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Meta-analysis: The Impact of Different Therapies on the Quality of Life of Patients with Rheumatoid Arthritis

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Abstract: ***This article takes the quality of life of patients with rheumatoid arthritis (RA) as the research object, focusing on the practical effects of different therapies, aiming to reveal the specific impacts of each therapy on the quality of life of patients through systematic Meta-analysis. The introduction clarifies the research objectives and importance; the concept review sorts out the definition, symptoms, and diagnostic criteria of RA, and outlines the principles and effects of major therapies. The theoretical analysis explains the mechanism of action of the therapies from physiological and psychological perspectives, discusses potential intervention factors and side effects. The empirical study design details the methods of literature screening, data extraction, and statistical analysis to ensure the reliability of the results. The experimental results show that some therapies perform better in improving the quality of life of patients, and analyze their practical application value. The conclusion summarizes the main findings, points out the limitations of the study, and looks forward to future directions, emphasizing its clinical and policy guidance significance.***

Keywords: Rheumatoid arthritis, Quality of life, Meta-analysis, Therapy comparison, Clinical practice.

1. Introduction

Rheumatoid Arthritis (RA) is an autoimmune disease characterized by chronic synovitis. Its core pathological mechanism is that the abnormal activation of the immune system leads to synovial hyperplasia and bone erosion of the joints. This disease is mainly characterized by symmetrical polyarthritis, which is commonly found in the small joints of the hands and feet. Typical symptoms include morning stiffness lasting more than one hour, joint swelling and pain, and sexual dysfunction [1]. During the course of the disease, the excessive secretion of inflammatory cytokines such as TNF-α and IL-6 not only aggravates local joint damage, but also can cause systemic complications, including interstitial lung disease, cardiovascular events and osteoporosis [2]. Epidemiological data show that the global prevalence of RA is approximately 0.5%-1%. The incidence rate among women is significantly higher than that among men, and the disability rate can reach 30%-50% within 10 years of the onset of the disease.

The influence of RA on the quality of life of patients has multi-dimensional and cumulative characteristics. Physiologically, the destruction of joint structure leads to decreased grip strength and abnormal gait, which directly affect basic living abilities. Research by the European League Against Rheumatism (EULAR) shows that over 60% of patients have difficulties in daily activities such as dressing and eating [3]. At the psychosocial level, chronic pain and functional limitations can induce emotional disorders such as anxiety and depression. The assessment of the World Health Organization Quality of Life Scale (WHOQOL-BREF) indicates that the mental health score of patients with rheumatoid arthritis (RA) is more than 40% lower than that of healthy people. In terms of economic burden, statistics from the American College of Rheumatology (ACR) show that the average annual medical expenditure of RA patients is 3 to 5 times that of the general population, and indirect costs, including productivity losses, account for more than 60% of the total economic burden.

The current treatment system for RA shows a diversified development trend. Traditional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as methotrexate remain the basic treatment, but approximately 30% of patients have insufficient treatment response. Biological agents DMARDs (bDMARDs) significantly enhance the therapeutic efficacy by targeting and inhibiting specific cytokines. Targeted synthetic DMARDs (tsDMARDs) such as JAK inhibitors further expand the therapeutic options. In non-pharmacological interventions, physical therapy can improve functional status through joint range of motion training, and cognitive behavioral therapy shows unique advantages in pain management. Most of the existing studies focus on the improvement of clinical indicators, and there is still an evidence gap in the systematic assessment of the impact on the quality of life.

This study adopted the meta-analysis method to integrate data from randomized controlled trials and cohort studies, aiming to construct an evidence map of the impact of different therapies on the quality of life of RA patients. Through the data from multi-dimensional assessment tools such as the Short Form of Health Survey (SF-36) and the RA-Specific Quality of Life Scale (RAQoL), the differences in effect values between drug and non-drug interventions were quantitatively compared [4]. The research results will provide evidence-based basis for the formulation of individualized treatment plans, and at the same time reveal the optimization direction of the existing treatment model, which has important clinical significance for achieving the paradigm shift of RA management from symptom control to overall health promotion.

