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Safety and Effectiveness of Traditional Chinese Medicine Compound in Treating Idiopathic Membranous Nephropathy Network Meta-analysis

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Abstract: ***Objective: To evaluate the clinical effectiveness and safety of different traditional Chinese medicine prescriptions combined with conventional western drugs to improve idiopathic membranous nephropathy (IMN) based on the Chinese medicine evidence system. METHODS: A computerized search of eight databases, including China Knowledge Network (CNKI), Wanfang, PubMed, and Web of Science, was conducted to collect randomized controlled trials (RCTs) of TCM compound formulas combined with conventional western medicines for the treatment of IMN, with a search timeframe of the period from the establishment of the database to 2023 October. The quality of the included literature was evaluated using the Cochrane Risk of Bias Assessment Tool version 2.0 (RoB2.0), reticulated Meta-analysis was performed using Stata 18.0 software, and the area under the cumulative ranking curve was used to rank the clinical efficacy and safety of the six interventions, with the aim of providing an evidence-based basis for the rational clinical selection of prescriptions for treating patients with IMN. RESULTS: Thirty-five RCTs involving 6 interventions and containing 2518 IMN patients were finally included. CONCLUSION: Thirty-five papers involving 2518 patients were finally included in the literature. The effect of the formula of tonifying deficiency and eliminating stasis + conventional western medicine was significant in lowering 24-hour urine protein quantification (SUCRA: 95.3%) and total cholesterol level (SUCRA: 98.2%); the formula of tonifying deficiency, eliminating stasis and dispelling dampness + conventional western medicine (SUCRA: 71.2%) was more effective in increasing the total effective rate; and the formula of tonifying deficiency, eliminating stasis and purging heat and dispelling dampness + conventional Western medicine was effective in lowering blood creatinine (SUCRA: 80.4%) and increased serum albumin level (SUCRA: 72.9%), while the formula for tonifying deficiency and clearing heat and dampness and conventional western medicine was more effective in lowering M-type phospholipase A2 receptor antibody titer (SUCRA: 86.0%). In terms of safety, the adverse effects of the TCM compound formula combined with conventional western drugs were overall less than those of conventional western drugs alone. The overall quality of the included RCTs was low, and more rigorous, large-sample size RCTs and basic studies are needed to verify the clinical applicability.***

Keywords: Compound Chinese medicine; Idiopathic membranous nephropathy; Mesh Meta-analysis; 24hUTP; ALB; PLA2R; SCr; TC.

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1. Introduction

Membranous nephropathy (MN) is one of the most common causes of nephrotic syndrome, of which the unknown cause is called idiopathic membranous nephropathy (IMN), which is mainly characterised by the deposition of immune complexes in the subepithelial cells of the glomerular epithelial layer accompanied by a diffuse thickening of the glomerular basement membrane. The main characteristic. In the past decade, the incidence rate of IMN has been increasing year by year, up to 51.02% in some areas, and it has a tendency to exceed IgA nephropathy [1]. Although about 1/3 of patients with IMN go into spontaneous remission, in most cases the disease has a long course and complete cure is relatively difficult. Commonly used drugs include alkylating agents (cyclophosphamide), glucocorticoids, calcium-regulated neural phosphatase blockers (cyclosporine, tacrolimus), rituximab and other immunosuppressants to reduce urinary protein and protect renal function. However, long-term

use of these drugs may increase the risk of cancer, lead to electrolyte disorders, blood glucose abnormality, or damage to the liver and kidneys, and the price of some biologics is very high, which puts a certain degree of stress on the physical and mental health of patients with IMN. pressure on IMN patients both physically and mentally [2].

More and more studies have shown that traditional Chinese medicine can be used as a single alternative therapy or adjuvant therapy for IMN [3]. According to the recommendations of the Clinical Practice Guidelines for Traditional Chinese Medicine in Idiopathic Membranous Nephropathy (2021), low and intermediate-risk patients are recommended to combine the use of Chinese herbal medicine combinations or Chinese herbal medicine monomers on the basis of conventional immunosuppressive therapy, which can help to improve and prevent the patients' oedema, tiredness, secondary infections, thromboembolism, and many other clinical manifestations, and to improve the quality of survival [4]. Chinese medicine compound formulas are complicated and diverse, and the identification and treatment varies from person to person. Although the effects and efficacy of Chinese medicine compound formulas in combination with conventional western medicines have been reported in a large number of literatures, there is still a lack of direct comparisons between Chinese medicine compound formulas, as well as dosing regimens that can improve the clinical performance or specific indicators of patients with IMN. Therefore, in this study, the effects of Chinese medicine compound formulas combined with conventional western medicines were investigated through network Meta-analysis (NMA), and the results were presented in the following table [5], Different clinical indicators such as total clinical efficiency, 24 hours urinary protein excretion (24 hUTP), serum albumin (ALB), Anti Phospholipase A2 Receptor Antibody (PLA2RAb), serum creatinine (SCr), total cholesterol (TC), and total cholesterol (TC) were investigated in different Chinese herbal medicinal compound treatments. Receptor Antibody (PLA2RAb), serum creatinine (SCr), total cholesterol (TC) and other efficacies were compared and ranked horizontally, with the aim of arriving at the optimal formula of Chinese herbal medicine compounding, avoiding full-coverage and large cohort drug use by clinicians, and providing evidence-based medical evidence for the clinical treatment of IMN. The aim of this study is to provide evidence-based medical evidence for the clinical treatment of IMN.

2. Information and Methods

2.1 Study Registration

This study was registered in the International Prospective Registry for Systematic Evaluation database (PROSPERO) under the registration number CRD42023487080.

2.1.1 Study subjects

Patients with confirmed diagnosis of membranous nephropathy after renal puncture biopsy and excluding other secondary factors, race, gender and age are not limited [6].

2.1.2 Type of study

Randomised controlled trial (RCT) of TCM compounding for IMN (R conventional western medicine), language limited to Chinese or English.

2.1.3 Intervention

The control group used conventional western drugs, including conventional basic treatment (anticoagulation, diuretic, antihypertensive, protein-lowering, lipid-lowering, etc.) and IMN general regimen treatment, such as glucocorticoids, immunosuppressants (tacrolimus, cyclosporine, cyclophosphamide, mycophenolate mofetil, etc.), angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, biologics (rituximab) and so on. The experimental group used conventional western medicines in combination with Chinese herbal medicine compounding.

2.1.4 Outcome indicators

① Overall clinical effectiveness rate Refer to the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines 2021: complete clinical remission of IMN is defined as urinary protein <0.3g/d and serum albumin ≥3.5g/dL, partial remission is defined as ≥50% reduction in urinary protein and final urinary protein of

0.3-3.5 g/d. Overall effective rate = (number of cases in complete remission + number of cases in partial remission)/(total number of cases × 100%) [7]; ② 24hUTP; ③ ALB; ④ SCr; ⑤ PLAR2; ⑥ TC; ⑦ 不良反应.

2.2 Exclusion Criteria

Interventions that used TCM therapies other than TCM compounding; more than one type of TCM preparation; no control group, or poor trial design, or inappropriate statistical methods; studies with less than 8 weeks of clinical efficacy observation; self-control studies; literature with obvious errors in the data; literature with no access to the full text; and literature with less than 2 articles of the same type of intervention.

2.3 Search Strategy

Computer searches were performed on databases such as China Knowledge (CNKI), Wanfang (Wanfang), Vip (VIP), SinoMed, PubMed, EMbase, Cochrane Library, MEDLINE, Web of Science, and so on, to search for the literature from the establishment of the database to October 2023. The search was conducted using a combination of subject terms and free words, and the Chinese search terms included "idiopathic membranous nephropathy", "primary membranous nephropathy", "traditional Chinese medicine", "Chinese medicine", "Chinese medicine", "Chinese medicine", "Chinese medicine", "Chinese medicine", and "Chinese medicine". "Chinese medicine", "Chinese herbal medicine", "Chinese medicine", "randomised controlled", "randomised Randomised controlled" "Randomised clinical trial", etc. The search terms in English include "Glomerulonephropathy, Membranouss" "Idiopathic Membranous Glomerulonephritis" "Glomerulonephritides, Idiopathic Membranous" "Chinese medicinal herb" "traditional chinese medicine" "randomised clinical controlled trial" "conventional western medicine", etc.

2.4 Literature Screening and Data Extraction

Two researchers imported the results of literature search into Endnote X9 software, which removed duplicates and then further read the titles and abstracts, and screened them according to the inclusion and exclusion criteria. Excel software was used to extract information on authors, year of publication, sample size, mean age, interventions, duration of treatment, and outcome indicators. If there was disagreement it was discussed or adjudicated by a third researcher.

