic manifestations|     |
| No abnormalities, n (%) | 20 (14.5)  |
| Anomalies, n (%)        | 118 (85.5) |
| Synovitis with/without bone erosion, n (%) | 35 (29.6) |
| TS with/without bone erosion, n (%) | 14 (11.9)  |
| Synovitis and TS with/without bone erosion, n (%) | 69 (58.5)  |
| Treatment               |       |
| One csDMARD plus bDMARD, n (%) | 15 (10.9) |
| One csDMARD plus CPM, n (%) | 54 (39.1) |
| One csDMARD plus glucocorticoids, n (%) | 16 (11.6) |
| Two csDMARD, n (%)      | 50 (36.2)  |
| Three csDMARD, n (%)    | 3 (2.2)    |

SD standard deviation, n absolute numbers, RF rheumatoid factor, anti-CCP anticyclic citrullinated peptide, AKA anti keratin antibody, DAS28 Disease Activity Score in 28 joints, TS tenosynovitis, csDMARD conventional synthetic disease-modifying antirheumatic drug, bDMARD biologic disease-modifying antirheumatic drug, CPM Chinese patent medicine
Comparison of baseline characteristics between the alleviation group and the progression group

As shown in Table 2, there were significant differences between the alleviation group and the progression group in CRP, synovitis, TS, GSUS synovitis, PDUS synovitis, PDUS TS, US total scores, and initial treatment options at baseline \((p < 0.05)\). There were no significant differences between the two groups in age, sex, ESR, RF, anti-CCP, AKA, DAS28-ESR, bone erosion, and erosion score \((p > 0.05)\).

Comparison of cutoff characteristics between the alleviation group and the progression group

Compared with the alleviation group, ESR, CRP, GSUS synovitis, PDUS synovitis, PDUS TS, and US total scores in the progression group were higher at the cutoff point. The frequency of US examinations was less in the progression group, there was a significant statistical difference between the two groups \((p < 0.05)\), and there were no significant differences between the two groups in age, sex, RF, anti-CCP, DAS28-ESR, and bone erosion score (Table 3).

Comparison of baseline characteristics between the pauciarticular group and the polyarticular group

According to the number of arthritis confirmed on US and clinical manifestations, the patients were classified into the pauciarticular group (1–4 joints) and the polyarticular group \((\geq 5 \text{ joints})\). There were statistically significant differences in ESR, CRP, DAS28-ESR, GSUS synovitis, PDUS synovitis, PDUS TS, bone erosion score, US total scores, initial treatment options, and outcomes between the pauciarticular group and the polyarticular group \((p < 0.05)\) (Table 4).

Association between baseline US manifestations and RA progression risk in regression models

Multivariate analysis showed that the presence of synovitis (odds ratio \([\text{OR}]\) 0.248, 95% confidence interval \([\text{CI}]\) 0.091 to 0.676, \(p = 0.006\)) and high GSUS synovitis score (OR 0.521, 95% CI 0.327 to 0.830, \(p = 0.006\)) at baseline were negatively correlated with RA progression (Table 5). These were the obstructive factors for RA progression when compared with the absence of synovitis and a lower GSUS synovitis score at baseline.

Discussion

Recently, the evaluation of RA progression has gained much attention. Several measures have been developed to assess disease progression using clinical, laboratory, and imaging data. In 2019, the EULAR established poor prognostic factors for RA, including persistently moderate or high disease activity despite csDMARD therapy, high acute phase reactant levels, more swollen joint counts, RF and/or anti-CCP antibody at high titers, presence of early bone erosion, and failure of two or more csDMARDs treatment \([2]\). It is reported that high levels of CRP, RF, anti-CCP positivity, and early bone erosion were strongly associated with radiographic joint damage \([17, 18]\). Bone edema detected by magnetic resonance imaging (MRI) was a predictor of radiographic progression \([19, 20]\). Rydell et al. \([21]\) showed the link between overweight or obesity and radiographic progression and reported that smoking was an independent predictor of bone erosion progression \([22]\). Smolen et al. \([23]\) founded that 28 swollen joint count, CRP, and physician global assessment at baseline associated with radiographic progression. They reported various characteristics that affect the prognosis of RA in arthritis, but only few studies have reported the usefulness of baseline US performance as a predictor of the prognosis of RA \([24, 25]\). Therefore, our study explored the importance of baseline MSUS findings in the prognosis of RA.

