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Musculoskeletal Ultrasonography for the Assessment of Combined Drug Therapy for Rheumatoid Arthritis

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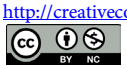

Abstract

Background: To evaluate the effect of treatment on musculoskeletal ultrasound (MSUS) and explore whether MSUS are associated with therapeutic response in rheumatoid arthritis (RA) patients treated with Tofacitinib in combination with methotrexate (MTX). **Methods:** We enrolled 102 RA patients treated with Tofacitinib in combination with MTX from a multicenter, exploratory, short-term, prospective and observational ultrasound cohort study of patients who received biologic or targeted synthetic disease-modifying antirheumatic drug (DMARD) therapy. We evaluated the patients' clinical disease activity and musculoskeletal ultrasound (MSUS) scores. The serum concentrations of two venous blood inflammatory indicators were evaluated (c-reactive protein [CRP], erythrocyte sedimentation rate [ESR]) by multiplex bead assays at baseline, 3, and 6 months: the change over 6 months was defined as the P value. Before MSUS score treatment, an associate chief physician tested the wrist joints of each patient at the first treatment, and the attending physician with 3 years of MSUS experience and 7 years of work experience also performed semi-quantitative scores on the same RA patients and tested the consistency of the results. **Results:** Tofacitinib in combination with MTX significantly improved the clinical disease activity and MSUS score over 6 months. Serum ESR and CRP were significantly elevated at 6 months after the Tofacitinib in combination with MTX introduction ($P < 0.01$). The DAS28-ESR and MSUS score DAS28-ESR and MSUS scores decreased significantly compared with no treatment, and the difference was statistically significant ($P < 0.01$). The correlation analysis results of Pearson's test showed that the semi-quantitative score of musculoskeletal ultrasound was positively correlated with the degree of rheumatoid arthritis and related inflammatory

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indexes (ESR, CRP) ($P < 0.05$). **Conclusions:** MSUS scores may be useful for predicting RA patients' therapeutic responses to abatacept.

Keywords

Rheumatoid Arthritis, Musculoskeletal Ultrasound, Tofacitinib, Methotrexate, C-Reactive Protein, Erythrocyte Sedimentation Rate

1. Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory joint disease that can cause cartilage, bone damage, and disability [1]. The tight control of RA disease activity by following the treat-to-target strategy to reach optimal outcomes is thus recommended. Advances in the treatment of RA such as the use of biological disease-modifying anti-rheumatic drugs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) have provided better clinical outcomes (including the achievement of clinical remission) and the prevention of joint damage and disability among individuals with RA [2].

Methotrexate (MTX) is a traditional disease control drug that can fundamentally delay the progression of rheumatoid arthritis disease and is considered one of the drugs of choice for the treatment of RA.

Tofacitinib was approved for marketing in China in March 2017 for the treatment of adult patients with moderate to severe active RA. Tofacitinib is a Janus kinase (JAK) inhibitor, a class of non-receptor tyrosine protein kinases that play a very important role in all stages of cell differentiation, proliferation, and survival. JAK protein is an important protein involved in transducing receptor signaling of a large number of cytokines and growth factors. Compared with other biological agents, tofacitinib is administered orally, compared with other intravenous or subcutaneous biological agents, because of the convenience of oral administration, tofacitinib is more acceptable to the majority of patients in the clinic. Tofacitinib has a half-life of about 3 hours, and the drug is eliminated from serum after hepatic metabolism (70%) and renal excretion (30%). Tofacitinib inhibits a variety of cytokines and hormones that are beneficial in reducing disease activity. The symptoms of patients can be significantly improved after medication, and it has good cost-benefit advantages, which will play an important role in the treatment of RA in the future [3].

The 2020 edition of the European League for Rheumatoid Arthritis Treatment Guidelines recommends the use of JAK inhibitors as an alternative to biologics for RA patients who do not respond to traditional DMARDS therapy and have poor prognostic factors, as well as those who fail to achieve certain efficacy through previous biologic therapy [4] [5]. Studies have shown that the oral bioavailability of Tofacitinib is 74%, and its dose is positively correlated with its metabolism, which can be rapidly absorbed and metabolized by patients.

