

# Research Progress on Traditional Chinese Medicine Intervention for Rheumatoid Arthritis Based on the Theory of Liver-Kidney Homology

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**Abstract:** Rheumatoid arthritis (RA) is an autoimmune disease characterized by joint erosion and destruction, protracted course, and high disability rate, which belongs to the typical categories of Bi syndrome and Lijie disease in traditional Chinese medicine (TCM). As the core framework for TCM syndrome differentiation of RA, the theory of Liver-Kidney Homology constructs the pathological correlation between liver-kidney function and the onset and progression of RA from three dimensions: essence-blood homology, mutual regulation of storage and drainage, and mutual nourishment of yin and yang, providing a core theoretical framework for TCM syndrome differentiation and intervention. Based on more than 70 literatures, this paper systematically reviews the connotation of the theory of Liver-Kidney Homology and its pathological association with RA, summarizes clinical evidence of different regimens from three intervention approaches: TCM compound prescriptions, acupuncture-moxibustion external therapy, and integrated traditional Chinese and Western medicine, analyzes their mechanisms of action, combines the research limitations mentioned in the literatures, and proposes future directions, so as to provide evidence-based support for the standardized TCM diagnosis and treatment of RA.

**Keywords:** Rheumatoid Arthritis, Liver-Kidney Homology, TCM Intervention, Integrated Traditional Chinese and Western Medicine, Literature Review.

## 1. Introduction

Rheumatoid arthritis (RA) mainly occurs in middle-aged and elderly people, with clinical manifestations of symmetrical joint swelling and pain, morning stiffness, and deformity. With the progression of the disease, it can involve multiple systems such as the lung and thyroid gland, and the disability rate increases significantly with the duration of the disease [1]. Western medicine treatments mainly include glucocorticoids, nonsteroidal anti-inflammatory drugs, and biological inhibitors. Although these drugs can relieve symptoms, long-term and high-dose administration easily causes drug-induced diseases. TCM has a long history of understanding RA. By sorting out literatures in the past 20 years, it is found that liver-kidney insufficiency is one of the core etiological and pathogenic factors of RA, which together with exogenous wind-cold-dampness-heat and intermingled phlegm and blood stasis constitutes the pathological characteristic of root deficiency and branch excess. In recent years, TCM intervention methods based on the theory of Liver-Kidney Homology have shown the advantages of toxicity attenuation and efficacy enhancement in the treatment of RA, and relevant studies have formed a multi-dimensional evidence system. This paper systematically reviews these advances combined with specific literatures.

## 2. Connotation of the Theory of Liver-Kidney Homology and Its Pathological Correlation with RA Onset

### 2.1 Core Essence of the Theory of Liver-Kidney Homology

The theoretical system of Liver-Kidney Homology (also

known as Yigui Homology) originated from Huangdi Neijing and was improved by physicians such as Zhang Zhongjing and Zhu Danxi. Its core includes three aspects: First, essence-blood homology: the kidney stores congenital essence, and the liver stores acquired blood; essence can transform into blood, and blood can generate essence. Suwen · Tiaojing Lun points out that “Qi and blood prefer warmth and dislike cold; when cold, they stagnate and fail to flow; when warm, they disperse and flow away”, and the two jointly nourish tendons, bones and joints [2]. Second, mutual regulation of storage and drainage: the kidney governs storage to consolidate essence and blood, and the liver governs drainage to regulate qi and blood circulation. Failure of renal storage leads to essence depletion, and dysfunction of hepatic drainage causes blood stasis, and imbalance between the two easily produces pathological products [3]. Third, mutual nourishment of yin and yang: kidney yin is the root of yin fluid in the body, and liver yin relies on the nourishment of kidney yin. Sufficient kidney yin prevents hyperactivity of liver yang; conversely, kidney yin deficiency leads to liver yin insufficiency, and deficient fire scorches tendons and vessels [4].

Physicians such as Zhang Linying et al. [5] further pointed out that the genetic predisposition of RA is related to “the kidney governing congenital endowment”, while impaired joint flexion and extension is directly related to “the liver governing tendons and fascia”, confirming the synergistic maintenance effect of the liver and kidney on joints in physiological functions.