2.5 Methods for Evaluating the Quality of Literature

Two researchers followed the preset criteria to evaluate the quality of the included literature using the Cochrane Risk of Bias Assessment Tool version 2.0 (RoB2.0) separately, evaluating the 5 dimensions of bias: randomised methods, interventions, missing data (≤10% of the total number of cases), outcome measures and selective reporting[8].The results were categorised as low risk, high risk and uncertain risk, and any disagreements were discussed and resolved by negotiation or adjudicated by a third researcher.

2.6 Statistical Analyses

This study used Stata 18.0 software for statistical analysis, and relative risk (RR) was used for dichotomous variable effects, and weight mean difference (WMD) was used for continuous variable effects, and 95% credibility intervals (CI) were calculated respectively. The 95% confidence intervals (CI) were calculated separately. If there was good homogeneity among the studies, the analysis was performed using a random-effects model; if there was heterogeneity among the studies ($I2 > 50\%$ or $P < 0.05$), further subgroup analyses were performed. Network evidence maps for each outcome indicator were plotted sequentially, publication bias was assessed using a corrected-funnel plot, and rank probability plots were produced using the area of the curve under the Cumulative Ranking of Probabilities (Sur Face Under the Cumulative Ranking Curveweight mean difference, WMDSUCRA) to rank the clinical efficacy of different interventions. Corrected-comparison funnel plots were used to detect publication bias, which was verified using Egger's test, and if bias existed, the impact of bias on the results was assessed using the cut-and-patch method.

3. Results

3.1 Basic Characteristics of the Included Literature

According to the PICOS search strategy, the search was carried out in accordance with the search method of subject words + free words. The preliminary search obtained 1736 pieces of literature, and 35 pieces of literature were finally included, of which 33 were in Chinese [9-41], 2 in English [42,43]. The total sample size was 2518 cases, 1267 cases in the test group and 1251 cases in the control group. The interventions were divided into 5 categories: 5 articles of formulae for tonifying deficiency + conventional western medicine (X + conventional western medicine); 9 articles of formulae for tonifying deficiency and eliminating blood stasis + conventional western medicine (XY + conventional western medicine); 2 articles of formulae for tonifying deficiency and clearing heat and dispelling dampness + conventional western medicine (XRS + conventional western medicine); 11 articles of formulae for tonifying deficiency and eliminating blood stasis and dispelling dampness + conventional Western medicine (XYS + conventional Western medicine); and 8 articles of formulae for tonifying deficiency, eliminating blood stasis and clearing heat and dispelling dampness + conventional Western medicine (XRSY +). (XRSY + conventional western medicine) 8 articles [13,19,20,25,29,36,38,42]. The literature screening process is shown in Figure 1 and the basic characteristics of the included literature are shown in Table 1.

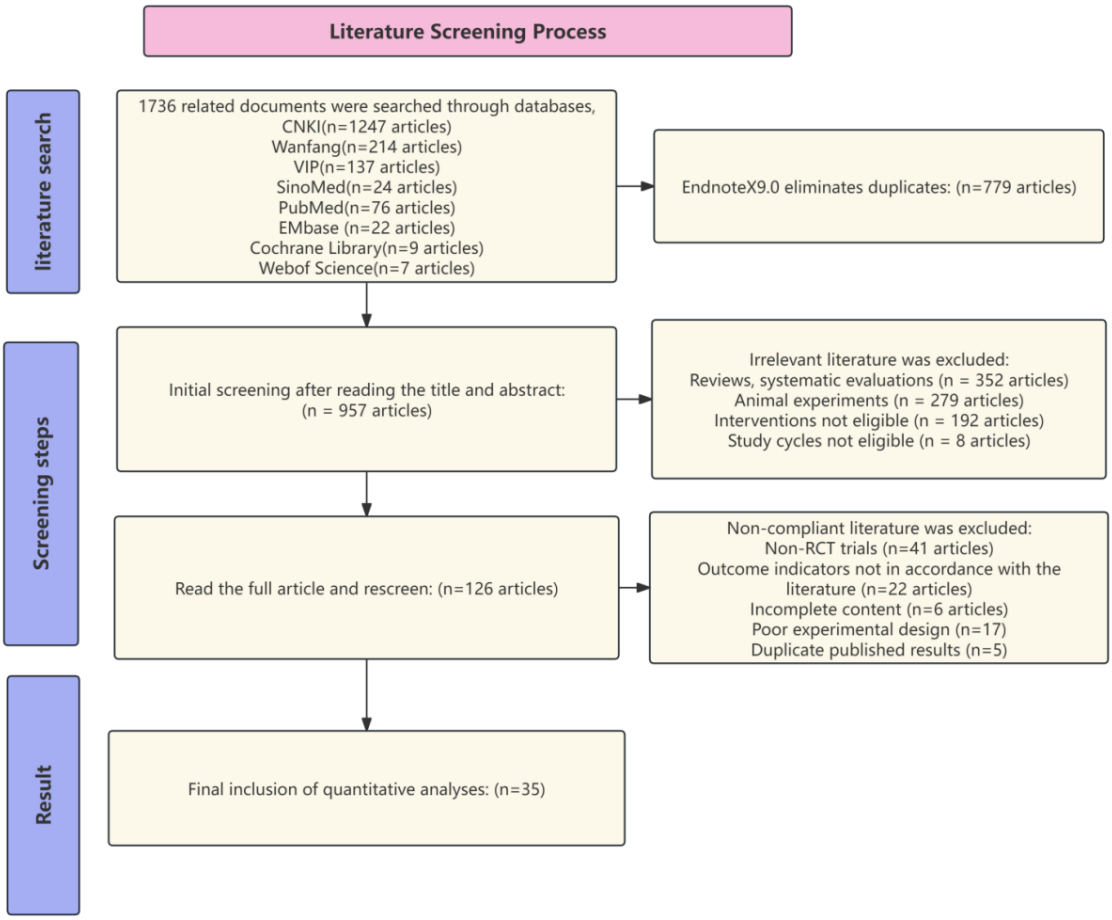

Figure 1: Article screening process

Table 1: Basic characteristics of included literature

Author/year	Sample size (male/female)/case		Mean age/(years)		Intervention	Sort	Course	Outcome indicator
	C	T	C	T				
Xing Yang 2023	28(21/7)	29(20/9)	53.96±9.24	54.66±10.06	Jiawei Zhenwu Tang + CT	X+CT	8 weeks	①②③⑤⑥⑦
Zhen Cai 2019	26(-)	32(-)	44.32±13.32	42.26±13.26	Radix Astragali Di Huang Tang + CT		24 weeks	①②③⑥
Lei Wang 2020	26(-)	28(-)	46.6±12.9	47.6±13.2	Radix Astragali Di Huang Tang + CT		24 weeks	①②③⑥
Chao Song 2020	30(22/8)	30(21/7)	47.90±11.43	45.33±9.97	Warming Yang and Lifting Water Formula +CT		3 months	①②③④⑤⑥⑦
Ling Huang 2023	33(17/16)	34(18/16)	51.48±7.31	52.41±6.41	Yiyuanjianzhong Formula+CT		9 months	①②③④⑤⑥⑦
Jieqi Zheng 2019	39(22/17)	38(20/18)	51.8±17.88	54.53±5.39	Zhen Wu Tang with Angelica Sinensis and Paeoniae Alba+CT	XY+CT	8 weeks	①②③④⑤⑥⑦