MSUS has three ways to assess the condition of RA: quantitative, semi- quan-

titative, and qualitative, but in terms of practicality, semi-quantitative scoring has gradually become the most important way [6]. Previous studies have commonly used to assess the disease activity of RA mainly related to joint tenderness, joint swelling, 28 joint rheumatoid arthritis activity (DAS28) score, American Rheumatology Association observation indicators 20%, 50%, 70% remission (ACR20, ACR50, ACR70), etc., these assessment methods are often greatly affected by the subjective feelings of patients and physicians, and can not directly observe and reflect the destruction of joint cartilage and bone by RA. The adequate management of disease activity requires a sensitive and accurate assessment of arthritis. Imaging plays an important role in this assessment. Musculoskeletal ultrasound (MSUS) has been widely applied in clinical settings as an imaging modality for patients with rheumatic diseases [5] [6]. Compared to clinical and radiographic examinations, MSUS provides a straightforward and more accurate detection of both inflammation and damage at the joint level [7] [8].

At present, most of the domestic studies are to evaluate musculoskeletal ultrasound combined with serological indexes to evaluate the activity and clinical efficacy of methotrexate combined with leflunomide or methotrexate alone or leflunomide tablets alone in the treatment of RA patients, but for musculoskeletal ultrasound evaluation, methotrexate combined with tofacitinib is still rare. Based on my observation experience in previous clinical work, I believe that MSUS is helpful for the monitoring and later efficacy evaluation of methotrexate combined with tofacitinib in the treatment of rheumatoid arthritis.

In the present study, this project determined the efficacy and safety of tofacitinib by first evaluating the consistency of MSUS semi-quantitative scores by different senior doctors, secondly evaluating the value of MSUS as an indicator of RA activity, conducting a correlation study between MSUS scores and common serological indicators of RA, and finally evaluating the efficacy of tofacitinib and MTX in the treatment of RA.

2. Methods

2.1. Patients

This study adopts a prospective cohort study of patients with RA who received bDMARD or tsDMARD therapy at one of the First People's Hospitals of Jingzhou. We evaluated the therapeutic efficacy by determining the patients' clinical disease activity, MSUS score, and serum biomarkers at baseline and at 3, 6 months starting from the initiation of treatment with a new bDMARD or tsDMARD. The patients' previous use of a bDMARD or tsDMARD was not restricted. For the present study, we enrolled from October 2021 to October 2022, 101 patients with RA were included as the study subjects, and all patients were adults over 18 years old. All patients met the 1987 American College of Rheumatology (ACR) [9] and/or 2010 ACR/EULAR (European League Against Rheumatism) criteria for RA [10]; Have stopped using antipathic agents other

than MTX 4 weeks prior to enrollment. The patients were randomly divided into 3 groups: control group (35 cases): MTX monotherapy (10 mg once a week); leflunomide group (35 cases): received MTX combined with leflunomide (MTX 10 mg once a week, leflunomide 10 mg tablet twice a day), and Tofacitinib group (31 cases): received MTX combined with Tofacitinib tablet (MTX 10 mg once a week, Tofacitinib 5 mg tablet twice a day). Oral administration of low-dose corticosteroids (20 mg of prednisone tablets in all patients, adjusted to prednisone tablets 10 mg maintenance after 1 week, and discontinued after 1 month). According to the Disease Activity Score (DAS28) score ≥ 3.2 [11], the disease is moderately active.

Our selection criteria: Tests of Cotolerate, Methotrexate, leflunomide tablets, etc.; In line with the clinical diagnostic criteria of RA, all of them used low-dose glucocorticoid anti-inflammatory, and both wrists were involved. Rheumatoid arthritis was consistent with a DSA28 score and the disease was moderate-high (DAS28 greater than 3.2) activity; Approved by the Ethics Committee of the hospital, patients and their families have informed consent and cooperated well.