Compared with baseline values of ESR, CRP, RF, anti-CCP, DAS28-ESR, GSUS synovitis, PDUS synovitis, PDUS TS, and US total scores in the alleviation group significantly decreased after treatment. However, bone erosion in the alleviation group increased when compared with that at baseline, indicating effective treatments could lower the levels of serological markers, reduce DAS28, and relieve arthritis, but it could not stop the progression of bone destruction. Surprisingly, the alleviation group had higher levels of CRP, synovitis, TS, GSUS synovitis, PDUS synovitis, PDUS TS, and US total scores at baseline than the progression group. The main reason might be that the patients with significant US manifestations at baseline received more aggressive treatment in their initial approach, with 85.5% receiving one csDMARD plus bDMARD or glucocorticoids, or a combination of two DMARDs. Particularly, the vast majority of patients maintained a review interval of 3 or
6 months by US during the subsequent follow-up. However, patients with no abnormalities or relatively mild abnormalities of the wrists and hands on US at baseline received one csDMARD plus CPM and underwent repeat US examinations at an interval of 12 months or more. The traditional view was that severe arthritis more likely promoted bone erosion progression, but our study demonstrated that aggressive treatment and regular MSUS assessment could improve RA outcome. On the contrary, patients with initial mild arthritis might be ignored and be compromised in the final treatment results due to mild treatment strategies and irregular US examinations.

In a survey from UK rheumatologists, for anti-CCP-positive patients with inflammatory symptoms but without clinical synovitis, 36/44 (82%) respondents usually requested an US scan to help guide management [26]. Patients with US synovitis receive the most intensive therapy, either treated as a standard patient with RA or given a DMARD. By contrast, 94% of patients with no US synovitis or US tenosynovitis are either observed in clinic without therapy or discharged. Therefore, more presence of synovitis may trigger rheumatologists to monitor patients closely and undertake specific laboratory testing or imaging examinations. Lukas et al. [27] indicated that early initiation of DMARD therapy reduces 12-month radiographic progression, and the potential benefits of DMARD treatment may be lost if the treatment is delayed. The MSUS-driven “T2T” strategy achieves low disease activity or remission in most patients and significantly improves clinical, functional, and imaging results [28]. Dale et al. [29] demonstrated that global RA disease activity evaluation utilizing a limited MSUS joint set provided new disease activity information, which led to revised therapy decisions in a large minority of cases. US and MRI, as sensitive imaging modalities, not only contribute to the therapy decisions, but also help to guide drug tapering or even discontinuing treatment [30]. But the costs of MRI examinations are expensive and inconvenient compared with the US.

Given that the number of arthritis may influence the prognosis of RA, we compared the baseline US findings and clinical manifestation between the pauciarticular group and the polyarticular group. Compared with the pauciarticular group, the baseline ESR, CRP, DAS28-ESR, GSUS synovitis, PDUS synovitis, PDUS TS, erosion, and US total scores of the polyarticular group were severe. Due to the high disease activity in patients with polyarthritis, there were differences in the choice of treatment options. Patients with more severe arthritis received aggressive treatment regimens (approximately 72.3%) including biologic agents, glucocorticoids, or csDMARD combinations at baseline. Patients with less severe arthritis received milder treatment, primarily one csDMARD plus CPM, and had a progression rate of above 50%. The alleviation ratio was more than 70% in the polyarticular group when compared with that of 46.2% in the pauciarticular group. This suggested that the choice of treatment was more important for prognosis.