Xueyan Sun 2022	39(21/18)	42(22/20)	58.05±12.27	57.14±13.92	Benefiting Qi, Nourishing Kidney and Promoting Blood+CT		6 months	①②③④⑥⑦
Xin Feng 2021	36(20/16)	36(22/14)		-	Benefiting Qi and Eliminating Crimes+CT		6 months	6 months
Yating Zhang 2022	39(26/13)	39(26/13)	52.53+11.69	50.97+10.42	Radix Astragali Di Huang Tang +CT	Radix Astragali, Radix et Rhizoma Ginseng, Radix et Rhizoma Polygoni Multiflori+ CT	6 months	①②③④⑥⑦
Guojun Tang 2020	34(16/18)	33(18/15)		-	Qi Jishen combined with Taohong Siwu Decoction + CT		3 months	3 months
Chongxia Zhao 2022	43(31/12)	43(30/13)	51.24±3.26	51.12±3.21	Add flavour to tonify Yang and restore the five elements+CT		6 months	①②④⑥
Xue Li 2022	25(14/11)	25(18/7)	57.12±12.54	55.61±9.52	Invigorate Blood and Promote Water Formula + CT		6 months	①②③④⑤⑥⑦
Changan Chen 2022	28(17/11)	28(15/13)	58.54±8.34	62.11±9.60	Tonifying Qi and Benefiting Kidney Formula + CT		6 months	①②③⑥⑦
Jiajiao Zuo 2018	80(47/33)		Average age 48		Qiling Tongluo Prescription + CT		6 months	①②③④⑤⑦
Zhou Shi 2022	40(22/18)	40(25/15)	57.38±12.35	57.90±13.14	Benefiting Qi, Tonifying the Kidneys and Clearing the Profit Formula + CT	XSR+ CT	12 weeks	①②③④⑤⑥⑦
Jia Liu 2021	24(15/9)	28(18/10)	55.35±10.65	55.75±11.081	Strengthening the spleen, benefiting the kidneys, clearing heat and inducing dampness formula + CT		12 weeks	①②③⑥⑦
Yun Ma 2023	26(-)	27(-)	47.56±14.03	45.32±12.15	Warming Yang and Clearing Dampness Formula + CT		24 weeks	①②③④⑥⑦
Jie Li 2020	6038/22	60(35/25)	44.83±10.56	45.23±10.07	Wen Yang Dispels Dampness and Circulates Dampness Formula + CT		6 months	①②③④⑤⑥⑦
Yanan Zhang 2023	33(22/11)	34(23/11)	43.58±11.45	42.47±10.98	Wen Yang Dispels Dampness and Circulates Dampness Formula + CT		6 months	①②③④⑤⑥⑦
Qiang Liu 2019	39(-)	39(-)	17.70±6.71	19.22±7.45	Warming Yang, Promoting Blood and Lifting Water+CT		48 weeks	①②③④⑤⑥⑦
Zheng Zhang 2022	28(14/11)	25(13/12)	54.28±10.84	54.45±10.28	Jin Qi Benefit Kidney Formula+CT	XSY+ CT	6 months	①②③④⑤⑥⑦
Kexin Wang 2022	30(18/12)	30(17/13)	42.31±8.05	41.63±7.31	Ginseng Astragali and Dihuang Tang+CT		6 months	①②③④⑤⑥⑦
Jianjun Guo 2022	46(30/16)	46(26/20)	45.67±13.45	49.79±12.50	Strengthening the spleen and dispelling dampness+CT		3 months	①②③④⑥⑦
Meng Ji 2021	28(20/8)	30(18/12)	48.1±8.8	49±9.0	Kun Xian Capsule±CT		6 months	①②③⑦
Jie Liu 2022	30(18/12)	30(16/14)	48.59±4.63	49.14±4.76	Rhizoma Ligustici Tongluo Capsule+CT		6 months	①②③④⑥⑦
Wu 2022	42(29/13)	42(31/11)	8.50±1.60	8.26±1.71	Strengthening the Spleen, Dispelling Dampness and Hepatoconjugate Formula+CT		2 months	①②③④⑥⑦
Leilei He 2022	84(45/39)	84(47/37)	54.56±5.03	53.96±5.12	Kidney Yikang+CT		3 months	①⑥⑦
Genping Lei 2019	30(19/11)	29(19/10)	48.97±11.61	51.69±11.31	Astragalus Di-Fixing Kidney Tablet+CT		6 months	①②③④⑤⑥⑦
Huaxia Liu 2019	29(19/10)	29(17/12)	46.34±14.38	47.41±13.60	Tonifying the Kidneys, Resolving Blood Stasis and Clearing Drainage Formula + CT		6 months	①②③④⑤⑥⑦
Lina Qiao 2020	29(16/13)	30(18/12)	43.07±9.083	47.27±9.938	Tonifying Qi, Resolving Dampness and Clearing Drainage+CT		8 weeks	①②③④⑤⑥⑦
Jin Wu 2021	49(27/22)	49(26/23)	53.69±3.63	52.38±3.76	Radix Astragali and Radix Rehmanniae Formula+CT	XSRY+CT	6 months	①②③④⑤⑥
Rong Zhao 2021	22(16/6)	22(14/8)	50.07±14.17	50.37±11.99	Huangtu Yi Kidney Granules+CT		6 months	①②③④⑤⑥⑦
Gaohua Ping 2021	35(19/16)	35(20/15)	44.1±10.2	8.9±4.2	Clearing and Resolving Turbidities Capsule+CT		16 weeks	②③④
Yaping Guo 2021	42(12/30)	42(13/29)	46.96±8.63	48.21±7.57	Qi Di Tao Hirch Er Cicada Formula+CT		3 months	①②③⑤
Lv W2021	42(38/4)	42(30/12)	61.56±7.11	62.01±6.89	Nephritis Rehabilitation Tablets+CT		12 weeks	①②③⑦

Notes:T. Test group; C. Control group; -. Conventional Western medicine; control group interventions were all conventional Western medicine; ① total effective rate; ② 24hUTP; ③ ALB; ④ Scr; ⑤ TC; ⑥ PLAR2; ⑦ adverse reactions; ⑧ X + CT. Regular formulae and western herbal remedies for tonifying deficiency, eliminating stasis and dispelling dampness; XRSY+CT.

3.2 Evaluation of the Quality of the Literature

Evaluation of randomisation methods included interventions, error in outcome data (≤10% of total cases), outcome measures, selective reporting and methodological aspects of random sequence generation 25 RCTs [9-13,15,16,18,20-23,25,26,28,30-33,35,36,39-41,43] 1 article by random number table method [14] Low risk based on random allocation; 8 articles[19,24,27,29,34,37,38,42]Mention of the word random only, 1 article [17] Grouping according to chronological order of admission was risk uncertain. For interventions and outcome measures, all studies did not mention the allocation of concealment programmes and the use of blinding by the investigator, subjects or outcome measures, as risk uncertain. For completeness of outcome data, 17 [13,15-18,24-27,30,36,38-43] Subjects were not dislodged in the RCTs, which is low risk; 17 articles [9-12,14,18-20,23,28,29,31-35,37] Subjects with a shedding rate of less than 10 per cent are at low risk; 1 article [21] Subjects with a shedding rate greater than 10% are at high risk. For selective reporting, 1 [40] The possibility of selective reporting was high risk, while no selective reporting was found in the remaining 34 papers, which was low risk. The results of literature quality evaluation are shown in Figure2.

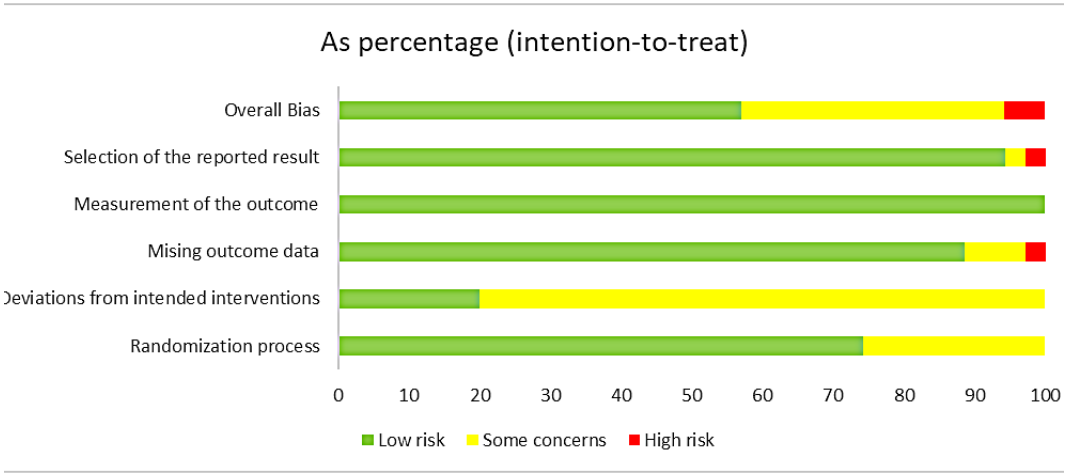

Figure 2: Proportion of items of included articles that produced risk of bias

3.3 Traditional Meta-analysis

Traditional Meta-analysis reported the total effective rate (31 RCTs), 24 hUTP (34 RCTs), ALB (32 RCTs), PLA2R (25 RCTs), SCr (23 RCTs), and TC (21 RCTs), respectively, and the fixed-effects model or the random-effects model was used according to the size of the I^2 between studies of the same intervention, respectively. The results were analysed and showed that in terms of total effective rate, 24 hUTP and ALB, the therapeutic measures of TCM compound combined with conventional western drugs were superior to conventional western drugs alone, and the differences were statistically significant ($P<0.05$), as shown in Table 2 (below). In addition, the conventional Meta-analysis in PLA2R, SCr and TC showed that, except for the formula for tonifying deficiency, clearing heat and dispelling dampness + conventional western medicine WMD=-20.353, 95% CI [-49.047, 8.340] in PLA2R, the formula for tonifying deficiency, clearing heat and dispelling dampness + conventional western medicine in TC (WMD=-0.610, 95% CI [-6.011, 4.791]), and the three interventions of the formula for tonifying deficiency and clearing heat and dampness in TC + conventional western medicine (WMD=-1.015, 95% CI [-6.039, 4.010]), the rest of the results could confirm the superiority of the effect of Chinese herbal medicine compounding in combination with conventional western medicine over the conventional western medicine alone, and the difference was statistically significant ($P<0.05$).