### 2.2 Pathological Correlation with RA Onset

TCM holds that the pathogenesis of RA is essentially root deficiency and branch excess, with liver-kidney deficiency as

the root and excess pathogenic obstruction as the branch. Moreover, concurrent liver-kidney disease can accelerate disease progression, which has been confirmed by multiple studies in literatures from different perspectives:

### 2.2.1 Liver-kidney deficiency as the internal cause of onset

Insufficient congenital endowment, aging-related debility, or prolonged illness consumption can lead to deficiency of liver-kidney essence and blood. Liu Xiaoning et al. [6] pointed out through clinical observation that RA of liver-kidney insufficiency type is mostly in remission stage, but the risk of joint destruction is still higher than that of other syndromes, because “insufficient kidney essence fails to nourish bone marrow, and deficient liver blood cannot moisten tendons and fascia”, resulting in decreased resistance of tendons and bones to pathogens and susceptibility to wind-cold-dampness invasion, which is consistent with the physiological characteristic of “kidney essence declining with age”. Li Yuling et al. [7] supplemented theoretically and proposed a pathogenesis chain of “liver-kidney deficiency as the root cause of RA onset, exogenous pathogenic invasion as the inducement, and intermingled phlegm and blood stasis as pathological products”, emphasizing that liver-kidney deficiency runs through the whole course of RA and is the key internal factor of joint deformity and bone destruction.

### 2.2.2 Excess pathogenic obstruction as the external cause of onset

On the pathological basis of liver-kidney deficiency, excess pathogenic obstruction is an important branch syndrome promoting RA progression. Liver-kidney deficiency leads to unsmooth circulation of qi and blood, endogenous damp-turbidity and blood stasis, superimposed with exogenous invasion of wind-cold-dampness pathogens (mixed invasion of three pathogens), forming “pain due to obstruction”. Based on the theory of “the kidney governing bones and the liver governing tendons”, physicians such as Zhang Liping pointed out that the essence of “joint cartilage and bone destruction” in RA progression is “kidney essence failing to generate bones and liver blood failing to nourish tendons”, and exogenous pathogenic invasion will further block meridians, aggravate qi and blood circulation disorder, form a vicious circle of “deficiency-pathogen-stasis”, and eventually lead to joint deformity.

### 2.2.3 Concurrent liver-kidney disease accelerates disease progression

RA has a protracted course; “prolonged illness involves the kidney” and “chronic pain enters the collaterals”. Dysfunction of the liver in drainage leads to qi stagnation and blood stasis, further consuming kidney essence; kidney yin deficiency results in liver yin insufficiency, and deficient fire burns tendons, eventually leading to joint stiffness and deformity. Combined with Jingui Yaolue, Zhan Jingyi et al. [8] proposed that early RA belongs to “damp Bi” (disease location superficial, healthy qi not declined), and if not treated in time, it will develop into “Lijie” (disease location involving the liver and kidney, tendons and bones damaged), which is highly consistent with the pathological process of “concurrent liver-kidney disease”. The five-zang Bi theory proposed by

Xu Run et al. [9] also pointed out that the root cause of multi-system involvement (such as interstitial lung disease, vasculitis) in RA is “liver-kidney deficiency and internal transmission of pathogenic toxins”, further confirming the core role of liver-kidney deficiency in RA progression.

## 3. TCM Intervention Strategies and Clinical Evidence Based on the Theory of Liver-Kidney Homology

### 3.1 TCM Compound Prescriptions: Focusing on Tonifying Liver-Kidney and Dredging Collaterals to Expel Pathogens

Oral administration of TCM is the main approach for RA intervention based on Liver-Kidney Homology, following the principle of “simultaneous regulation of essence and blood, expelling pathogens without injuring healthy qi”, covering modified classic prescriptions, self-designed prescriptions and Chinese patent medicines. Different regimens target different complicated syndromes of liver-kidney deficiency (such as cold-dampness, damp-heat, blood stasis), with abundant clinical evidence:

#### 3.1.1 Classic Prescription: Centered on Duhuo Jisheng Decoction

Duhuo Jisheng Decoction, originated from Beiji Qianjin Yaofang, takes “dispelling wind-dampness, relieving Bi pain, tonifying liver-kidney, and supplementing qi and blood” as the core, and is the core prescription for clinical treatment of RA of liver-kidney deficiency type. Wang Haoyang et al. [10] randomly divided 60 RA patients of liver-kidney deficiency type (with serum 25(OH)D < 30 ng/mL) into two groups. The control group was treated with methotrexate + folic acid + alfacalcidol, and the treatment group was additionally treated with modified Duhuo Jisheng Decoction (15g of *Angelicae Pubescentis Radix*, 12g of *Taxilli Herba*, 10g of *Eucommiae Cortex*, etc.). After 12 weeks, the total effective rate of the treatment group (93.33%) was significantly higher than that of the control group (76.77%), and the improvement of joint tenderness count (3.2±1.1 vs 5.6±1.5), morning stiffness time (28.5±8.3 min vs 45.2±10.1 min) and ESR (22.1±5.4 mm/h vs 35.6±6.7 mm/h) was better (P<0.05), suggesting that it can improve efficacy by tonifying liver-kidney and regulating immunity.

Through systematic review of literatures in the past 15 years, Tang Rui et al. [11] found that Duhuo Jisheng Decoction can inhibit synovocyte proliferation and release of inflammatory factors (TNF- $\alpha$ , IL-6) by regulating multiple signaling pathways such as MAPK, WNT, NF- $\kappa$ B, and PI3K/Akt, and improve immune function of RA patients, with a significantly lower incidence of adverse drug reactions than pure Western medicine treatment.

#### 3.1.2 Application of Self-designed Prescriptions and Chinese Patent Medicines

##### Bushen Qiangjin Capsules

Bushen Qiangjin Capsules are an empirical prescription of Professor Xu Xuemeng, composed of *Eucommiae Cortex*,

Psoraleae Fructus, Drynariae Rhizoma, Rehmanniae Radix Praeparata, Sanguis Draxonis, Scorpio, etc., with the efficacy of tonifying kidney to strengthen bones, activating blood circulation to dredge collaterals [12]. Li Chunyi et al. [13] divided 100 RA patients of liver-kidney insufficiency type into two groups. The Bushen Qiangjin group was treated with methotrexate + Bushen Qiangjin Capsules, and the placebo group with methotrexate + placebo. After 6 months, the total effective rate of the Bushen Qiangjin group (93.48%) was higher than that of the placebo group (78.72%), and the improvement of serum NLRP3 level and synovial thickness was better ( $P<0.05$ ), suggesting that it can inhibit inflammasome activation and delay synovial lesions.

### Compound Qiqiong Prescription

This prescription [14] is an empirical prescription used for many years in the Department of Integrated Traditional Chinese and Western Medicine, General Hospital of Central Theater Command of the Chinese People's Liberation Army for the treatment of RA. Jiang Meihua et al. [15] retrospectively analyzed 105 RA patients of liver-kidney yin deficiency type. The observation group was treated with Compound Qiqiong Prescription combined with methotrexate. After 3 months, the total effective rate (92.45%) was higher than that of the control group (75.00%) ( $P<0.05$ ); the levels of IgG, IgM, RF, TNF- $\alpha$ , IL-8 and joint tenderness/swelling count in the observation group were better improved without additional adverse reactions.

### Wangbi Tablets

Gao Yu et al. [16] divided 120 RA patients of liver-kidney insufficiency type into two groups. The treatment group was treated with Wangbi Tablets combined with Yuxuebi Capsules, and the control group with Tripterygii Wilfordii Polyglycosidum Tablets. After 6 months, the total effective rate of the treatment group (84.7%) was higher than that of the control group (72.4%) ( $P<0.05$ ), and the improvement of joint tenderness/swelling count and DAS28 score was more significant.

## 3.2 Acupuncture-Moxibustion External Therapy: Focusing on Regulating and Tonifying Liver-Kidney

### 3.2.1 Warm Acupuncture

Lv Jianmin et al. [17] divided 80 RA patients into two groups. The control group was treated with methotrexate + meloxicam, and the observation group with warm acupuncture (acupoints: Shenshu, Zusanli, Ashi points) + Duhuo Jisheng Decoction. After 1 month, DAS28 score and joint tenderness count in the observation group were lower than those in the control group ( $P<0.05$ ), and serum IL-17 level decreased and Tregs level increased ( $P<0.05$ ).

### 3.2.2 Electroacupuncture

Jia Cheng et al. [18] selected 50 RA patients of liver-kidney yin deficiency type and treated them with electroacupuncture (acupoints: Ganshu, Shenshu, Taixi) + Compound Qiqiong Granules. After 12 weeks, the total effective rate was 90.00%, and serum NLRP3 level and MMP-3 level decreased

significantly ( $P<0.05$ ).