Several studies have analyzed the relationship between US findings and structural damage in RA. For example, PDUS is a predictor of erosive progression and disease flare [20, 31]. Bone erosion detected on baseline US was an independent predictor of radiographic erosion at the same joint level at 1 year (p < 0.001) [32]. The baseline total GS synovitis score (GS ≥ grade 2) was predictive of progression to RA [33]. El Miedany et al. [9] found that the rates of disease relapse were significantly higher in patients whose US scores (both GS and PD scores) raised within 3 months of stopping their medications. Möller et al. [34] also confirmed that GSUS appears to be an essential component of synovitis assessment, higher levels of GSUS are associated with the development of erosion. Sundin et al. [35] reported that the systematic use of MRI or US detected inflammation, both at diagnosis and in remission is associated with the elements of future disease development. However, Andrea et al. [36] reported that in anti-CCP + at-risk individuals with musculoskeletal symptoms, CR-detected erosion is uncommon and does not predict the development of inflammatory arthritis (IA). In our study, we also found that the presence of synovitis at baseline and higher GSUS synovitis score does not necessarily imply poor prognosis of RA. Compared with patients with normal or slightly abnormal US at baseline, these more severe abnormalities were important indicators for rheumatologist to enhance...
treatment and increase MSUS follow-up frequency. Kawashiri et al. [37] also found that anti-CCP antibody positivity/high titer and high swollen joint counts or the presence of synovial hypertrophy with GS grade 3 at baseline were associated with the use of b/tsDMARDs therapy, and MSUS scores at baseline were not associated with SDAI remission at 1 year post-diagnosis. This conclusion was similar with our findings to some extent. According to the patient’s clinical manifestation to implement intensive treatment might be more important than only thinking about MSUS scores at baseline.

In conclusion, our results indicate that RA patients should undergo US assessment not only at baseline but also in the follow-up. US manifestations should be interpreted with great caution, because synovitis and higher GSUS synovitis score at baseline do not always mean worse prognosis. All of these may be reversed by aggressive treatment leading to better prognosis. It is easy to overlook the patients with mild synovitis and low GSUS synovitis, who receive routine treatment and without ultrasonic reexamination may result in bad prognosis. This is a real-life retrospective observational study from China that reflects the actual clinical situation and can provide references for the clinical treatment and prognosis of RA patients.

Table 2 Comparison of baseline characteristics between alleviation group and progression group

| Characteristics                              | Alleviation (n=76) | Progression (n=62) | p value |
|----------------------------------------------|-------------------|--------------------|---------|
| Age, years (mean ± SD)                       | 45.61 ± 11.75     | 44.11 ± 12.29      | 0.468   |
| Female/male, n                               | 66/10             | 52/10              | 0.622   |
| ESR, median (min.–max.)                      | 26.5 (3,113)      | 20.5 (2,101)       | 0.064   |
| CRP, median (min.–max.)                      | 13 (1.42,146)     | 7.96 (1.33,108)    | 0.035   |
| RF, median (min.–max.)                       | 156 (12.6,2830)   | 91.75 (15,3430)    | 0.267   |
| Anti-CCP, median (min.–max.)                 | 526.81 (5.3,1933) | 457.06 (3.14,3484.6) | 1.000 |
| DAS28-ESR (mean ± SD)                        | 4.00 ± 1.21       | 3.94 ± 1.15        | 0.625   |

Synovitis

| Presence, n (%)                              | 54 (71)           | 29 (47)            | 0.004   |
| Absence, n (%)                               | 22 (29)           | 33 (53)            |         |

TS

| Presence, n (%)                              | 68 (89)           | 36 (58)            | 0.000   |
| Absence, n (%)                               | 8 (11)            | 26 (42)            |         |

Bone erosion

| Presence, n (%)                              | 25 (33)           | 18 (29)            | 0.626   |
| Absence, n (%)                               | 51 (67)           | 44 (71)            |         |
| GSUS synovitis, median (min.–max.)           | 6 (0,42)          | 2 (0,28)           | 0.000   |
| PDUS synovitis, median (min.–max.)           | 4 (0,40)          | 2 (0,28)           | 0.000   |
| PDUS TS, median (min.–max.)                  | 2 (0,22)          | 0.5 (0,50)         | 0.009   |
| Bone erosion score, median (min.–max.)       | 0 (0,14)          | 0 (0,12)           | 0.516   |
| US total score, median (min.–max.)           | 15.5 (0,92)       | 5.5 (0,90)         | 0.000   |

