

Effectiveness of Acupuncture Combined with Medicine in Treatment of Hashimoto's Thyroiditis: A Systematic Research and Meta-Analysis of Randomized Controlled Trials

Zhili Dou^{1,2}, Lei Zhao², Yixing Liu³, Dongran Han^{2*}, Jinzhu Jia^{1,4*}

¹Department of Biostatistics, School of Public Health, Peking University, Beijing, China; ²Department of Dermatology, The School of Life Science of Beijing University of Chinese Medicine, Beijing, China; ³Department of Dermatology, The School of Management of Beijing University of Chinese Medicine, Beijing, China; ⁴Department of Dermatology, Center for Statistical Science, Peking University, Beijing, China

ABSTRACT

Objectives: The aim of this study was to evaluate the efficacy and safety of acupuncture in treating Hashimoto's thyroiditis. It provides some reference value for clinic.

Methods: PubMed, Cochrane Library, Embase, and Scopus databases were searched from their inception to March 28, 2023. Seven databases including CNKI, WangFang Data, VIP, PubMed, The Cochrane Library, CBM and EmBase were searched by computer. Randomized Controlled Trials (RCTs) on acupuncture in the treatment of Hashimoto's thyroiditis from their inception to March 2023 were searched, and the results were screened and data extracted independently by two investigators.

Results: A total of 9 RCTs with a total of 704 patients were included in this study. There were 349 cases in the treatment group and 355 in the control group. 1 of them mentioned no adverse reactions, 5 of them did not mention, and 3 of them had no adverse reactions. The results of meta-analysis showed that: (1) Total effective rate: $I^2=0.0\%$, $P=0.99$, (OR=4.27, 95%CI [2.716,7.3]), $Z=6.25$, $P<0.00001$; (2) FT3: $I^2=93\%$, $P<0.05$ (SMD=1.21, 95%CI [0.55, 1.86]), $Z=3.59$, $P=0.0003$; (3) FT4: $I^2=94\%$, $P<0.05$, (SMD=1.25, 95%CI [0.58, 1.91]), $Z=3.69$, $P=0.0002$; (4) TSH: $I^2=94\%$, $P<0.05$, (SMD=-1.58, 95%CI [-2.34, -0.81]), $Z=4.04$, $P<0.0001$; (5) TgAb: $I^2=94\%$, $P<0.05$, (SMD=-2.04, 95%CI [-2.86, -1.23]), $Z=4.92$, $P<0.00001$; (6) TPOAb: $I^2=94\%$, $P<0.05$, (SMD=-2.18, 95%CI [-3.04, -1.32]), $Z=4.96$, $P<0.00001$; (7) TT4: SMD=0.65, 95%CI [0.13, 1.17], $P=0.01$; (8) Thyroid volume: $I^2=22\%$, $P=0.27$, (SMD=-0.93, 95%CI [-1.15, -0.71]), $Z=8.13$, $P<0.00001$; (9) Isthmus thickness: $I^2=68\%$, $P=0.03$, (SMD=-1.77, 95%CI [-2.29, -1.26]), $Z=6.80$, $P<0.00001$; (10) Total scores of TCM syndromes: $I^2=91\%$, (SMD=-1.30, 95%CI [-2.57,-0.03]), $Z=2.01$, $P=0.04$.

Conclusion: Acupuncture and moxibustion has certain curative effect on Hashimoto's thyroiditis, and the effect is better than that of single western medicine.

Keywords: Acupuncture; Hashimoto's thyroiditis; Randomized controlled trial; Efficacy; Systematic research

INTRODUCTION

Hashimoto's Thyroiditis (HT), proposed by Hashimoto in 1912, is the most common autoimmune thyroid disease and one of the most common endocrine diseases [1]. The thyroid tissue of HT patients is infiltrated by lymphocytes or plasma cells, interstitial fibrosis, and degeneration and destruction of thyroid follicular

epithelial cells, eventually leading to hypothyroidism and a series of symptoms of hypothyroidism. The hallmark of autoimmune disorder in HT is higher Thyroid Peroxidase Antibody (TPOAb) and Thyroglobulin Antibody (TgAb). The annual incidence of HT worldwide is about 0.3-1.5 per 1000, and women are 5-10 times more likely to be affected than men [2]. This disease can occur at all ages primarily in women aged 30-50. The incidence