Table 2: Traditional Meta-analysis of each outcome indicator

Intervention	Total effectiveness rate			24UTP			ALB		
	RCT	RR(95%CI)	I^2	RCT	WMD(95%CI)	I^2	RCT	WMD(95%CI)	I^2
X+CT	4	**1.348 * (1.140,1.595)**	0.00%	5	**-0.502 * (-0.577,-0.428)**	0.00%	5	**2.229* (1.255,3.204)**	23.40%
XY+CT	8	**1.338 * (1.203, 1.488)**	0.00%	9	**-1.414 * (-2.124,-0.705)**	94.40%	8	**2.8269* (2.310,3.341)**	0.00%
XSY+CT	9	**1.271 * (1.176,1.373)**	16.30%	10	**-1.022* (-1.387,-0.657)**	96.60%	9	**3.810* (2.365,5.255)**	90.30%

XSR+CT	2	**1.410 * (1.068,1.862)**	0.00%	2	**-0.592* (-0.885,-0.300)**	0.00%	2	**3.663* (1.302,6.024)**	78.10%
XSRY+CT	8	**1.235 * (1.137,1.341)**	0.00%	8	**-0.731* (-1.074,-0.388)**	78.40%	8	**4.336* (3.075,5.598)**	64.10%
Intervention		**PLA2R**			**SCr**			**TC**	
	RCT	WMD (95%CI)	I^2	RCT	WMD (95%CI)	I^2	RCT	WMD (95%CI)	I^2
X+CT	5	**-13.381* (-24.315,-2.448)**	88.20%	2	-1.015 (-6.039,4.010)	0.00%	3	**-0.342 * (-0.619,0.066)**	19.80%
XY+CT	6	**-27.027* (-42.059,11.995)**	96.50%	7	**-6.592 * (-9.875,-3.308)**	54.50%	5	**-1.513 * (-2.226,0.800)**	88.20%
XSY+CT	7	**-10.233* (-14.334,-6.131)**	87.60%	6	**-6.383 * (-10.949,-1.818)**	93.30%	7	**-0.603* (-1.068,0.138)**	96.20%
XSR+CT	2	-20.353 (-49.047,8.340)	58.20%	2	-0.610 (-6.011,4.791)	-	1	-	-
XSRY+CT	5	**-6.705* (-8.490,-4.920)**	0.00%	6	**-7.653 * (-14.567,-0.739)**	89.60%	5	**-0.252* (-0.368,0.136)**	13.20%

3.4 Network Meta-analysis

In this study, an evidence network diagram was produced for each outcome indicator, with the size of the dots representing the size of the sample size, and the thickness of the line representing the size of the standard error, and no closed loops were formed between the interventions, so there was no need for inconsistency testing, and the results are shown in Figure 3. The relative effect values of the results of the two-by-two comparisons of the six interventions are shown in Figure 4. Based on the SUCRA values of each intervention, a rank probability plot was drawn to more intuitively rank the cumulative probability of each intervention in terms of its superiority or inferiority, as shown in Figure

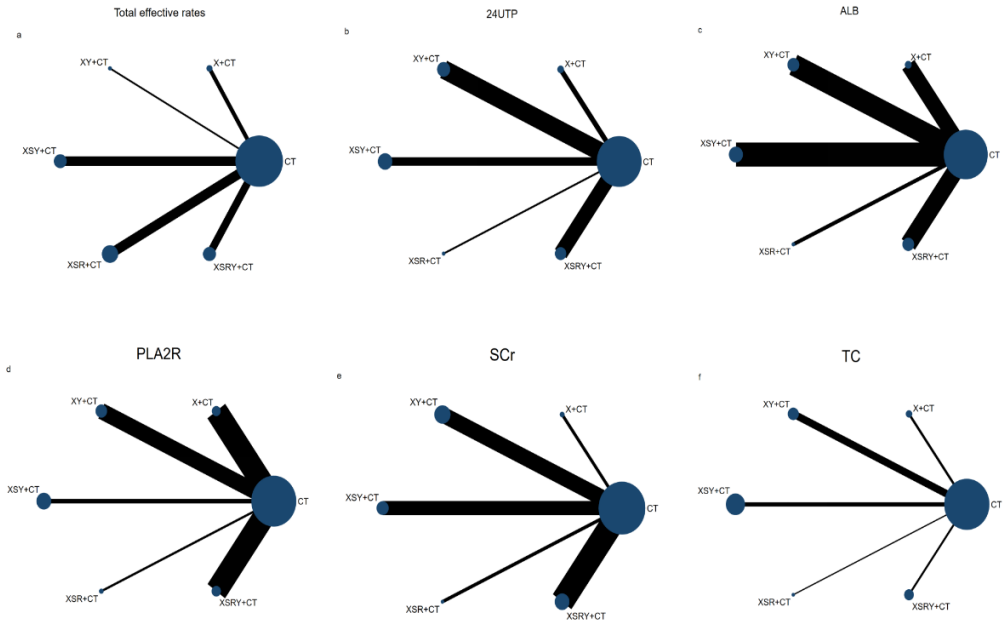

Figure 3: The Evidence network diagram

3.4.1 Total effectiveness rate

31RCTs [9-13,16,17,19-29,31-43] used overall effectiveness as the primary outcome metric of the study and included a total of 2195 patients. The evidence network showed that: six interventions, a total of 15 directly comparable outcomes were formed. Net Meta-analysis showed that: tonifying deficiency, clearing heat and dispelling dampness class formula + conventional western medicine (RR=1.03, 95% CI [0.55, 1.93]), tonifying

deficiency, eliminating stasis and dispelling dampness class formula + conventional western medicine (RR=3.28, 95% CI [2.03, 5.29]), tonifying deficiency class formula + conventional western medicine RR=3.10 (95% CI [1.67, 5.76]), and tonifying deficiency and elimination of blood stasis and clearing heat and dampness category formula + conventional western medicine (RR=1.17, 95% CI [0.51, 2.69]), deficiency tonifying and elimination of blood stasis category formula + conventional western medicine (RR=2.53, 95% CI [1.22, 5.28]), and were superior to conventional western medicine alone, with a statistically significant difference (P<0.05). The difference between the two-by-two comparisons of the remaining types of interventions was not statistically significant. According to the rank probability plot, the interventions were ranked as tonifying deficiency, clearing heat and dispelling dampness class formula + conventional western medicine > tonifying deficiency, eliminating stasis and dispelling dampness class formula + conventional western medicine > tonifying deficiency class formula + conventional western medicine > tonifying deficiency, eliminating stasis and clearing heat and dispelling dampness class formula + conventional western medicine > tonifying deficiency, eliminating stasis and dispelling dampness class formula + conventional western medicine > tonifying deficiency, eliminating stasis and dispelling dampness class formula + conventional western medicine. The calibration-comparison funnel plot showed fair symmetry, with no studies distributed outside the 95% CI, and no significant bias was considered.