Treatments

| One csDMARD plus bDMARD, n (%)               | 15 (19.7)         | 0 (0)              | 0.000   |
| One csDMARD plus CPM, n (%)                 | 9 (11.8)          | 44 (71)            |         |
| One csDMARD plus glucocorticoids, n (%)     | 14 (18.4)         | 3 (4.8)            |         |
| Two csDMARD, n (%)                           | 36 (47.4)         | 14 (22.6)          |         |
| Three csDMARD, n (%)                         | 2 (2.6)           | 1 (1.6)            |         |

ESR erythrocyte sedimentation rate, CRP C reactive protein, RF rheumatoid factor, anti-CCP anticyclic citrullinated peptide, AKA anti keratin antibody, DAS28 Disease Activity Score in 28 joints, TS tenosynovitis, GSUS grey scale ultrasound, PDUS power Doppler ultrasound, US ultrasound, csDMARD conventional synthetic disease-modifying antirheumatic drug, bDMARD biologic disease-modifying antirheumatic drug, CPM Chinese patent medicine
Table 3  Comparison of the cutoff characteristics between alleviation group and progression group

| Characteristics                                             | Alleviation (n = 76) | Progression (n = 62) | p value |
|-------------------------------------------------------------|----------------------|----------------------|---------|
| Age, years (mean ± SD)                                      | 48.04 ± 11.84        | 47.1 ± 12.38         | 0.650   |
| Female/male, n                                              | 66/10                | 52/10                | 0.622   |
| ESR (mm/h), median (min.–max.)                              | 10 (1.80)            | 16 (3.84)            | 0.017   |
| CRP (mg/L), median (min.–max.)                              | 4.79 (1.803)         | 7.86 (1.41,169)      | 0.003   |
| RF (KIU/L), median (min.–max.)                              | 58.8 (15,1390)       | 104 (15,2160)        | 0.188   |
| Anti-CCP (RU/mL), median (min.–max.)                        | 267 (3.65,1305.65)   | 358 (1.26,1681.65)   | 0.411   |
| DAS28-ESR (mean ± SD)                                       | 2.62 ± 1.37          | 4.23 ± 1.16          | 0.107   |
| GSUS synovitis, median (min.–max.)                          | 1 (0.30)             | 6 (0.56)             | 0.000   |
| PDUS synovitis, median (min.–max.)                          | 0 (0.20)             | 4 (0.38)             | 0.000   |
| PDUS TS, median (min.–max.)                                 | 0 (0.7)              | 2 (0.19)             | 0.000   |
| Bone erosion score, median (min.–max.)                      | 2 (0.20)             | 2 (0.23)             | 0.139   |
| US total score, median (min.–max.)                          | 5 (0.65)             | 18 (1,130)           | 0.000   |
| Frequency of ultrasound examination                         |                      |                      |         |
| Interval 3 months, n (%)                                    | 11 (14.5)            | 3 (4.8)              | 0.000   |
| Interval 6 months, n (%)                                    | 41 (53.9)            | 11 (17.7)            |         |
| Interval 12 months, n (%)                                   | 24 (31.6)            | 48 (77.4)            |         |

ESR erythrocyte sedimentation rate, CRP C reactive protein, RF rheumatoid factor, anti-CCP anticyclic citrullinated peptide, DAS28 Disease Activity Score in 28 joints, GSUS grey scale ultrasound, PDUS power Doppler ultrasound, TS tenosynovitis, US ultrasound

Table 4  Comparison of the baseline characteristics between pauciarticular group and polyarticular group