Correspondence to: Jinzhu Jia, Department of Biostatistics, School of Public Health, Peking University, Beijing, China, E-mail: jzjia@math.pku.edu.cn

Dongran Han, Department of Dermatology, The School of Life Science of Beijing University of Chinese Medicine, Beijing, China, E-mail: handongr@gmail.com

Received: 10-Aug-2023, Manuscript No. JYPT-23-26076; **Editor assigned:** 14-Aug-2023, Pre QC No. JYPT-23-26076 (PQ); **Reviewed:** 28-Aug-2023, QC No. JYPT-23-26076; **Revised:** 04-Sep-2023, Manuscript No. JYPT-23-26076 (R); **Published:** 11-Sep-2023, DOI:10.35248/2157-7595.23.13.396.

Citation: Dou Z, Zhao L, Liu Y, Han D, Wang Y, Jia J (2023) Effectiveness of Acupuncture Combined with Medicine in Treatment of Hashimoto's Thyroiditis: A Systematic Research and Meta-Analysis of Randomized Controlled Trials. J Yoga Phys Ther.13:396.

Copyright: © 2023 Dou Z, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

of HT in China is about 0.5%-1.5%, which is higher than that in the world and gradually increasing. HT accounts for 20%-25% of thyroid diseases [3]. Currently, thyroid hormone replacement therapy, immunotherapy, and surgery are mainly used in western medicine for HT. Western medicine often restores thyroid function to normal, but the clinical symptoms do not improve significantly, and thyroid antibody levels remain high and long-term medication will bring many side effects to patients, affecting their everyday life and work [4]. Although many studies have focused on the role of selenium supplementation in treating HT in recent years, its efficacy is still being determined [5-8]. Therefore, it is of great significance to seek more effective treatment methods and early active intervention to treat HT and delay disease development.

Thus, modern approaches to the treatment of HT require further exploration. According to ancient books, Traditional Chinese Medicine (TCM) has unique advantages in treating HT. In TCM, HT belongs to the category of "thyroid nodule" disease, which is caused by deficiency of the spleen and kidney, Qi stagnation of the liver, phlegm, and blood stasis, mainly using soothing the liver and regulating Qi, promoting blood circulation and removing blood stasis, eliminating phlegm and gall, warm and tonify the spleen and kidney and other treatments. Acupuncture is a surgical treatment of TCM, mainly through regulating the balance of the neuroendocrine-immune network, reducing serum antibody levels, and inhibiting the destruction of thyroid cells to promote the recovery of thyroid function [9]. In addition, acupuncture treatment can also regulate the immune imbalance of the body [10-12], especially moxibustion can correct the autoimmune abnormalities of HT patients by adjusting the proportion of T lymphocyte subsets and inhibiting the level of anti-thyroid antibodies produced by B lymphocytes. Finally, HT patients' immune function, clinical symptoms, and quality of life can be effectively improved [13-15].

The overview is a novel method for assessing the scientific quality of published systematic research and meta-analyses in a specific domain [16,17]. This method has been applied in many medical fields, including acupuncture [18,19], benign thyroid nodules, moxibustion, parkinson's disease, etc. In recent years, acupuncture combined with medicine or moxibustion combined with treatment has had a remarkable clinical effect on HT. Several meta-analyses based on Randomized Controlled Trials (RCTs) of HT have assessed its association with TCM.

However, despite the number of systematic research and meta-analyses that have evaluated the association between HT and TCM, where need to be comprehensive research to assess the reporting and methodological quality and summarize the evidence. There need to be more evidence-based medical evidence for the efficacy of acupuncture in treating HT. Also, guidance for clinical users and physicians is limited. Consequently, this research aims to provide more references and a basis for clinical treatment and research.

MATERIALS AND METHODS

Search strategy

Literature was retrieved from CNKI, WangFang, VIP, PubMed, The Cochrane Library, CBM and Embase self-established databases until March 2023. Chinese search term: Hashimoto's thyroiditis, chronic lymphocytic thyroiditis, Hashimoto's disease, Hashimoto's thyroiditis, autoimmune thyroiditis, acupuncture, acupuncture and moxibustion, electric acupuncture, fire

acupuncture, needle, moxibustion, acupoint, randomized controlled trial, RCT.

Inclusion criteria

Type of study: Published randomized controlled clinical trial of acupuncture in Hashimoto's thyroiditis, the language is Chinese or English, whether blind or not

Object of study: The patients diagnosed with Hashimoto's thyroiditis are not limited to nationality, age, gender and course of disease.