3.4.2 24hUTP

34RCTs [9-39,41-43] reported on 24 hUTP and included a total of 2350 patients. The evidence network showed that: six interventions with a total of 15 directly comparable outcomes were formed. Net Meta-analysis showed that compared with conventional western medicine alone, the formula for tonifying deficiency and eliminating stasis + conventional western medicine (WMD = -1.48, 95% CI [-1.93, -1.04]), the formula for tonifying deficiency and eliminating stasis and expelling dampness + conventional western medicine (WMD = -1.13, 95% CI [-1.53, -0.74]) and the formula for tonifying deficiency + conventional western medicine (WMD = -0.93, the 95% CI [-1.50, -0.36]) were both more effective than conventional western medicine alone in reducing 24 hUTP, in addition, compared to the formula for tonifying deficiency and eliminating stasis, clearing heat and dispelling dampness class formula + conventional western medicine, the formula for tonifying deficiency and eliminating stasis class formula + conventional western medicine (WMD = -1.00, 95% CI [-1.65, -0.35]) and the formula for tonifying deficiency and eliminating stasis, dispelling dampness class formula + conventional western medicine (WMD = -0.65 , 95% CI [-1.27, -0.03]) had better clinical efficacy, and the rest of the differences between the two were not statistically significant. According to the rank probability plot, the interventions were ranked as tonifying deficiency and eliminating blood stasis class formula + conventional western medicine > tonifying deficiency and eliminating blood stasis and dispelling dampness class formula + conventional western medicine > tonifying deficiency class formula + conventional western medicine > tonifying deficiency and eliminating heat and dispelling dampness class formula + conventional western medicine > tonifying deficiency and eliminating blood stasis and dispelling heat and dispelling dampness class formula + conventional western medicine > conventional western medicine. The calibration-comparison funnel plot showed general symmetry, with some studies distributed outside the 95% CI, and Egger's test p=0.166, suggesting no significant publication bias (p>0.05).

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3.4.3 ALB

32RCTs [9-14,16-25,27-39,41-43] reported on ALB and included a total of 2214 patients. The evidence network showed that the six interventions yielded a total of 15 two-by-two directly comparable outcomes. Net Meta-analysis showed that, compared with conventional western medicine alone, the formula for tonifying deficiency, eliminating stasis, clearing heat and dispelling dampness + conventional western medicine (WMD = 4.12, 95% CI [2.59, 5.65]), the formula for tonifying deficiency, eliminating stasis and dispelling dampness + conventional western medicine (WMD = 3.96, 95% CI [2.51, 5.41]), the formula for tonifying deficiency, eliminating stasis and dispelling dampness + conventional Western medicine (WMD = 3.91 95% CI [2.36, 5.45]), and the formula for tonifying deficiency and clearing heat and dampness + conventional western medicine were superior to conventional western medicine alone, and the rest of the differences between the two comparisons were not statistically significant. According to the rank probability plot, the interventions were ranked as tonifying deficiency, clearing heat and dispelling dampness class formula + conventional western medicine > tonifying deficiency, clearing heat and dispelling dampness class formula + conventional western medicine > tonifying deficiency, clearing blood stasis class formula + conventional western medicine > tonifying deficiency, clearing heat and dispelling dampness class formula + conventional western medicine > tonifying deficiency class formula + conventional western medicine > conventional western medicine. The calibration-comparison funnel plot

showed general symmetry, with some studies distributed outside the 95% CI, and Egger's test p=0.82, suggesting no significant publication bias (p>0.05).

3.4.4 PLA2RAb

25RCTs [9-14,16-31,33-35] reported on PLA2R and included a total of 1663 patients. The evidence network showed that the 6 interventions yielded a total of 15 directly comparable outcomes. Net Meta-analysis showed that the combination of only two formulas, namely the formula for tonifying deficiency + conventional western medicine (WMD=-40.26, 95% CI [-69.41, -11.11]) and the formula for tonifying deficiency and eliminating blood stasis + conventional western medicine (WMD=-26.47, 95% CI [-49.59, -3.34]), was more effective than the combination of conventional western medicine alone, and the difference was statistically significant (P< 0.05). The rest of the two-by-two comparison differences were not statistically significant. According to the rank probability plot, the interventions were ranked as formula for tonifying deficiency + conventional western medicine > formula for tonifying deficiency and eliminating blood stasis + conventional western medicine > formula for tonifying deficiency and clearing heat and dispelling dampness + conventional western medicine > formula for tonifying deficiency and eliminating blood stasis and dispelling dampness + conventional western medicine > formula for tonifying deficiency and eliminating blood stasis and clearing heat and dispelling dampness + conventional western medicine > conventional western medicine. The calibration-comparison funnel plot showed that the symmetry was fair, and some studies were distributed outside the 95% CI, and the Egger's test p=0.005 suggested the existence of publication bias, and the clipping method was repeated to evaluate the effect of publication bias on the results, and the clipping method results showed that 0 clippings occurred, and 0 negative papers were included additionally, which, combined with the results of the Egger's test, indicated that the possibility of publication bias was small.

3.4.5 SCr

23RCTs [12-17,19-21,23,25-27,29-34,36,39,41,42] reported on SCr and included a total of 1582 patients. The evidence network showed that the six interventions produced a total of 15 directly comparable outcomes. Net Meta-analysis showed that only the formula of tonifying deficiency, eliminating stasis, clearing heat and dispelling dampness + conventional western medicines (WMD=-7.86, 95% CI [-13.53, -2.18]) and the formula of tonifying deficiency, eliminating stasis and dispelling dampness + conventional western medicines (WMD=-6.41, 95% CI [-12.42, -0.40]) were more effective than conventional western medicines alone in lowering the SCr, and the difference was statistically significant (P<0.05), and the rest of the two-by-two comparisons were not statistically significant. According to the rank probability plot, the interventions were ranked as tonifying deficiency, eliminating stasis and clearing heat and dispelling dampness class formula + conventional western medicine > tonifying deficiency, eliminating stasis and dispelling dampness class formula + conventional western medicine > tonifying deficiency, eliminating stasis and clearing heat and dispelling dampness class formula + conventional western medicine > tonifying deficiency, eliminating stasis and dispelling dampness class formula + conventional western medicine > conventional western medicine. The corrected-comparison funnel plot showed poor symmetry, with some studies distributed outside the 95% CI, and Egger's test p=0.521, suggesting no significant publication bias (p>0.05).

3.4.6TC

21RCTs [9,12-14,16,17,9,20,22-24,26,27,29,31,33,35,38-40,43] reviewed SCr and included a total of 1538 patients. The evidence network showed that: the 6 interventions yielded a total of 15 directly comparable outcomes. Net Meta-analysis showed that, compared with the application of conventional western medicine alone, the formula for tonifying deficiency + conventional western medicine (WMD=-1.52, piecewise 95% CI [-2.03, -1.00]) and the formula for tonifying deficiency, eliminating stasis, and dispelling dampness + conventional western medicine (WMD=-0.66, 95% CI [-1.07, -0.24]) were able to reduce TC more than the application of conventional western medicine alone, and, between the two, the formula for tonifying deficiency, eliminating stasis, and dispelling dampness + conventional Western medicine WMD=-1.32, 95% CI [-2.15, -0.50] was more effective, and the difference was statistically significant (P<0.05). In addition, the clinical efficacy of the formula for tonifying deficiency and eliminating blood stasis to improve TC was better than that of the formula for tonifying deficiency and eliminating blood stasis to clear heat and dispel dampness + conventional western medicine (WMD=-1.28, 95% CI [-2.00, -0.57]) and the formula for tonifying deficiency and eliminating blood stasis to dispel dampness + conventional western medicine (WMD=-0.86, 95% CI [-1.52, -0.20]), and the rest of the two two-measure comparisons did not have a statistically significant difference. According to the rank probability plot,

the interventions were ranked as tonifying deficiency and eliminating stasis class formula + conventional western medicine > tonifying deficiency and eliminating stasis and dispelling dampness class formula + conventional western medicine > tonifying deficiency and eliminating heat and dispelling dampness class formula + conventional western medicine > tonifying deficiency and eliminating stasis and dispelling heat and dispelling dampness class formula + conventional western medicine > tonifying deficiency class formula + conventional western medicine > conventional western medicine. The calibration-comparison funnel plot showed poor symmetry, with some studies distributed outside the 95% CI, and Egger's test p=0.061, suggesting no significant publication bias (p>0.05).

a.

XSR+CT					
1.03(0.55,1.93)	XSY+CT		RR(95%CI)		
1.09(0.52,2.29)	1.06(0.48,2.31)	X+CT			
1.15(0.65,2.02)	1.11(0.60,2.07)	1.05(0.50,2.19)	XSRY+CT		
1.34(0.58,3.09)	1.29(0.54,3.11)	1.22(0.47,3.20)	1.17(0.51,2.69)	XY+CT	
3.39(2.26,5.08)	**3.28(2.03,5.29)**	**3.10(1.67,5.76)**	**2.96(1.98,4.41)**	**2.53(1.22,5.28)**	CT

b.

XY+CT					
-0.35 (-0.95,0.25)	XSY+CT		RR(95%CI)		
-0.55 (-1.27,0.17)	-0.20 (-0.89,0.49)	X+CT			
-0.91 (-1.90,0.09)	-0.56 (-1.53,0.42)	-0.36 (-1.41,0.70)	XSR+CT		
-1.00 (-1.65,-0.35)	**-0.65 (-1.27,-0.03)**	-0.45 (-1.19,0.29)	-0.09 (-1.10,0.92)	XSRY+CT	
-1.48 (-1.93,-1.04)	**-1.13 (-1.53,-0.74)**	**-0.93 (-1.50,-0.36)**	-0.58 (-1.47,0.31)	**2.53 (1.22,5.28)**	CT

c.