We excluded criteria: women with fertility requirements; Recently taking immunosuppressants; Complications and other connective tissue diseases such as sjogren's syndrome; Malignant tumor, severe mental illness; Patients who have been treated with tocilizumab or adalimumab in the past; Having severe comorbidities, such as liver and kidney insufficiency, heart disease, etc.; Severe blood system involvement, severe leukopenia, severe anemia, thrombocytopenia; None of the subjects were related to each other.

We remove the criteria: patients who interrupted treatment due to adverse reactions during the course of administration; The subjects who had poor compliance and failed to follow the doctor's advice; During the course of other serious diseases, such as coronary heart disease, researchers believe that it is not appropriate to continue the drug; Failure to complete all inspection items on time as required, resulting in failure to evaluate.

Treatment was with control patients taking only MTX (10 mg once a week); Patients in the leflunomide group were combined with the application of leflunomide tablets 10 mg twice a day on the basis of methotrexate; Patients in the tofacitinib group were given tofacitinib tablets 5 mg twice a day on the basis of methotrexate. Each group of patients can be treated with corticosteroids as appropriate for joint swelling and pain. The total duration of treatment was 6 months, and the patient's clinical symptoms, laboratory test indicators, DAS28 score, and ultrasound semi-quantitative score were recorded as 0, 3 months, and 6 months, respectively.

The study was approved by the Ethics Committee of the First Affiliated Hospital of Yangtze University (ethics review number: KY202334), all enrolled patients were informed and signed informed consent, and the study strictly adhered to ethical principles such as the Helsinki Declaration and the International Ethical Guidelines for Human Biomedical Research.

2.2. Clinical and Laboratory Assessments

Disease activity was evaluated by each patient's attending physician and was based on the Disease Activity Score (DAS) 28-joint C-reactive protein (CRP) value and the Simple Disease Activity Index (SDAI) value at baseline and every 3 months after the introduction of to facitinib group the treating physicians were different from the MSUS evaluators. The patients' baseline MSUS scores were evaluated after the decision regarding the introduction of b/tsDMARD therapy.

2.3. Musculoskeletal Ultrasound Assessment

The attending physician (researchers himself) who is experienced by MSUS has completed the MSUS examination of the two joints of the two wrist joints, including 3 months, 6 months after treatment, 3 months, and 6 months after treatment. Muscle Bone Ultrasonic score: The four-level scoring method is used to calculate the three time periods of the underlying joint changes in the joints of the muscle-bone ultrasound, including four aspects of joint section, synovial blood flow signal, synovial hyperplasia, and bone erosion. Get a total score. (1) Jelly stabilization, normally 0 points, a small number of joint effusions is 1 point, the medium-sized joint effusion is 2 points, and a large number of joint effusions is 3 points; The single blood flow signal appears 1 point, the blood flow signal is less than 50% of the sliding film area of 2 points, and the blood flow signal is greater than 50% of the sliding film area of 3 points; The slim membrane hyperplasia in the angle of the joint clamping does not exceed the highest point of the drum surface to 1 point. The synovial hyperplasia exceeds the highest point of the bone surface, but it does not extend to the backbone of 2 points. 3 points; (4) Bone erosion, normally 0 points, rough surface of the bone cortex, but no defects is 1 point, Obvious bone defect is 2 points, and the bone defect area is large 3 points. Each score is added to the total score. In addition, a MSUS experienced deputy chief physician and a resident who worked for 3 years were selected to conduct MSUS scores before the treatment of all patients.

Use Konica Minea color Doppler ultrasound diagnostic to check. The 9L4 line array probe, frequency of 7 - 12 MHz, MSK conditions, imaging depth and focus point to near the field. The wall filter is set to a low-pass filter, the pulse repetitive frequency is 977 Hz, the energy Doppler is set to the best sensitivity and the pseudo-image is not produced in the osteology. Patients take a seat, place their hands on the inspection table, and detect the bilateral wrist joints.