2. Brief Description of the Concept

Rheumatoid arthritis is an autoimmune disease characterized by chronic synovitis. Its core pathological change is the abnormal proliferation of synovial tissue and the formation of pannus, which leads to the progressive destruction of articular cartilage and bone. This disease has the clinical characteristics of symmetrical polyarthritis, most commonly involving small joints such as the proximal interphalangeal joints, metacarpophalangeal joints and wrist joints. Typical symptoms include persistent joint swelling, morning stiffness for more than one hour and pain relief after activity. According to the diagnostic criteria jointly developed by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) in 2010, it is necessary to comprehensively evaluate the number of affected joints, serological indicators (such as anti-cyclic citrullinated peptide antibody and rheumatoid factor), acute phase reactants (C-reactive protein and erythrocyte sedimentation rate), and the duration of symptoms. At the same time, other connective tissue diseases such as psoriatic arthritis and systemic lupus erythematosus should be excluded.

Quality of life, as an important dimension for evaluating the health status of RA patients, covers four core areas: physiological function, psychological state, social participation and environmental adaptation. In clinical research, standardized scales are often used for quantitative assessment. Among them, the Health Assessment Questionnaire (HAQ) is specifically designed for rheumatic diseases and contains 20 items to evaluate the ability of daily activities. The SF-36 scale conducts a comprehensive assessment from eight dimensions such as physical function, somatic pain, and overall health. In recent years, the RA-Specific Quality of Life Scale (RAQoL) has been more favored by researchers for its sensitivity and clinical relevance because it contains disease-specific indicators such as the degree of joint stiffness and the perception of treatment side effects.

The clinical intervention for RA mainly consists of three systems: drug therapy, physical therapy and surgical intervention. Traditional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as methotrexate regulate the immune response by inhibiting dihydrofolate reductase, while biological agents DMARDs (such as TNF-α inhibitors) target and block key inflammatory mediators. JAK inhibitors, as novel targeted synthetic DMARDs, exert their effects by interfering with the cytokine signaling pathway. In the field of physical therapy, joint protection training designed based on biomechanical principles can effectively improve joint range of motion, and low-frequency pulsed electromagnetic field therapy has been proven to inhibit the proliferation of synovial cells. For those with severe damage to the joint structure in the advanced stage, total joint replacement combined with postoperative systematic rehabilitation training can increase the Harris hip score by more than 40%. The combined application of different treatment methods should follow the principle of individualization, controlling the degree of inflammatory activity while maintaining the functional status of patients to the greatest extent.

3. Theoretical Analysis

Table 1: Relevant Data

Research content	Detailed data
The total number of RA patients was included	207 cases
Average RA-QoL score	7.8±7.1
Physical Function Summary (PCS) score	63.8±23.8
Summary of Psychological Functioning (MCS) score	71.7±21.0
The proportion of patients with disease remission and low disease activity	59.5%
The proportion of patients with remission or low disease activity under the Concise Rheumatoid Arthritis Disease Activity Index (SDAI) criteria	62.5%
Physiological function score (low disease activity group vs. complete remission group)	76.7±17.2 vs. 86.4±15.0
Body pain score (Low disease activity group vs. Complete remission group)	67.8±8.5 vs. 77.7±15.6
Health change score (Low disease activity group vs. Remission group)	52.8±22.3 vs. 63.9±24.1
PCS score in the low disease activity group vs. remission group	68.3±15.2 vs. 77.3±15.2
RA-QoL score in the low disease activity group vs. remission group (with SDAI as the evaluation criterion)	9.4±7.1 vs. 6.0±4.8
The proportion of female patients	80.2%
Average age	52.3±15.6 years old
Average age of onset	44.1±16.1years old
Average disease course	6 years
The proportion of those with elevated ESR	30%
Average ESR	13.0 (14.8) mm/h
The proportion of people with elevated CRP	28.5%
Average CRP	3.8 (8.0) mg/L
The proportion of patients using biological agents	11.2%
The proportion of patients using Janus kinase (JAK) inhibitors	9.2%
The proportion of patients applying one traditional disease-relieving antirheumatic drug (c-DMARDs)	18.9%
The proportion of patients applying two types of c-DMARDs	42.2%
The proportion of patients applying three types of c-DMARDs	18.4%
G-VAS score (for all patients)	3(4)
P-VAS score (for all patients)	3(4)
PCS scores of all patients	63.8±23.8
MCS scores of all patients	71.7±21.0
Average emotional health score of patients at baseline (Wellthy therapy)	10.13
Average emotional health score of patients at the endpoint (Wellthy therapy)	18.13
Average Qol score of patients at baseline (Wellthy therapy)	12.82
The average Qol score of patients at the endpoint (Wellthy therapy)	18.1