XSRY+CT					
0.16 (-1.95,2.26)	XSY+CT		RR(95%CI)		
0.21 (-1.96,2.38)	0.05 (-2.06,2.17)	XY+CT			
0.62 (-2.79,4.03)	0.46 (-2.91,3.83)	0.41 (-3.00,3.82)	XSR+CT		
1.48 (-1.01,3.97)	1.32 (-1.12,3.76)	1.27 (-1.22,3.76)	0.86 (-2.76,4.48)	X+CT	
4.12 (2.59,5.65)	**3.96 (2.51,5.41)**	**3.91 (2.36,5.45)**	**3.50 (0.45,6.54)**	**2.64 (0.68,4.60)**	CT

d.

X+CT					
-13.79 (-50.90,23.31)	XY+CT		RR(95%CI)		
-12.91 (-60.01,34.18)	0.88 (-42.87,44.63)	XSR+CT			
-23.99 (-59.06,11.07)	-10.20 (-40.56,20.16)	-11.08 (-53.11,30.95)	XSY+CT		
-27.12 (-66.26,12.01)	-13.33 (-49.05,22.39)	-14.21 (-60.25,31.83)	-3.13 (-36.72,30.47)	XSRY+CT	
-40.26 (-69.41,-11.11)	**-26.47 (-49.59,-3.34)**	-27.35 (-64.50,9.80)	-16.27 (-35.94,3.41)	-13.14 (-40.42,14.14)	CT

e.

XSRY+CT					
-1.45 (-9.72,6.82)	XSY+CT		RR(95%CI)		
-3.92 (-11.87,4.02)	-2.47 (-10.66,5.72)	XY+CT			
-4.68 (-16.48,7.11)	-3.23 (-15.20,8.73)	-0.76 (-12.50,10.98)	X+CT		
-7.34 (-23.18,8.50)	-5.89 (-21.85,10.08)	-3.41 (-19.21,12.38)	-2.65 (-20.70,15.39)	XSR+CT	
-7.86 (-13.53,-2.18)	**-6.41 (-12.42,-0.40)**	-3.93 (-9.49,1.62)	-3.17 (-13.51,7.17)	-0.52 (-15.31,14.27)	CT

f.

XY+CT					
-0.86 (-1.52,-0.20)	XSY+CT		RR(95%CI)		
-0.90 (-2.14,0.35)	-0.04 (-1.24,1.17)	XSR+CT			
-1.28 (-2.00,-0.57)	-0.42 (-1.07,0.22)	-0.39 (-1.62,0.85)	XSRY+CT		
-1.32 (-2.15,-0.50)	-0.46 (-1.23,0.31)	-0.43 (-1.73,0.88)	-0.04 (-0.85,0.77)	X+CT	
-1.52 (-2.03,-1.00)	**-0.66 (-1.07,-0.24)**	-0.62 (-1.75,0.51)	-0.23 (-0.73,0.26)	-0.19 (-0.84,0.45)	CT

Figure 4: Relative effect analysis of outcomes.
green. Interventions; yellow. Indicating statistical significance

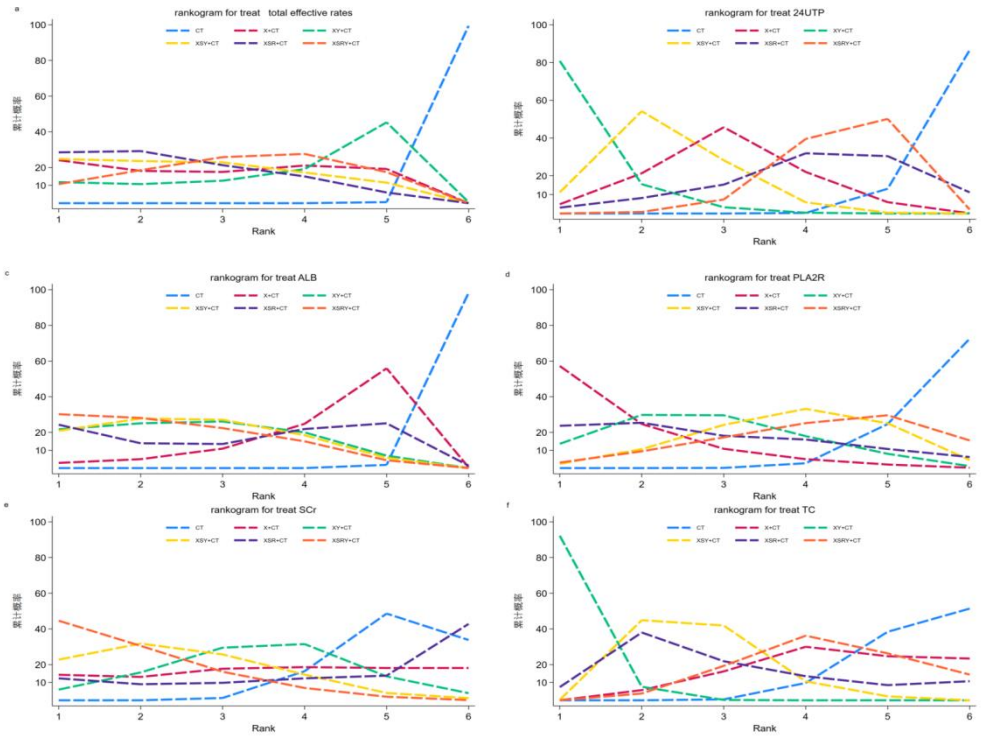

Figure 5: Rank probability of each outcome indicator

3.5 Publication Bias Detection

As shown in Figure 6, we plotted a corrected-comparison funnel plot for all outcomes to assess potential publication bias. In Egger's test, p = 0.962 for total clinical effectiveness, p = 0.166 for 24h UTP reduction, p = 0.82 for ALB increase, p = 0.521 for SCr decrease, and p = 0.061 for TC reduction. The funnel plots of each of the above mentioned metrics showed an essentially symmetrical distribution pattern of the chromatic dispersion points, which were further analysed by Egger's test. The results all showed no significant publication bias (p > 0.05). In addition, although the reduction rate of PLA2R was p=0.005, after analysed by the cut-and-patch method, we considered that the possibility of publication bias was small.

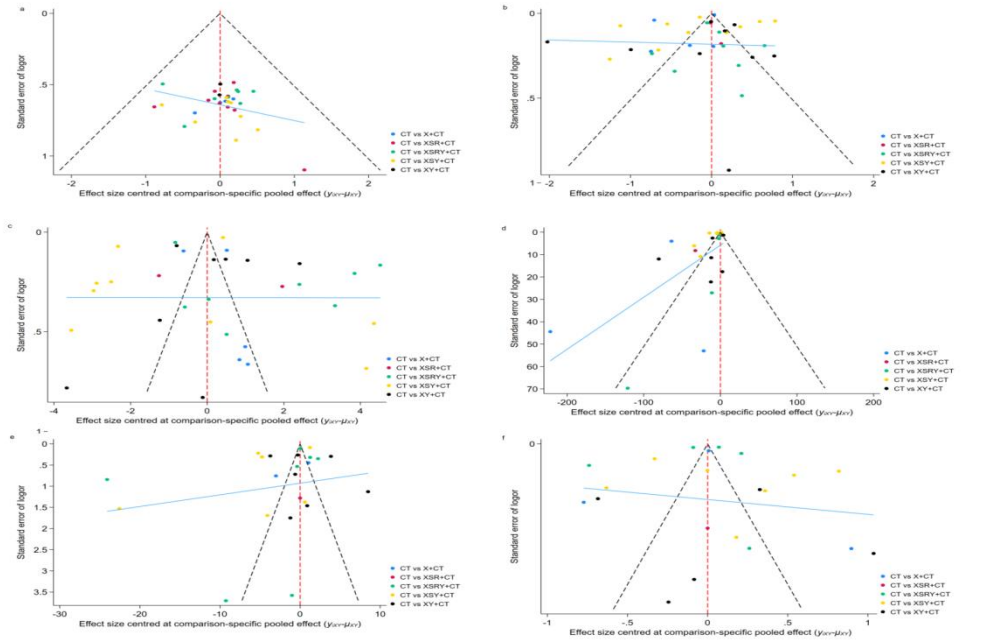

Figure 6: Comparison-correction funnel plot of each outcome indicator

3.6 Adverse Reactions

The occurrence of adverse reactions was mentioned in 22 RCTs, of which 10 described the specific manifestations of adverse reactions in detail, mainly including infections, liver function abnormalities, gastrointestinal reactions, elevated blood pressure, blood glucose abnormalities and so on, and the patients were treated promptly and the subjects did not withdraw from the trial as a result. The occurrence of adverse reactions is shown in Table 3.