2.4. Statistical Analyses

The application of SPSS25.0 statistical software for statistical analysis. Among them, the measurement data is tested with Shapiro-Wilk, which is expressed in compliance with the normal distribution ± standard deviation (x ± s). The number of dividends [m (*P*25, *P*75)] is expressed; the calculation data usage rate or composition ratio indicates that the comparison between the group is tested; Mori symbol norm test; comparative analysis of single factors between the three

groups (data conforms to normal, independent, neutrality); $P < 0.05$ is of statistical significance.

3. Results

3.1. Loss of the Pathogenesis

There are 101 people in this study and randomly distributed into 3 groups. For 6 months as of the treatment, 33 people in the control group completed the follow-up, 2 people retreated, and 34 people came to the leflunomide group to complete the follow-up, with 1 retreat; 28 people to the treatment group of tofacitinib completed the follow-up of the follow-up group; The loss rate was 5.94%, and a total of 95 people were included in the analysis. The loss rates of the three groups were 5.71%, 2.86%, and 9.67%. The difference was not statistically significant ($P > 0.05$).

3.2. MSUS Consistency Analysis

Three doctors of different levels of seniority conducted a semi-fixed score of 190 joints before 95 patients were treated before treatment. In order, the deputy chief physician score is 10.3 ± 2.9, and the bilateral wrist joint MSUS score is distributed between three observers without statistical differences ($P > 0.05$).

3.3. Clinical Data of Three Groups of Patients

General information: 33 cases in the control group, 27 women, 6 men, age 26 - 81 years old, and the course of the disease is 2-360th; 34 cases of the Leflunomide group, 29 women, 5 men, 5 cases At the age of 76, the course of the disease is from 3rd to 24th; there are 28 cases of Tofacitinib, 23 women, 5 cases, and 5 cases. The age is 23 - 79 years old. The proportion, age and course of men and women between the three groups are statistically different, $P > 0.05$ (Table 1). Diseases during admission: CRP, ESR, DAS28-ESR, MSUS scores, and anti-CCP antibodies, RF, HGB, AST, ALT have no statistical differences, $P > 0.05$ (Table 1).

3.4. Three Groups of RA Patients for Treatment after March Efficacy Comparison

ESR, CRP and DAS28-ESR in Tofacitinib group and Leflunomide group were significantly decreased compared with the control group, with statistical difference ($P < 0.05$). Compared with the Leflunomide Group, the Tofacitinib Group declines more obvious, and the differences are statistically significant ($P < 0.05$). (Table 2).

3.5. The Comparison of Efficacy after 6 Months of Treatment for Patients with RA Patients

Compared with the control group in ESR, CRP, and DAS28-ESR, the Toffib Group has a significant decline in the control group, with statistical differences ($P < 0.05$). Compared with the Fluorite Group, the Torfani Favorizer declines

more obvious, and the differences are statistically significant ($P < 0.05$). (Table 3).

3.6. MSUS Scores Are Positively Correlated with CRP and DAS28

Pearson test results show that muscle bone ultrasonic semi-quantitative scores are positively correlated with the degree of rheumatoid arthritis and related inflammatory indicators (ESR, CRP) ($P < 0.05$). (Table 4).

3.7. Treatment Effect Comparison

Three groups of patients with DAS28-ESR < 2.6 after 3 months of treatment. In order to achieve clinical relief, the relief rate has statistical differences ($\chi^2 = 6.99$, $P = 0.03$) and the 6-month relief rate of treatment ($\chi^2 = 10.81$, $P = 0.004$), of which the Tofacitinib Group has a clinical relief rate of 78.6% and 96.4% after treatment of 3 months and 6 months (Table 5).

Table 1. Clinical data of three groups of patients.