| Characteristics                                             | Pauciarticular group (n = 91) | Polyarticular group (n = 47) | p value |
|-------------------------------------------------------------|-------------------------------|-------------------------------|---------|
| Age, years (mean ± SD)                                      | 44.45 ± 11.87                 | 45.87 ± 12.25                 | 0.469   |
| Female/male, n                                              | 76/15                         | 42/5                          | 0.355   |
| ESR (mm/h), median (min.–max.)                              | 20 (2.92)                     | 40 (3,113)                    | 0.000   |
| CRP (mg/L), median (min.–max.)                              | 7.17 (1.33,108)               | 25.3 (1.67,146)               | 0.000   |
| RF (KIU/L), median (min.–max.)                              | 107 (12,6,3430)               | 124(15,2830)                  | 0.478   |
| Anti-CCP (RU/mL),median (min.–max.)                         | 456.72 (3.14,3484.6)          | 513.4(4.8,1933)               | 0.849   |
| AKA positive, n (%)                                         | 18 (19.8)                     | 16 (34)                       | 0.065   |
| DAS28-ESR (mean ± SD)                                       | 3.77 ± 0.95                   | 5.65 ± 1.05                   | 0.000   |
| GSUS synovitis, median (min.–max.)                          | 2 (0.11)                      | 14 (0.42)                     | 0.000   |
| PDUS synovitis, median (min.–max.)                          | 1 (0.9)                       | 12 (0.40)                     | 0.000   |
| PDUS TS, median (min.–max.)                                 | 1 (0.20)                      | 4 (0.50)                      | 0.009   |
| Bone erosion score, median (min.–max.)                      | 0 (0.12)                      | 2 (0.14)                      | 0.000   |
| US total score, median (min.–max.)                          | 5 (0.26)                      | 36 (5,92)                     | 0.000   |
| Treatments                                                  |                               |                               |         |
| One csDMARD plus bDMARD, n (%)                              | 6 (6.6)                       | 9 (19.1)                      | 0.024   |
| One csDMARD plus CPM, n (%)                                 | 43 (47.3)                     | 11 (23.4)                     |         |
| One csDMARD plus glucocorticoids, n (%)                     | 11 (12.1)                     | 5 (10.6)                      |         |
| Two csDMARD, n (%)                                          | 30 (32.9)                     | 20 (42.6)                     |         |
| Three csDMARD, n (%)                                        | 1 (1.1)                       | 2 (4.3)                       |         |
| Outcomes                                                    |                               |                               |         |
| Alleviation                                                 | 42 (46.2)                     | 34 (72.3)                     | 0.003   |
| Progression                                                 | 49 (53.8)                     | 13 (27.7)                     |         |

ESR erythrocyte sedimentation rate, CRP C reactive protein, RF rheumatoid factor, anti-CCP anticyclic citrullinated peptide, AKA anti keratin antibody, DAS28 Disease Activity Score in 28 joints, GSUS grey scale ultrasound, PDUS power Doppler ultrasound, TS tenosynovitis, US ultrasound, csDMARD conventional synthetic disease-modifying antirheumatic drug, bDMARD biologic disease-modifying antirheumatic drug, CPM Chinese patent medicine
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Author contribution CS, LL, and YY performed the US scans. XQ was responsible for the data collection. LG analyzed data. CS wrote the manuscript. HG was responsible for the study design. All authors contributed to revision of the report and approved the final version.

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Data availability The dataset used and/or analyzed during the current study is available from the corresponding author on reasonable request.

Table 5 Association between baseline US and RA progression

| Variables          | B     | SE   | Wald | Exp (B) | 95% CI          | p value |
|--------------------|-------|------|------|---------|-----------------|---------|
| CRP                | −0.008| 0.010| 0.654| 0.992   | 0.974 to 1.011  | 0.419   |
| Presence of synovitis | −1.394| 0.512| 7.430| 0.248   | 0.091 to 0.676  | 0.0006  |
| Presence of TS     | −1.091| 0.604| 3.266| 0.336   | 0.103 to 1.097  | 0.071   |
| GSUS synovitis score | −0.652| 0.238| 7.539| 0.521   | 0.327 to 0.830  | 0.0006  |
| PDUS synovitis score | 0.262 | 0.212| 1.529| 1.300   | 0.858 to 1.971  | 0.216   |
| PDUS TS score      | −0.101| 0.107| 0.901| 0.904   | 0.733 to 1.114  | 0.342   |
| US total score     | 0.170 | 0.099| 2.982| 1.186   | 0.977 to 1.438  | 0.084   |
| Constant           | 2.518 | 0.593| 18.038| 12.403  | 0.000           | 0.000   |

SE standard error, CI confidence interval, CRP C reactive protein, TS tenosynovitis, GSUS grey scale ultrasound, PDUS power doppler ultrasound, US ultrasound

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