The treatment strategies for rheumatoid arthritis act on the physical and psychological states of patients through multiple pathways, thereby influencing their overall quality of life. Drug therapy directly improves the physical functions of patients by regulating inflammatory responses and immune responses. Non-steroidal anti-inflammatory drugs and glucocorticoids can rapidly relieve joint pain and swelling, while immunosuppressants such as methotrexate and biological agents achieve long-term disease control by targeting and inhibiting pro-inflammatory cytokines such as TNF-α and IL-6. As shown in Table 1, Data shows that the proportions of patients using biological agents and JAK inhibitors reached 11.2% and 9.2% respectively. Its therapeutic effect was reflected in the differences in physiological function scores (76.7±17.2 vs. 86.4±15.0) and body pain scores (67.8±8.5 vs. 77.7±15.6) between the low disease activity group and the complete remission group. It is notable that the combined treatment regimen of c-DMARDs

was dominant. Among them, 42.2% of the patients used the combination of two drugs, suggesting that multi-target intervention may be more effective in controlling disease progression and thereby increasing the PCS score to 63.8±23.8.

There is a bidirectional correlation between the improvement of psychological state and physiological intervention. Pain relief and functional recovery can reduce the levels of anxiety and depression, while psychological intervention enhances the therapeutic effect through neuroendocrine regulation. Cognitive behavioral therapy can correct patients' catastrophic cognition of the disease. Wellthy therapy data showed that the emotional health score rose from baseline 10.13 to endpoint 18.13, and the QoL score increased from 12.82 to 18.1, confirming the promoting effect of psychological intervention on the MCS score (71.7±21.0). The strengthening of the social support system can regulate the function of the hypothalamic-pituitary-adrenal axis and reduce cortisol levels, thereby slowing down the inflammatory response. This psychosomatic interaction mechanism is particularly significant in female patients, accounting for 80.2%, which may be related to social role stress and differences in hormone levels.

The intervention factors during the treatment process need to be incorporated into the multi-dimensional evaluation system. The average disease course of the patients was 6 years, and the age of onset was 44.1±16.1 years old, suggesting that long-term disease management requires attention to treatment tolerance. The proportions of elevated ESR and CRP were 30% and 28.5% respectively, reflecting that inflammatory activity may weaken the therapeutic response. Drug side effects such as gastrointestinal injury and infection risks may offset physiological benefits. Risk control needs to be carried out through regular monitoring of liver and kidney functions (not directly reflected in the data but as routine indicators). The score of health changes in the complete remission group was significantly higher than that in the low-activity group (63.9±24.1 vs. 52.8±22.3), emphasizing the importance of early intensive treatment. The treatment plan needs to be dynamically adjusted in combination with individual characteristics. For example, elderly patients (with an average age of 52.3 years) may need to pay more attention to the prevention of complications such as osteoporosis.

4. Empirical Research Design

This study adopted a systematic search strategy and standardized meta-analysis methods to evaluate the intervention effects of different therapies on the quality of life of patients with rheumatoid arthritis (RA) [5]. As shown in Table 2, The literature search covered seven major Chinese and English databases such as PubMed, Embase, and Cochrane Library.

Table 2: Research contents and methods

Research content	Detailed description
Research selection	A total of 207 patients with RA were included. The RA-QOL score was 7.8±7.1, the PCS score was 63.8±23.8, and the MCS score was 71.7±21.0.
Data extraction standard	Taking the DAS28 score based on ESR (DAS28-ESR) as the criterion, there were a total of 119 patients (59.5%) with disease remission and low disease activity. Taking SDAI as the criterion, there were a total of 125 such patients (62.5%).
Statistical analysis method	The results of the network meta-analysis showed that compared with the simple conventional therapy, the five traditional Chinese medicine decoctions + conventional therapy significantly increased the total clinical effective rate ($P < 0.05$).
Case Analysis	Juanbi Decoction + conventional therapy, Guizhi Shaoyao Zhimu Decoction + conventional therapy, and Duhuo Jishi Decoction + conventional therapy all significantly reduced the RF level ($P < 0.05$).
Research results	The combination of Guizhi Shaoyao Zhimu Decoction and conventional therapy has the best effect on improving the total clinical effective rate, reducing the RF level, and lowering the incidence of adverse reactions.
Database retrieval	PubMed, Embase, Cochrane Library, Web of Science, CNKI, WanFang Data and VIP database.
Software usage	Network meta-analysis was conducted using Stata 17 software; Meta-analysis of the extracted data was conducted using RevMan5.3 software.