Intervention measures: The treatment group was treated with acupuncture, acupuncture combined with western medicine, the control group was treated with standard western medicine

Outcome index: Total effective rate; FT3; FT4; TSH; TgAb; TPOAb; TMAb; TT4; Thyroid volume; Isthmus thickness; Total scores of TCM syndromes.

Exclusion criteria

(1) Republished literature; (2) Full text literature is not available; (3) Non-RCTs, summary, animal experiments, case report, the literature of clinical experience; (4) Unable to extract data or incomplete literature; (5) Studies that do not specify the diagnostic criteria.

Data extraction

Two researchers independently screened the literature according to inclusion and exclusion criteria, then extracted the data and cross-checked it. When researchers Dong, et al. [15] had a disagreement, other researcher Lv, et al. [9], would judge and help resolve it.

Assessing the quality of included studies and the reporting quality

We used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system to assess evidence quality [20]. According to the bias risk assessment tool provided by the Cochrane evaluator's manual, the included literature was assessed for bias risk. The contents of bias risk assessment include the generation of random sequences, allocation hiding, implementation bias, follow-up bias, measurement bias, reporting bias. According to the literature content, it was evaluated as "low risk", "high risk" and "unclear".

We evaluated the reporting quality using the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 statement [21], and the Assessment of Multiple Systematic Researchs (AMSTAR) 2 checklist [22]. The PRISMA 2020 (Supplementary Data) statement consists of 27 items in seven domains: Title, abstract, introduction, methods, results, discussion, and funding. According to the reported completeness, each item was answered as "yes", "partial yes" or "no".

Statistical analysis

Meta-analysis was performed using Revman5.3 software. Odds Ratio (OR) and 95% Confidence Interval (CI) of dichotomous variables are applied. Continuous variables were Weighted Mean Value (WMD) and 95% CI were used as therapeutic analysis statistics. Heterogeneity among studies was examined. If $P < 0.1$ and $I^2 \leq 50\%$, the heterogeneity is good, and the fixed effect model is selected. If $P \leq 0.1$ and $I^2 > 50\%$, the heterogeneity is large and the source of heterogeneity is found. If the cause still cannot be determined, the random effect model is selected and the funnel plot is used to analyze publication bias, and the funnel plot is further tested for bias. If the funnel plot is symmetrical

($P \geq 0.05$ according to Egger's test), it indicates that there is no publication bias. If the funnel plot is asymmetrical ($P < 0.05$ according to Egger's test), suggesting the existence of publication bias, correction bias should be used.

RESULTS

Literature search results

Initially, 1,852 literatures were retrieved, among which 1,852 literatures were retrieved through database and 0 literatures were retrieved through other resources. Using note express software, 632 articles were deleted after research, then 622 articles were deleted after reading the title and abstract and 319 articles were deleted after browsing the full text. Finally, 9 literatures were included in this research (Figures 1).

Basic characteristics of the included literature

9 literatures were finally included in this study [23-31], a total of 714 cases were included, 355 of which were in the control group the patients were treated with eutolol or levothyroxine sodium

tablets or Rhatix. Treatment group 359 cases, on the basis of the control group by acupuncture or acupuncture combined with medicine intervention.

Baseline data such as sample size, gender and course of disease were compared between the control group and the treatment group, and it was found that the two groups were well similar and comparable. 9 of them [23-31] described the effectiveness of clinical treatment, 8 literatures [23-25,27-31] described the change of FT3, 9 literatures [23-31] described the changes of FT4, 8 literatures [24-31] described the change of TSH, 8 literatures [24-31] described the change of TgAB, 8 literatures [24-31] described the change of TPOAb, 1 literature [31] described the change of TT4, 5 literature [23-25,27,29] described the change of thyroid volume, 4 literatures [23-25,27] described the change of the variation of isthmus thickness, 2 literatures [23,28] described the change of the total score of TCM syndroms, 1 literature [30] described adverse reactions (Table 1) (Supplementary Table S1 and Supplementary Table S2).