### 3.2.3 Moxibustion and Acupoint Application

Liu Zhichao et al. [19] showed that Qianghuo Dihuang Granules combined with acupoint application in the treatment of RA of liver-kidney yin deficiency and cold-dampness obstruction type, the ACR20 response rate of the treatment group (50.0%) was higher than that of the control group (28.6%) ( $P<0.05$ ).

### 3.2.4 Midnight-Noon Ebb-Flow Acupuncture

Yin Juan et al. [20] divided 90 RA patients of liver-kidney deficiency type into two groups. The study group was treated with Midnight-Noon Ebb-Flow Acupuncture + chronic disease management. After 3 months, morning stiffness time and 20m walking time in the study group were shorter than those in the control group ( $P<0.05$ ), and serum  $Ca^{2+}$  level increased significantly ( $P<0.05$ ).

## 3.3 Integrated Traditional Chinese and Western Medicine

Du Dingyi [21] divided 96 RA patients of liver-kidney deficiency type into two groups. The control group was treated with methotrexate + hydroxychloroquine, and the experimental group was additionally treated with Duhuo Jisheng Decoction. After 12 weeks, VAS score and ESR in the experimental group were lower than those in the control group ( $P<0.05$ ), and the total effective rate increased significantly ( $P<0.05$ ).

## 4. Mechanism Research of TCM Intervention for RA Based on Liver-Kidney Homology

### 4.1 Regulating Immune and Inflammatory Responses

TCM intervention can multi-targetedly regulate the immune-inflammatory network of RA: Yang Juntao et al. [22] confirmed that Bushen Shujin Decoction can reduce the levels of IL-6 and RF in RA patients of kidney-yang deficiency type ( $P<0.05$ ); the warm acupuncture regimen of Lv Jianmin et al. can increase Tregs level and inhibit Th17 cell activation ( $P<0.05$ ).

### 4.2 Protecting Joint Structure and Delaying Bone Erosion

The moxibustion regimen of Zhang Min et al. [23] can increase serum  $Ca^{2+}$  level and enhance bone mineral density; Bushen Naqi Formula of Luo Qiming [24] can reduce the levels of MMP-1, MMP-3 and reduce cartilage destruction; Duhuo Jisheng Decoction of Wang Haoyang et al. [10] can up-regulate serum 25(OH)D level and promote osteoblast activity.

### 4.3 Improving Endocrine and Metabolic Status

Huanglian Ejiao Decoction regimen of Luo Xiaoguang et al. [25] can increase serum E2, HDL levels and improve sex hormone and lipid metabolism; Chen Wenjia et al. [26] found through transcriptome analysis that key target genes (such as NR3C1, ESR1) in RA patients of liver-kidney deficiency type are enriched in hormone regulation pathways.

## 5. Research Deficiencies and Future Prospects

### 5.1 Current Research Deficiencies

1) Inconsistent syndrome differentiation standards [28]: Existing studies lack unified norms for syndrome differentiation of RA of liver-kidney deficiency type.

2) Insufficient depth of mechanism research [26]: Most studies focus on a single pathway or indicator, lacking systematic explanation of the overall regulatory mechanism.

3) Limited quality of clinical research: Most clinical studies have small sample sizes, few multi-center, large-sample RCTs.

4) Insufficient preparations and popularity [29]: TCM is dominated by decoctions, leading to low patient compliance.

### 5.2 Future Research Directions

1) Standardize syndrome differentiation standards and formulate Guidelines for TCM Syndrome Differentiation of RA of Liver-Kidney Deficiency Type [28].

2) Deepen mechanism research using omics technologies [11].

3) Carry out high-quality multi-center, large-sample, long-term follow-up RCTs [28].

4) Develop convenient intervention regimens and home-based tools [29].

## 6. Conclusion

The theory of Liver-Kidney Homology profoundly reveals the pathogenesis essence of RA of liver-kidney deficiency as the root and excess pathogenic obstruction as the branch. A large number of clinical studies have confirmed that oral TCM, acupuncture-moxibustion external therapy, and integrated traditional Chinese and Western medicine regimens can significantly improve joint symptoms, reduce inflammatory indicators, delay bone erosion, and have better safety than pure Western medicine. With the standardization of research design and modernization of technical means, the value of the theory of Liver-Kidney Homology in the precise TCM treatment of RA will be further highlighted.

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