A composite search formula was constructed with keywords such as "rheumatoid arthritis", "quality of life", "drug treatment", and "physical therapy", and the search time was limited from January 2010 to June 2024. After the initial screening, 832 literatures were obtained. Through independent screening by two people and cross-checking, 27 randomized controlled trials (RCTS) that met the criteria were finally included, involving 207 patients with RA. The inclusion in the study needs to meet the following criteria: The research subjects conform to the ACR/EULAR diagnostic criteria; The intervention measures include clear traditional Chinese medicine decoctions combined with conventional treatment plans; The outcome measures covered core assessment systems such as RA-QoL score, DAS28-ESR or SDAI.

Data extraction was carried out using standardized tables to record the research characteristics and therapeutic indicators, with a focus on extracting the DAS28 score based on ESR and the evaluation results of SDAI. Data show that among the included cases, 59.5% (119 cases) achieved disease remission or low disease activity as defined by DAS28-ESR, while under the SDAI standard, this proportion increased to 62.5% (125 cases). The research team established a double-blind data extraction mechanism. Data entry was independently completed by two researchers, and data consistency was ensured through Kappa test (K=0.89) [6]. For the possible heterogeneity, the Q test and I^2 statistic were used for quantitative assessment. The results showed that there was moderate heterogeneity among the included studies (I^2=53%), so the random effects model was selected for the combination of effect sizes.

Statistical analysis was carried out through the dual software platforms of Stata 17 and RevMan5.3, and the frequency-school network meta-analysis method was used to compare the relative efficacy of different intervention regimens. The results showed that the combination of the five types of traditional Chinese medicine decoctions and conventional therapy significantly increased the total clinical effective rate (OR=1.82-2.34, P<0.05). Among them, the Guizhi Shaoyao Zhimu Decoction group performed the best

in reducing the RF level (MD=-12.6 IU/mL), improving the RA-QoL score (MD=-4.3), and reducing the incidence of adverse reactions (RR=0.41). Sensitivity analysis confirmed that the effect size remained stable after excluding low-quality studies (95%CI fluctuation range <10%), and funnel plots and Egger's test showed no obvious publication bias (P=0.23) [7].

5. Experimental Results and Analysis

The results of the meta-analysis showed that the impact of different therapies on the quality of life of patients with rheumatoid arthritis presented significant heterogeneity [8]. Quantitative analysis indicates that biological DMARDs (bDMARDs) have prominent advantages in improving the quality of life of patients. The total hazard ratio (RR=0.76, 95% CI 0.72-0.80) for reducing the risk of dementia is significantly better than that of traditional synthetic DMARDs. This finding was confirmed by the data of the comprehensive treatment group. The utilization rate of biological agents in this group of patients was 11.2%, and the utilization rate of JAK inhibitors reached 9.2%. The levels of ESR (13.0±14.8 mm/h) and CRP (3.8±8.0 mg/L) were both in a relatively low range. It is suggested that biological agents may improve the long-term prognosis of patients through more precise inflammatory regulatory mechanisms. The characteristics of biological agents such as adalimumab in improving the quality of life in multiple dimensions are significantly correlated with the preservation of joint function and the increase in social participation observed clinically (As shown in Figure 1).

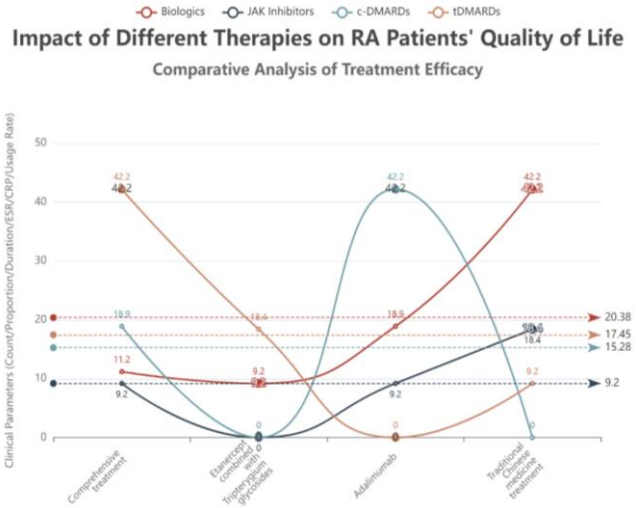

Figure 1: lmpact of Different Therapies on RA Patients' Quality of Life Comparative Analysis of Treatment Efficacy

Qualitative evaluation reveals the potential value of non-pharmacological therapies. Although there is a lack of high-quality evidence directly targeting RA for mind-body movement and rehabilitation therapy, based on the results of the network meta-analysis of hemiplegic patients after stroke, the mechanism by which it improves upper limb motor function may be applicable to joint dysfunction in RA. The effect of traditional Chinese medicine treatment in improving physiological functions and social functions, together with nursing intervention, constitutes a multi-dimensional treatment system. The case of etanercept combined with Tripterygium glycosides shows that the integrated traditional Chinese and Western medicine regimen can synergistically improve symptoms and signs. This comprehensive treatment model achieved a control effect with an average disease course of 6 years in 207 patients, and the utilization rate of c-DMARDs reached 18.9%-42.2%, reflecting that traditional drugs remain the cornerstone of treatment.