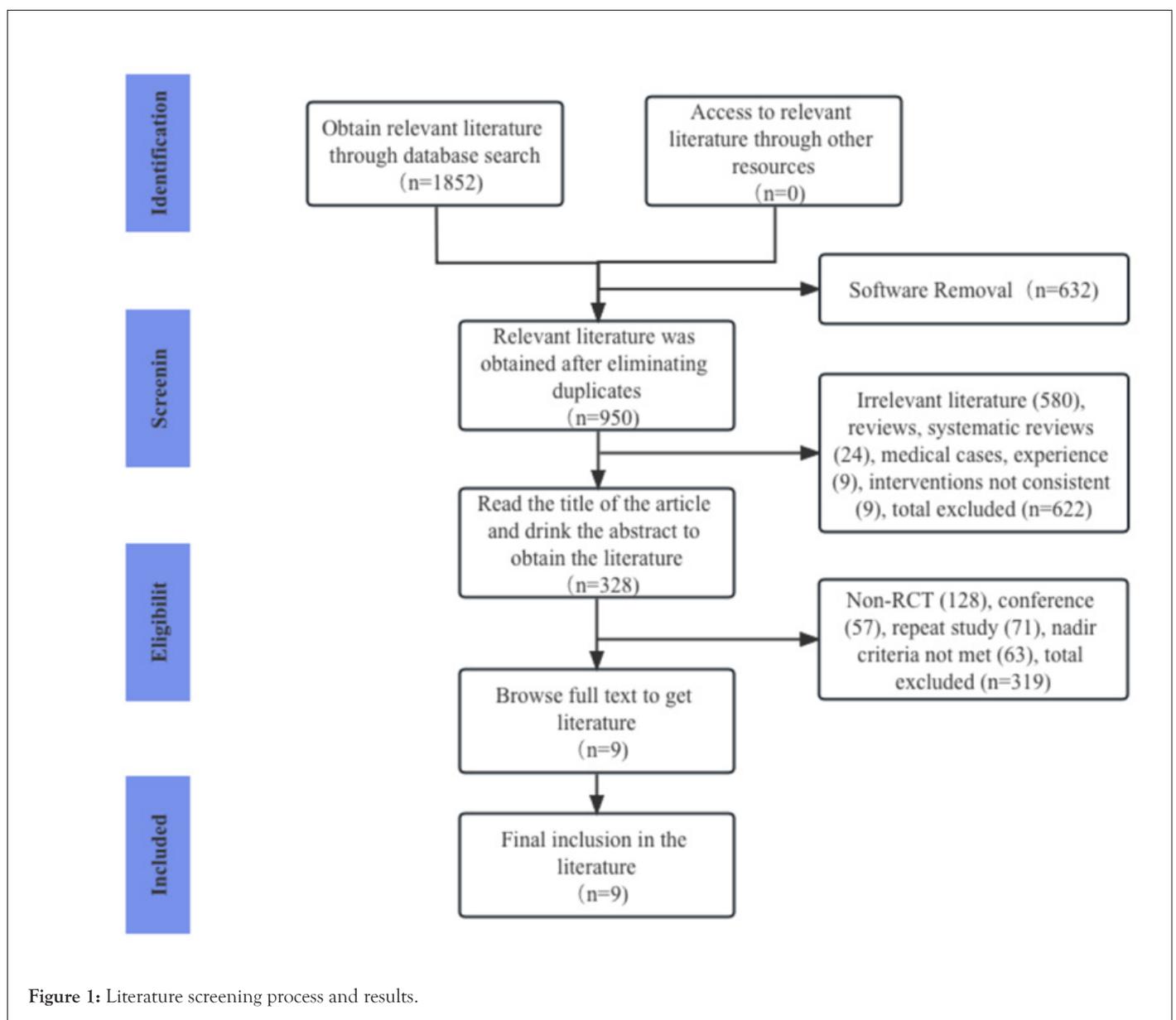


Table 1: Demographic characteristics of participants (N=210). **Note:** T: Interventions; C: Comparations; ①: FT3; ②: FT4; ③: TSH; ④: TgAb; ⑤: TPOAb; ⑥: Thyroid volume; ⑦: Isthmus thickness; ⑧: Total scores of TCM syndromes; ⑨: Total effective rate; ⑩: TMAB