4. Discussion

A total of 35 studies were included in this paper, involving 2,518 IMN patients, of which 1,267 were in the experimental group and 1,251 were in the control group, and the differences between the experimental group and the control group in terms of gender and age were not statistically significant. A total of 5 types of interventions of Chinese medicine compound preparation + conventional western medicine were investigated in this paper, aiming to objectively assess their efficacy and effectiveness in clinical application. The data were analysed using a random-effects model, and the overall heterogeneity was low among all the included studies. The results showed that compared with other types of TCM compound preparations + conventional western drugs, the formula for tonifying deficiency, eliminating heat and stasis and dispelling dampness + conventional western drugs (SUCRA: 71.2%) was more effective in improving the overall clinical efficacy; the formula for tonifying deficiency, eliminating heat and stasis + conventional western drugs was more effective in lowering the quantitative 24-hour urinary protein (SUCRA: 95.3%) and total cholesterol (SUCRA: 98.2%); the formula for tonifying deficiency, eliminating heat and stasis and dispelling dampness + conventional Western drugs The formula for clearing heat and eliminating dampness + conventional western medicine ranked the highest in lowering blood creatinine (SUCRA: 80.4%) and increasing serum albumin level (SUCRA: 72.9%).

Based on the above results, we further explored in depth the therapeutic mechanism of various types of TCM compound formulas + conventional western drugs. The reason why the formulae of the category of tonifying deficiency, eliminating stasis and dispelling dampness + conventional western medicines could improve the overall clinical effectiveness rate may be related to the fact that the formulae of this category are more in line with the basic etiology and pathogenesis of IMN patients, i.e., deficiency of spleen and kidney qi coupled with the interconnection of dampness and stasis. Blood stasis and water stagnation are the cause and effect of the same source of fluid and blood, as mentioned in "The Essentials of the Golden Chamber", "When blood is not favourable, it becomes water." Clinical patients often present with dark skin colour, swelling of the lower limbs, skin ecchymosis, purple and dark tongue, white moss, and sunken and fine pulse. The formulas for tonifying deficiency, eliminating stasis and dispelling dampness included in this study, such as "Warming Yang and Passing the Lumps Formula", "Warming Yang and Dispelling Dampness and Passing the Lumps Formula" and "Strengthening the Spleen and Inducing Dampness Formula", are mostly based on the methods of benefiting qi, warming yang, inducing dampness and invigorating blood circulation and promoting circulation of blood. The most frequently used medicines include: Astragalus, Angelica sinensis, Salvia miltiorrhiza, leeches, Poria, motherwort, etc., to regulate Qi and blood and to treat blood and water at the same time. Huang Han medicine" has said: "astragalus can stretch the positive qi, back to the fluid, solid and dense coupling, then the stagnant water from the back down, urinary fluency, slippery skin and get moist", so the patients with this evidence mostly with large doses of astragalus with the application of qi, qi and blood, replenish the qi and water, modern pharmacological studies have shown that astragalus has an anti-oxidative stress, improve immunity, protection of renal tissues and other effects[52,53].In addition, Kun Xian capsule, which represents dispelling wind and removing dampness and activating blood circulation, can reduce foot cell damage and proteinuria level by inactivating β-catenin protein in mice with diabetic nephropathy, and inhibit disease progression [54].

Clinical findings show that IMN patients with predominantly deficiency evidence tend to have a long history of illness, recurrent and prolonged illness, with the most severe deficiency of the lungs, spleen and kidneys. The pathogenesis of the disease is mostly identified as deficiency of lung and kidney yin, lung and spleen qi, and spleen and kidney yang, and oedema, fatigue and proteinuria are common in the clinic. Zhang Jiebin of the Ming Dynasty mentioned in Class Classic - Treatment of Deficiency: "For Qi deficiency, it is appropriate to tonify its upper part; for essence deficiency, it is appropriate to tonify its lower part; for Yang deficiency, it is appropriate to tonify and warm at the same time; and for Yin deficiency, it is appropriate to tonify and clear at the same time." The formulas included in this study for tonifying deficiency are Chinese medicinal preparations represented by "Zhenwu Tang," "Ginseng Astragali and Dihuang Tang," and "Sijunzi Tang," with commonly used medicines including Codonopsis pilosulae, Astragalus membranaceus, Poria cocos, and Chinese yam, The commonly used herbs include Radix Astragali, Poria, Chinese yam, Radix Rehmanniae Praeparata, Cornus Officinalis, etc. These herbs tonify qi and

blood, nourish the spleen and kidneys, and help to correct the imbalance of qi and blood and the internal organs of patients with IMN from the perspective of "supporting the right side of the body". 70%—80% of patients with IMN are positive for the antibody to PLA2R, and most cross-sectional studies have shown that the high level of antibody to PLA2R Most cross-sectional studies have shown that high levels of PLA2R antibodies are one of the main reasons for the decrease in spontaneous remission rate, increase in disease activity and accelerated progressive loss of renal function in patients with IMN, and that lowering the titer of PLA2R antibodies as early as possible can help improve the long-term prognosis of patients [45-47]. Modern pharmacological studies have shown that deficiency tonic formulas have the effect of lowering urinary protein, reducing inflammatory factors and enhancing immunity [48,49]. However, there are few reports in the literature on the association between deficiency tonic formulae and PLA2R antibodies, which need to be further explored.

Deficiency and stasis are the most common clinical conditions in IMN patients. If there is deficiency in qi, the blood flow will not be smooth and the renal channels will be stagnant; if there is stagnation in blood, the deficiency will be even worse, which will lead to a vicious circle, and it usually manifests itself as thickening of the glomerular basement membrane or formation of tubular microthrombosis [50]. Clinical patients are mostly manifested as fatigue and lethargy, swelling of the face and limbs, and skin and nail mistakes. Wang Qingren in the Qing Dynasty in the "medical forest correction - on the wind is not the wind" cloud: yuan qi is weak, will not be able to reach the blood vessels, blood vessels without gas, will stay and stasis. Formulas for replenishing deficiency and eliminating stasis, such as "Benefiting Qi and Eliminating Crimes Formula", "Plus Flavour Tonic Yang Returning Five Soup", and "Ginseng Astragali and Di Huang Combined with Peach and Red Four Substances Soup", which were included in this study, are one of the best interventions for lowering TC and 24 hUTP, and have been used most frequently. The most frequently used drugs include: Astragalus, Codonopsis pilosula, Radix et rhizoma, Radix Rehmanniae Praeparata, Radix Angelicae Sinensis, Rhizoma Ligustici Chuanxiong, Radix et Rhizoma Polygoni Multiflori, Radix et Rhizoma Polygoni Multiflori, and so on, which benefit the qi and promote water retention, nourish and invigorate blood. Modern pharmacological studies have shown that such formulas not only help to increase renal blood flow and reduce podocyte damage, but also slow the progression of renal disease [44]. A retrospective clinical study based on 495 patients with IMN found that high levels of TC were positively associated with glomerular injury and increased urinary protein, and that improving lipid levels could help reduce urinary protein [51].

IMN patients with deficiency of both qi and yin, and interlocking of dampness and heat as the main evidence often show swollen face and limbs, soreness and weakness of waist and knees, redness and astringency of urine, foul-smelling breath, or skin boils, sores and ulcers, and so on. The Jingyue Encyclopaedia states, "For the disease of dampness-heat, it is appropriate to clear and benefit, and the heat goes away, so does the dampness." Most of the literature included in this study is based on the method of benefiting qi and nourishing yin, clearing heat and inducing dampness, such as "Benefiting qi and tonifying the kidneys to clear dampness" and "Strengthening the spleen and the kidneys to clear heat and induce dampness", etc. Commonly used medicines include: Astragalus, Cornu Cervi Pantotrichum, raspberry, Cuscuta chinensis, cypress, Plantago ovata, Poria cocos, and Jiexue cao. This formula benefits Qi and nourishes Yin, nourishes the liver and kidneys, and clears heat and relieves dampness. Modern pharmacological studies have shown that these medicines can reduce renal pathological damage by inhibiting endoplasmic reticulum stress and repairing foot cell damage, thus improving clinical efficacy [55,56].