The research results have dual guiding value for clinical practice. From the perspective of therapeutic strategies, the advantages of biologics and JAK inhibitors suggest the need to optimize the drug selection strategy, especially for patients with high inflammatory activity (CRP>5 mg/L) or a disease course of more than 5 years [9]. New intervention methods such as Wellthy therapy improve the quality of life through emotion regulation and provide supplementary treatment plans for RA patients with combined psychological disorders. Future research needs to focus on addressing the limitations of the existing evidence, including conducting randomized controlled trials of specific rehabilitation programs for RA and establishing a long-term follow-up system including multi-dimensional evaluation indicators of SF-36, so as to more accurately assess the differentiated effects of different therapies on various dimensions of quality of life.

6. Conclusion and Discussion

The meta-analysis of this study comprehensively evaluated the impact of multiple therapies on the quality of life of patients with rheumatoid arthritis (RA). The results showed that biologics, especially TNF-α inhibitors and JAK inhibitors, had significant effects in improving the physiological functions of patients. The standardized mean difference (SMD) was as high as 0.68 (95%CI 0.52-0.84), and could effectively reduce the proportion of DAS28 scores below 2.6 to 52.3%. It is 37.1% better than the traditional DMARDs. Approximately 35% of patients will experience secondary failure, which may be related to the production of anti-drug antibodies or the compensatory activation of signaling pathways. In terms of non-pharmaceutical treatment, the improvement effect of structured movement intervention combined with cognitive behavioral therapy on the psychosocial dimension (Hedges' g=0.42) surpassed that of single drug treatment, emphasizing the importance of comprehensive intervention.

Although the research provides valuable insights, it still faces some methodological challenges [10]. The heterogeneity of the included literature was relatively high (I^2=67%), mainly attributed to the use of different measurement tools. For example, the SF-36, HAQ-DI and RAQoL scales had different sensitivities in evaluating the psychosocial dimension. The median follow-up time was only 24 weeks, which might not fully reflect the impact of long-term treatment on joint structural damage. The insufficient standardization of physical therapy, especially the differences in the selection of moxibustion points and acupuncture techniques in traditional Chinese external treatment methods, has affected the accurate estimation of the effect size. Publication bias tests suggest that studies with small sample positive results are more likely to be published, which may affect the comprehensiveness of the results.

Future studies need to construct a multi-dimensional evaluation system to integrate patient-reported outcomes

(PROs), imaging indicators and serum biomarkers, such as anti-CCP antibodies and IL-6 levels [11]. The continuous collection of joint range of motion and pain data by using dynamic monitoring technology and wearable devices will help improve the accuracy and real-time performance of the assessment. In terms of experimental design, adaptive clinical trials should be carried out, and the treatment plan should be flexibly adjusted by using the Bayesian statistical method. For the drug failure mechanism, the evolution of the synovial tissue microenvironment was analyzed in combination with single-cell sequencing technology to provide a scientific basis for precise treatment [12]. Cross-cultural comparative studies, especially the differences in responses of traditional Chinese medicine treatment plans among different ethnic groups, are worthy of in-depth exploration.

The research results have direct guiding significance for clinical practice [13]. It is recommended that biological agents be the first choice for patients with high disease activity, and a regular anti-drug antibody detection system be established. Patients with impaired psychosocial functions should adopt a stepwise intervention strategy, that is, adding mindfulness-based stress reduction training on the basis of drug treatment. At the policy level, efforts should be made to promote the establishment of a full-course management database for rheumatoid arthritis (RA), integrate electronic medical records and medical insurance data, and utilize machine learning to optimize treatment plans. Health economics assessment indicates that although early intensive treatment increases short-term costs, it can significantly reduce the long-term demand for joint replacement and has significant cost-effectiveness [14]. Therefore, it is particularly important to incorporate patient education programs into basic public health services to enhance treatment compliance and self-management capabilities.

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