Reference	Year	Sample size		Gender (male/female)		Average age(year)		Course of disease		Intervention		Acupoint	Frequency	Duration	Outcomes	Safety	Follow-up
		T	C	T	C	T	C	T	C	T	C						
Chen(27)	2019	30	30	6, 24	7, 23	39.07 ± 2.45	38.17 ± 2.29	1.20 ± 0.18	1.19 ± 0.22	Acupuncture/ Manipulation	Euthyrox	ST36,SP9,GB34,SP6,KI3,LR3,LI11,SJ13,LU7	qid	3 Weeks	①②③④⑤ ⑥⑦⑧⑨	NR	NR
Zhou(28)	2021	40	40	21, 19	18, 22	34.15 ± 5.74	36.12 ± 4.22	-	-	Acupuncture/ Manipulation/ Euthyrox	Euthyrox	RN4,LR3,RN22,SP6,ST36,ST40,LI4,SJ13	3 times per week	8 Weeks	①②③④⑤ ⑥⑦⑨	NR	NR
Zhou(29)	2019	30	32	8, 22	7, 25	32.5	33.2	-	-	Acupuncture/ Manipulation	Euthyrox	ST36,SP9,GB34,SP6,LR3,SJ5,LU7	qid	30 Days	①②③④⑤ ⑥⑦⑧⑨	NR	3months
Deng(30)	2022	60	60	11, 49	9, 51	41.65 ± 5.49	43.13 ± 5.18	41.65 ± 5.49	3.84 ± 1.43	Jshaped needle knife	Euthyrox	-	1Week,bid;	3 Weeks	①②③④⑤	Yes	NR
Qi(31)	2022	30	32	8, 22	7, 25	31.54 ± 2.53	33.96 ± 3.49	2.67 ± 1.24	2.98 ± 1.65	Acupuncture	Euthyrox	ST36,SP9,GB34,SP6,KI3,LR3,LI11,SJ5	2-3Week,tid	3 Months	①②③④⑤ ⑥⑦⑧⑩	NR	NR
Zheng(23)	2019	50	52	9, 41	4, 48	44.5	42.5	60	36	Moxibustion	Euthyrox	RN22,RN17,RN12,RN4,DU14,BL23,DU4	qod	12 Weeks	①②③④ ⑤⑧⑨	NR	NR
Huang(24)	2022	40	40	4, 36	3, 37	41.43 ± 7.67	39.82 ± 7.21	3.21 ± 1.44	3.42 ± 1.47	Prescription combined with acupuncture	Euthyrox	ST36,SP9,GB34,SP6,KI3,LR3,LI11,SJ5,LU7	Week 1,tid	3 Months	①②③④ ⑤⑧⑨	N	NR
Wu(25)	2021	39	39	25, 14	24, 15	42.86 ± 5.63	42.33 ± 5.34	1.51 ± 0.92	1.46 ± 0.88	Acupuncture	Euthyrox	ST36,SP6,ST40,LI4,LR3,KI3	qid	3 Months	①②③ ④⑤⑨	N	NR
Lin(26)	2017	30	30	2, 28	3, 27	35.27 ± 3.39	34.87 ± 9.16	-	-	Warm acupuncture	Retis	BL20,BL23,DU4,ST40,LR3	qod	12 Weeks	②③④ ⑤⑧⑨	N	NR

Methodological quality evaluation of the included literature

The way random sequences are produced: This study included 9 studies, 7 used random number table method with low risk of bias; the other two studies were only summarized as randomization without specifying the grouping method, so the risk of bias could not be judged.

Allocation hiding: None of the 9 studies described whether random sequences were hidden or not, so bias risk could not be judged (Figure 2).

The implementation of the blind method: Due to the particularity of acupuncture and moxibustion intervention therapy, no blind method was applied to researchers and subjects in the 9 studies, which resulted in a high risk of bias. 9 studies did

not describe whether the outcome of the study was evaluated by blind method, so the risk of bias could not be judged.

Integrity of outcome data: In 3 studies, shedding personnel were explained, and the risk of bias was low; the remaining 6 studies did not describe the absence of personnel, so the risk of bias could not be determined.

Selective reporting outcome: All the 9 studies were described and counted according to the outcome indicators included in the methodology, and there was no selective reporting of outcomes, with a low risk of bias.

Other bias: All the 9 studies had different degrees of information loss, and it was impossible to determine whether there was any other bias (Figure 3).