Group	Control group (n = 33)	Leflunomide group (n = 34)	Tofacitinib group (n = 28)	*P* value
Women (Example (%))	27 (81.8)	29 (85.3)	23 (82.1)	0.063
Age (age)	57.4 ± 10.5	59.2 ± 8.9	59.3 ± 12.9	0.735
The course of disease (month)	87.2 ± 92.2	76.9 ± 71.3	82.6 ± 100.1	0.520
ESR (mm/h)	62.7 ± 30.4	67.6 ± 32.3	64.8 ± 23.6	0.253
CRP (ug/ml)	31.4 ± 30.1	34.2 ± 34.5	29.9 ± 28.9	0.564
RF (IU/ml)	177.0 ± 171.5	196.0 ± 161.8	186.7 ± 244.9	0.922
Anti-CCP antibody	39.4 ± 22.4	36.8 ± 25.0	32.5 ± 21.3	0.458
HGB (g/L)	106.0 ± 14.3	101.0 ± 14.3	100.0 ± 13.4	0.166
AST (U/L)	20.2 ± 8.6	18.6 ± 7.9	18.4 ± 6.5	0.611
ALT (U/L)	20.0 ± 20.1	16.8 ± 16.8	15.5 ± 10.1	0.533
DAS28-ESR	5.7 ± 2.6	5.5 ± 2.0	6.1 ± 2.2	0.742
MSUS score	10.4 ± 3.2	9.6 ± 3.9	9.8 ± 3.8	0.641

Table 2. Comparison of ESR, CRP, DAS28 and MSUS among the three groups after 3 months of treatment.

Group	ESR (mm/h)	CRP (ug/ml)	DAS28	MSUS score
Control group	44.5 ± 20.6	20.1 ± 7.4	4.9 ± 2.2	8.5 ± 2.9
Leflunomide group	30.4 ± 14.3	15.7 ± 6.8	3.7 ± 1.1	6.9 ± 2.3
Tofacitinib group	20.3 ± 9.4	10.3 ± 3.6	2.5 ± 0.8	5.6 ± 1.3
*P*1	0.021	0.012	0.028	0.039
*P*2	<0.001	<0.001	<0.001	<0.001
*P*3	0.024	0.019	0.041	0.048

Note: The comparison between the three groups is analyzed by a single factor variance, the *P*1 control group is compared with the Leflunomide group; the *P*2 control group is compared with the Tofacitinib group; the P3 Leflunomide group is compared with the Torfaibett group; $P < 0.05$ means that the difference is statistically significant.

Table 3. Comparison of ESR, CRP, DAS28 and MSUS among the three groups after 6 months of treatment.

Group	ESR (mm/h)	CRP (ug/ml)	DAS28	MSUS score
Control group	30.8 ± 16.4	13.4 ± 7.9	3.4 ± 1.8	6.1 ± 1.6
Leflunomide group	19.3 ± 13.5	7.3 ± 4.1	2.5 ± 1.2	4.8 ± 0.9
Tofacitinib group	13.2 ± 7.1	4.6 ± 2.3	1.4 ± 0.6	3.9 ± 0.8
*P*1	0.026	0.027	0.043	0.048
*P*2	<0.001	<0.001	<0.001	<0.001
*P*3	0.041	0.023	0.027	0.036

Note: The comparison between the three groups is analyzed by a single factor variance, the *P*1 control group is compared with the Leflunomide group; the *P*2 control group is compared with the Tofacitinib group; the *P*3 Leflunomide group is compared with the Torfaibett group; $P < 0.05$ means that the difference is statistically significant.

Table 4. Correlation analysis of MSUS with ESR, CRP and DAS28.

