INPLASY

Efficacy Comparison of Traditional Chinese Medicine in Treating Rheumatoid Arthritis from the Spleen: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 April 2025 and was last updated on 29 April 2025.

INTRODUCTION

Review question / Objective P: Adults with rheumatoid arthritis (RA). I: Spleen-strengthening TCM therapies. C: Conventional drugs or placebo. O: Clinical response rate, ACR20,DAY28, VAS, Duration of morning stiffness; RF/ESR/CRP/hs-CRP levels;Score of joint pain degree,Score of joint swelling degree; adverse events. S: RCTs. Objective: To compare efficacy/safety of spleen-strengthening TCM for RA and explore its role in combined therapy.

Condition being studied Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease characterized by synovial inflammation, which leads to joint pain, swelling, stiffness, and progressive joint destruction, and in severe cases, deformity and loss of function.The pathogenesis of RA involves the interaction of genetic, immune, and environmental factors. Abnormally activated immune cells (e.g. T-cells, B-cells, macrophages) trigger synovial hyperplasia and bone erosion through the release of pro-inflammatory cytokines (e.g. TNF-α, IL-6, IL-1β). The global prevalence is about 0.46%, with a significantly higher prevalence in women than in men (2-3 times), and a high prevalence age of 50-59 years.
Existing treatments include traditional synthetic disease-improving antirheumatic drugs (e.g., methotrexate), biologics (e.g., TNF-alpha inhibitors), and targeted drugs (e.g., JAK inhibitors), but long-term use may be accompanied by infections, hepatotoxicity, and other adverse effects. Based on the theory of “spleen deficiency causes paralysis”, Chinese medicine has demonstrated unique advantages in treating RA from the spleen perspective by strengthening the spleen and enhancing qi, regulating immune-inflammatory responses (e.g., lowering RF, CRP, etc.), and improving joint symptoms. In this study, we evaluated the efficacy and safety of the spleen-based treatment of RA with Chinese medicine

through meta-analysis system to provide evidence-based basis for clinical practice.

METHODS

Participant or population The systematic review and meta-analysis will focus on patients diagnosed with rheumatoid arthritis (RA), specifically those receiving Traditional Chinese Medicine (TCM) interventions targeting the spleen . Participants will include adults (age ≥18 years) of any gender or ethnicity, with active or stable RA, regardless of disease duration or prior treatments. Studies involving pediatric populations,the elderly population, non-RA diagnoses, or non-spleen-targeted TCM approaches will be excluded.
Key characteristics of participants:
Diagnosis: Confirmed RA per recognized criteria (e.g., ACR/EULAR).
Intervention Groups: Patients treated with TCM spleen-regulating therapies alone or combined with conventional Western drugs.
Control Groups: Patients receiving conventional Western drugs alone or placebo.
Outcomes: Clinical response rate, ACR20,DAY28, VAS, Duration of morning stiffness; RF/ESR/CRP/hs-CRP levels;Score of joint pain degree,Score of joint swelling degree; adverse events.
Rationale: This selection aligns with the review's objective to evaluate the comparative efficacy and safety of spleen-targeted TCM therapies for RA, ensuring homogeneity in the analyzed population.

Intervention The interventions of Chinese medicine in treating rheumatoid arthritis (RA) from the spleen theory mainly include the following programs:
Combined drug group: TCM spleen therapy combined with conventional western drugs .
Single-medication group: only using Chinese medicine to strengthen the spleen .
The specific formula composition is based on spleen-healthy and qi-benefiting TCM , with additions and subtractions according to the pattern of evidence (e.g., tonifying the kidneys, invigorating the blood, clearing heat, and dispelling wind, etc.). The intervention period ranged from 4 to 24 weeks.

Comparator Conventional drugs or placebo: Conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs)、Non-steroidal anti-inflammatory drugs (NSAIDs)、Biologics.

Study designs to be included This systematic review and meta-analysis will include randomized controlled trials (RCTs) that evaluate the comparative efficacy of Traditional Chinese Medicine (TCM) focusing on spleen-strengthening therapies for rheumatoid arthritis (RA). Only studies with a parallel-group design, published in Chinese or English, will be considered. Non-randomized studies, observational studies, case reports, and reviews will be excluded.