IMN patients with multiple pathological factors such as deficiency, stasis, dampness and heat are mostly seen in the middle and late stages of the disease, which is often summarised by the TCM theory of "poisonous evil". Clinical manifestations include fatigue, oedema, urine and turbidity repeatedly, and the condition is stubborn and difficult to be cured; if the disease is prolonged, it will be caused by the deficiency, and become a syndrome of mixed deficiency and reality. The Political Parameters states, "Poisonous evils cannot enter without deficiency, and if the stomach qi is weak again, the poisonous evils will sink in, and the treatment will not cure the disease for years and months." The Chinese medicinal preparations included in this study, such as "Qi Di Ku Kidney Formula", "Huang Cu Yi Kidney Pill", and "Yi Qi, Dampness and Collaterals Soup", were mainly used to strengthen the spleen and the kidneys, and at the same time, they were also used to detoxify and relieve dampness, and to remove blood stasis and clear the collaterals. The most frequently used medicines include: Astragalus, Radix Rehmanniae Praeparata, Salviae Miltiorrhizae, Leeches, Radix et Rhizoma Alba, Zedoariae, etc. Modern pharmacological studies have shown that such formulas can help to reduce SCr levels, reduce the micro-inflammatory state of the kidneys, increase renal blood flow and delay the progression of chronic kidney disease [57,58].

Table 3: Occurrence of adverse reactions

Author/year	intervention measures in the test group	negative reaction	
		T	C
Xing Yang 2023	Jiawei Zhenwu Tang + CT	Not present	Not present
Zhen Cai 2019	Radix Astragali Di Huang Tang + CT	-	-
Lei Wang 2020	Radix Astragali Di Huang Tang + CT	-	-
Chao Song 2020	Warming Yang and Lifting Water Formula +CT	Not present.	1 case of acute renal failure
Ling Huang 2023	Yiyuanjianzhong Formula+CT	Not present.	Not present
Jieqi Zheng 2019	Zhen Wu Tang with Angelica Sinensis and Paeoniae Alba+CT	Failure to appear.	Not present
Xueyan Sun 2022	Benefiting Qi, Nourishing Kidney and Promoting Blood+CT	Not present	Not present
Xin Feng 2021	Benefiting Qi and Eliminating Crimes+CT	Infection 3 cases, deep vein thrombosis 1 case, and	Infection 10 cases, deep vein thrombosis 5 cases, and
Yating Zhang 2022	Radix Astragali Di Huang Tang+ CT	3 cases of facial acne	Facial acne 12 cases
Guojun Tang 2020	Qi Jishen combined with Taohong Siwu Decoction + CT	Elevated blood sugar 8 cases, peptic ulcer 3 cases, and	Elevated blood sugar 9 cases, peptic ulcer 4 cases, and
Chongxia Zhao 2022	Add flavour to tonify Yang and restore the five elements+CT	Hypertension 9 cases, Infection 7 cases	Hypertension 12 cases, Infection 16 cases
Xue Li 2022	Invigorate Blood and Promote Water Formula + CT	Acute kidney injury, 1 case.	Liver function abnormality 1 case
Changan Chen 2022	Tonifying Qi and Benefiting Kidney Formula + CT	-Gastrointestinal symptoms	-Gastrointestinal reactions.
Jiajiao Zuo 2018	Qiling Tongluo Prescription + CT	Gastrointestinal symptoms 2 cases	Digestive tract reaction 5 cases, urinary tract reaction 1 case
Zhou Shi 2022	Benefiting Qi, Tonifying the Kidneys and Clearing the Profit Formula + CT	-Gastrointestinal symptoms.	-Lung infection 2, leukocyte reaction 1
Jia Liu 2021	Strengthening the spleen, benefiting the kidneys, clearing heat and inducing dampness formula + CT	Digestive tract symptoms 2 cases	lung infection 2 cases, leukopenia 2 cases, and
Yun Ma 2023	Warming Yang and Clearing Dampness Formula + CT	Not present	Gastrointestinal symptoms in 3 cases, abnormal liver function in 1 case
Jie Li 2020	Wen Yang Dispels Dampness and Circulates Dampness Formula + CT	Not present	Not present
Yanan Zhang 2023	Wen Yang Dispels Dampness and Circulates Dampness Formula + CT	Not present	Not present
Qiang Liu 2019	Warming Yang, Promoting Blood and Lifting Water+CT	Liver function abnormalities 2, leukopenia 2, gastrointestinal reaction 1, infection 1	Not present
Zheng Zhang 2022	Jin Qi Benefit Kidney Formula+CT	Not present	Liver function abnormality 3 cases, leukopenia 10 cases, gastrointestinal reaction 7 cases, infection 5 cases
Kexin Wang 2022	Ginseng Astragali and Dihuang Tang+CT	Not present	Not present
Jianjun Guo 2022	Strengthening the spleen and dispelling dampness+CT	Dizziness 1 case, nausea 1 case, diarrhoea 1 case	Not present
Meng Ji 2021	Kun Xian Capsule±CT	Elevated blood sugar 2 cases, peptic ulcer 3 cases, and	Dizziness 2 cases, nausea 1 case, diarrhoea 2 cases
Jie Liu 2022	Rhizoma Ligustici Tongluo Capsule+CT	2 cases of hypertension, 1 case of infection	9 cases of elevated blood glucose, 4 cases of peptic ulcer, and
Wu 2022	Strengthening the Spleen, Dispelling Dampness and Hepato conjugate Formula+CT	Liver function abnormality 1 case, digestive symptoms 2 cases	Hypertension 8 cases, infection 5 cases
Leilei He 2022	Kidney Yikang+CT	4 cases of menstrual disorders in women; 1 case of gastrointestinal reaction; 1 case of alanine aminotransferase elevation	Liver function abnormality 3 cases, digestive symptoms 5 cases, lung infection 1 case, urinary tract infection 1 case
Genping Lei 2019	Astragalus Di-Fixing Kidney Tablet+CT	-1 case of alanine aminotransferase elevation	3 cases of gastrointestinal reactions; 2 cases of abnormal liver function; 3 cases of abnormal glucose metabolism; 2 cases of lung infection, 1 case of urinary tract infection; 1 case of venous thrombosis;

Huaxia Liu 2019	Tonifying the Kidneys, Resolving Blood Stasis and Clearing Drainage Formula + CT	Diarrhoea 2 cases	2 cases of new-onset hypertension
Lina Qiao 2020	Tonifying Qi, Resolving Dampness and Clearing Drainage+ CT	Renal vein thrombosis 1 case	-
Jin Wu 2021	Radix Astragali and Radix Rehmanniae Formula+CT	Infection 1 case	3 cases of vomiting, 1 case of nausea, 2 cases of diarrhoea
Rong Zhao 2021	Huangtu Yi Kidney Granules +CT	Liver function abnormality 1 case, drug-induced hyperglycaemia 2 cases	1 case of renal vein thrombosis, 0 cases of deep vein thrombosis, and pulmonary embolism 1 case, renal failure 1 case
Gaohua Ping 2021	Clearing and Resolving Turbidities Capsule+CT	Not present	
Yaping Guo 2021	Qi Di Tao Hirch Er Cicada Formula+CT	-Not occurring	Infection 2 cases
Lv W2021	Nephritis Rehabilitation Tablets+CT	Not present	Liver function abnormality 1 case, drug-induced hyperglycaemia 4 cases

There are some limitations in this study: (1) the quality of the literature varies, and some studies did not describe the randomisation method and the allocation concealment scheme; (2) no direct comparison between TCM compound prescriptions was formed, which may have some errors; (3) no statistical comparison of drug dosages of similar prescriptions was performed, which may affect the authenticity of the results.

In conclusion, this study provides evidence-based medical evidence for the treatment of IMN through reticulated Meta-analysis, which can be used by clinicians to quickly select the most efficacious TCM compound formula with the best efficacy based on the clinical manifestations of IMN patients under the premise of evidence identification. However, there is some variability in the selection of drugs in the included studies, especially in the activation of blood circulation and elimination of blood stasis, which is affected by geographic factors or the personal medication habits of physicians, with large differences in the types and dosages of drugs, and it is recommended that clinicians can make lateral comparisons when selecting drugs in the future, so as to formulate the optimal formulas that are in line with the clinical indexes of patients with IMN. In addition, there is still a lack of high-quality, large-sample R-conventional western drugs in clinical studies of TCM, and it is hoped that research specifications can be further clarified and the quality of research can be improved in the future, so as to provide a higher level of evidence-based medical evidence for the treatment of IMN with TCM.

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