Index	MSUS score	
	r	*P*
ESR	0.68	<0.01
CRP	0.70	<0.01
DAS28 score	0.69	<0.01

Table 5. Comparison of DAS28-ESR remission rate after treatment among three groups.

treatment time	DAS28-ESR Score remission rate			*P* value
	Control group (%)	Leflunomide group (%)	Tofacitinib group (%)	
3 months	15 (45.5)	19 (55.9)	22 (78.6)	0.03
6 months	20 (60.1)	26 (76.4)	27 (96.4)	0.004

4. Discussion

This study adopts a prospective cohort study of patients with RA. A total of 95 patients with active RA patients were entered in this study, including 33 people in the control group, 34 people in the Leflunomide group, and 28 Tofacitinib group. Sexual indicators such as ESR, CRP, Anti-CCP antibodies, DAS-28 and muscle ultrasound scores have no statistical differences. They ensure the relative consistency of patients in each group, and can compare clinical results through different treatment plans. After 3 and 6 months of treatment, regardless of inflammatory indicators, MSUS scores, or disease activity in terms of torrential cloth groups, they must be significantly better than that of the control group and Leflunomide group. The differences are statistically different. Especially with the DAS28-ESR < 2.6 as the standard of clinical relief, the relief rate of the Tofacitinib group can reach 78.6% and 96.4%, respectively, which is also significantly increased compared to the alleviating rate of the control group and the Lefluno-

mide group. Oral Strategy [12] in a one-year study, it was found that the efficacy of the Tofacitinib for the combined MTX was comparable to the Adalimumab for the combined MTX.

The most widely used in MSUS is the semi-quantitative scoring method proposed by the Szkudlark team [13]. By observing the changes in ultrasound, according to the severity of the lesions, sloling membrane hyperplasia, joint effusion, and blood flow signals are divided into level 0 - 3, and level 0 arteritis changes. Level 3 represents severe lesions. The rates are 86%, 79%, and 87%, all of which have good consistency of observer. In this study, it is found that the score high and low are positively correlated with the degree of activity of the disease. In this study, different years of doctors use doctors to score MSUS on different patients. It is found that the scores between the three have no differences and are consistent. It shows that the MSUS operation should be unlimited.

The commonly used RA therapy drugs can be divided into non-steroidal anti-inflammatory drugs, glucocorticoids, and improving the disease anti-rheumatic drug (DMARDS) is the basis of the treatment and alleviating of rheumatoid arthritis. It is mainly divided into Traditional synthetic types: methotrexate, willow nitroglycerine, etc.; Biological formats: Ada Mutterumoplasty, Tupu Mipoid, etc., and targeted synthetic types: Todfatta cloth and other three types.

Folic acid restoration enzyme inhibitors can prevent the synthesis of cell DNA, further inhibit the division and proliferation of lymphocytes, and have a strong anti-inflammatory and immunosuppressive effect. Ahotate can be used as anchor drug in RA treatment. 2/3 RA patients can use a single methotrexate, or use it with other traditional synthetic DMARDS to achieve the treatment target [14] [15]. Related studies have shown that the adverse reactions of small doses of metarotreate (≤10 mg/week) generally have good adverse reactions and good long-term tolerance. However, in clinical practice, many RA patients have no obvious effect on MTX, so they need to conduct joint medications to improve the efficacy.

In addition to the synthesis of pyrine, Lepomit also has other functions such as inhibiting the activity of hypertrophonase and cell adhesion, the generation and secretion of antibodies, and inhibiting inflammatory medium. Studies and analysis show that methotrexate and Latelit can significantly inhibit the synthesis of purine and pyrine. In addition, the two drugs are used in combination, which is significantly better than the single medication [4] [16]. In this study, the decline of MTX combined Lieflutrait in the inflammatory indicators and the DAS28 score is significantly better than the control group, indicating that when the MTX treatment effect is not good, it can be used with Lomit to use it. The DAS28 score and inflammatory indicators have positive correlations, and MSUS can be used to evaluate the efficacy. In addition, the clinical relief rates of 3 months and 6 months after MTX were used in this study to reach 45.5% and 60.1%, respectively, and the clinical relief rate of 3 months and 6 months after the combination of MTX and Lipmit was treated. It reaches 55.9% and 76.4%,

which indicates that the combined treatment of Lipmite treatment is better.