Eligibility criteria Additional inclusion criteria:
Intervention: Treatment groups must employ TCM therapies explicitly targeting spleen-strengthening .
Control: Control groups must use conventional Western drugs or placebo.
Outcomes: Studies must report at least one of the predefined efficacy outcomes (e.g., Clinical response rate, ACR20,DAY28, VAS, Duration of morning stiffness; RF/ESR/CRP/hs-CRP levels;Score of joint pain degree,Score of joint swelling degree) or safety outcomes (adverse event rates).
Duration: Minimum intervention duration of 4 weeks to ensure measurable therapeutic effects.
Additional exclusion criteria:
Non-spleen-focused TCM: Studies where spleen-strengthening is not the primary therapeutic principle .
Incomplete data: Studies lacking key data for meta-analysis (e.g., missing standard deviations, unreported baseline characteristics).
Studies with drug intervention duration of less than 1 month;
Dissertations, reports, conference abstracts, and non-peer-reviewed literature.

Information sources China National Knowledge Infrastructure、Wanfang Data、VIP Information、Chinese Biomedical Literature Database、PubMed、Embase、Cochrane library、Web of Science.

Main outcome(s) This systematic review and meta-analysis evaluated the comparative efficacy of Traditional Chinese Medicine (TCM) focusing on spleen-strengthening therapies for rheumatoid arthritis (RA). The outcomes included clinical total effectiveness rate , ACR20 response , DAY28 score, VAS score , morning stiffness duration, and inflammatory markers (RF, ESR, CRP, hs-CRP), joint pain/swelling scores and adverse events .
Key Details:
Timing: Outcomes assessed at intervals from 4 weeks to 24 weeks.
Effect Measures: Risk ratios (RR), mean differences (MD) with 95% CIs, using random/fixed-effects models per heterogeneity (I^2).
Clinical Relevance: Demonstrates TCM's role in RA management, aligning with "spleen deficiency leading to Bi syndrome" theory.

Quality assessment / Risk of bias analysis The methodological quality of the included randomized controlled trials (RCTs) was assessed using the Cochrane Risk of Bias Tool (version 5.1.0).

Strategy of data synthesis Data synthesis was performed using Review Manager 5.2:
Effect measures:
Dichotomous outcomes were pooled as risk ratios (RR) with 95% confidence intervals (CI).
Continuous outcomes were analyzed as mean differences (MD) or standardized mean differences (SMD) for inconsistent scales.
Heterogeneity:
Assessed via I^2 statistic and χ^2 test ($P < 0.10$ indicated significance).
Fixed-effect models were used if $I^2 \leq 50\%$; otherwise, random-effects models were applied .
Sensitivity analysis: Excluding high-risk bias studies confirmed robustness.
Subgroup analysis: Stratified by intervention type (TCM-alone vs. TCM + Western medicine) to explore heterogeneity.
Publication bias: Funnel plots were generated for outcomes with ≥10 studies.

Subgroup analysis Subgroup analyses were conducted to address clinical and methodological heterogeneity: Patients treated with TCM spleen-regulating therapiesalone or combined with conventional Western drugs.

Sensitivity analysis Sensitivity analysis will be conducted to assess the robustness of the meta-analysis results by:
Sequential Exclusion of Individual Studies: Removing one study at a time to evaluate its impact on pooled effect sizes and heterogeneity.
Subgroup Analysis by Study Quality: Comparing results from high-quality vs. low-quality studies (based on Cochrane risk-of-bias assessment).
Subgroup Analysis by Intervention Type: Separating studies into "combination therapy (TCM + conventional drugs)" and "TCM monotherapy" subgroups to examine consistency.
Alternative Statistical Models: Repeating analyses using fixed-effect models when random-effects models were initially applied (or vice versa) to check for model dependency.
Outcome Metric Consistency: Verifying results by switching between different effect measures (e.g., RR to OR for dichotomous outcomes) where applicable.
Exclusion of Outliers: Identifying and excluding studies with extreme effect sizes or high weight influence.
Rationale: This approach addresses potential biases from study quality, intervention heterogeneity, and statistical methods, ensuring conclusions are reliable. For example, if exclusion of a specific study significantly alters heterogeneity (I^2) or effect direction, results will be interpreted with caution.

Country(ies) involved China.

Keywords Traditional Chinese Medicine (TCM), spleen-oriented therapy, rheumatoid arthritis (RA), randomized controlled trial (RCT), meta-analysis, clinical efficacy, immune inflammation, safety, spleen-strengthening.

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