Some patients have poor responses to traditional anti-rheumatic drugs or intolerances, such as methotrexate, non-steroidal anti-inflammatory drugs, glucocorticoids, and thundervan vine. At the same time, due to the long-term use of biological agents, some patients have resistance to object preparations, and only a small number of patients can completely alleviate it. Because the pathogenesis of reactive T cells, B cells, macrophages, fibroblast-like synovial cells, and endothelial cells is the pathogenesis of RA as the pathogenesis of RA. The phosphorylation of hyperasezine kinase plays an important role in the combination of inflammatory cytokine in the combination of the corresponding receptor, so targeted drugs are mostly based on limousine kinase as an important target. Among them, the JAK kinase family (mainly JAK1, JAK2, JAK3) in non-intravinopase kinases, through signal pathways of various cytokines, growth factors, and hormones to promote the incidence of RA. In 2017, the State Administration of Food and Drug Administration approved by the State Administration of Food and Drug Administration to be listed in the country, Tofacitinib, Baricitinib [13] [14].

At present, whether the muscle ultrasound semi-quantitative score can reflect the level of inflammation response in the body of rheumatoid arthritis, and lack of relevant reports. The results of the research show that the muscle ultrasonic semi-quantitative score of patients with rheumatoid arthritis is positively correlated with the degree of rheumatoid arthritis and the level of related inflammatory indicators and the level of C-reactive protein. In addition, it can also reflect the patient's inflammatory factor and inflammation damage level [17]. Studies have shown that the muscle ultrasound semi-quantitative score is positively correlated with disease activity 28 scores, that is, increased with the muscle ultrasonic semi-quantitative score, and the 28 scores of disease activity also increased significantly. This study also shows that the muscle ultrasonic semi-quantitative score is positively correlated with rheumatoid arthritis DAS28 score and related inflammatory indicators (ESR, CRP), which is consistent with the results of appeal research. Evaluation of rheumatoid arthritis.

There are also some shortcomings in this study. First of all, there are fewer research samples in the three research groups, and the Torfa Daibu Group RA patients have fewer samples due to the choice of treatment plans. Secondly, there is less time to observe. Due to the tedious operation and time, time, cost, and patient acceptance, the patients have only conducted a MSUS examination on the patient's wrist joints, thereby a certain deviation on the ultrasonic score of the whole body. Finally, for the degree of relief of the disease, only the DAS28-ESR score is used, and the ACR20/50/70 relief index is not used. At the same time, the time for follow-up in this study is too short, and the alleviation of the images of rheumatoid arthritis may not be obvious within half a year. At the same time, due to the short follow-up time, the common cardiovascular risk of Torfa for clothes is not included in statistics. For the above deficiencies, in the future re-

search, the number of case samples can be increased, the number of research joint examinations is increased, the indicators of clinical relief are increased, the follow-up time of the follow-up time will be more comprehensively evaluated.

5. Conclusion

This is the first study of the impact of MTX and Tofacitinib for the effects of inflammation indicators in RA patients, and uses data exploration of data exploration in preview research whether the combined treatment is related to the patient's inflammatory indicators. In particular, the uniqueness of this survey is that it evaluates the treatment response confirmed by MSUS. In addition, MSUS may help predict the condition of RA patients.

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Availability of Data and Materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' Contributions

YY designed and managed the whole study. MW wrote the manuscript and performed the all figures and tables.MW helped to revise the manuscript. All the authors have read and approved the final manuscript.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of the First Affiliated Hospital of Yangtze University (ethics review number: KY202334). All patients gave signed informed consent.

Patient Consent for Publication

Consent for publication.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

RA	Rheumatoid Arthritis
US	Ultrasound
MSUS	Musculoskeletal ultrasound
MTX	Methotrexate
LF	Leflunomide
ALT	Alanine transaminase
AST	Aspartate transaminase
RF	Rheumatoid factor
Anti-CCP	Anti-cyclic peptide containing citrulline
DAS	Disease Activity Score
CRP	C-Reactive Protein
ESR	Erythrocyte Sedimentation Rate.