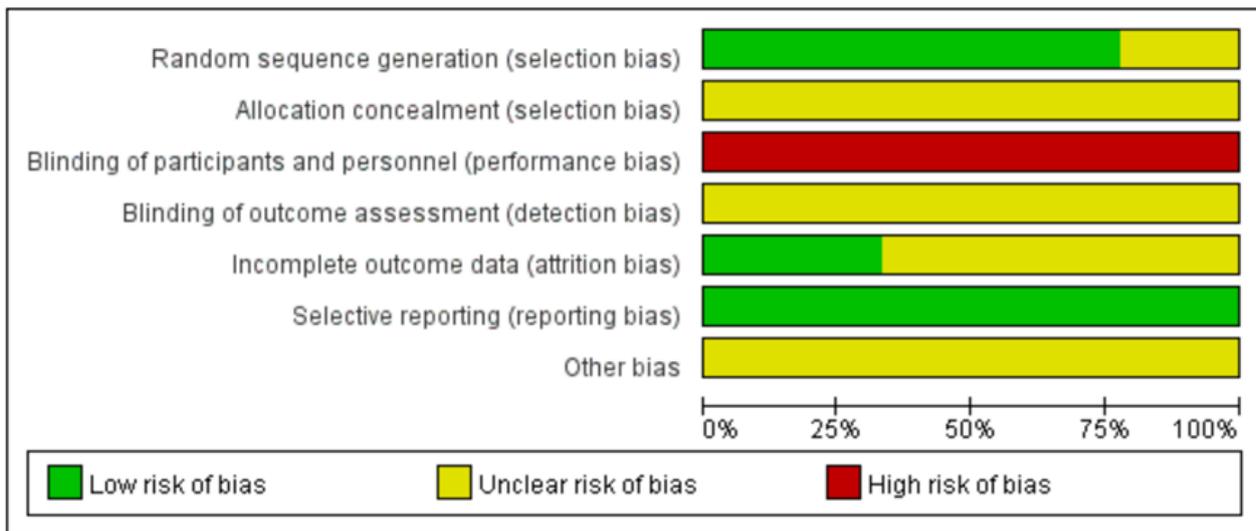


Figure 2: The bias risk assessment of included studies. Note: (Green) Low risk of bias; (Yellow) Unclear risk of bias; (Red) High risk of bias.

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Chen2019	+	?	-	?	+	+	?
Deng2022	+	?	-	?	?	+	?
Huang2022	+	?	-	?	?	+	?
Lin2017	+	?	-	?	?	+	?
Qi2022	?	?	-	?	?	+	?
Wu2021	+	?	-	?	+	+	?
Zheng2019	+	?	-	?	?	+	?
Zhou2019	?	?	-	?	+	+	?
Zhou2021	+	?	-	?	?	+	?

Figure 3: Include methodological quality evaluation.

Meta-analysis

Total effective rate: A total of 9 studies [23-31] described the clinical efficacy of acupuncture in the treatment of Hashimoto's thyroiditis. The heterogeneity of the 9 studies was $I^2=0.0\%$ and $P=0.99$, indicating that the data were homogenous and fixed effect model was adopted. The combined effect size was (OR=4.27, 95%CI [2.71, 6.73]), and the combined effect size test $Z=6.25$, $P<0.00001$. These results indicated that acupuncture and moxibustion had obvious advantages over western medicine in improving the total effective rate of HT (Figure 4a).

FT3: A total of 8 studies [23-25, 27-31] described FT3 in the treatment of Hashimoto's thyroiditis by acupuncture. The heterogeneity of 8 studies was $I^2=93\%$ ($P<0.05$), indicating that the data had heterogeneity and a random effects model was adopted. The combined effect size was (SMD=1.21, 95%CI [0.55, 1.86]), and the combined effect size test $Z=3.59$, $P=0.0003$. It indicated that acupuncture and moxibustion had advantages over western medicine in increasing FT3 in HT treatment (Figure 4b).

FT4: A total of 9 studies [23-31] described FT4 in the treatment of Hashimoto's thyroiditis by acupuncture and moxibustion. The

heterogeneity of the 9 studies was $I^2=94\%$, $P<0.05$, indicating that the data had heterogeneity, and the random effects model was adopted. The combined effect size was (SMD=1.25, 95%CI [0.58, 1.91]), and the combined effect size test $Z=3.69$, $P=0.0002$. It indicated that acupuncture and moxibustion had advantages over western medicine in increasing FT4 in HT treatment (Figure 4c).

TSH: A total of 8 studies [24-31] described the TSH of acupuncture in the treatment of Hashimoto's thyroiditis, and the heterogeneity of 8 studies was $I^2=94\%$, $P<0.05$, indicating that the data had heterogeneity, and random effects model was adopted (Figure 5).

TgAb: A total of 8 studies [24-31] described TgAb in the treatment of Hashimoto's thyroiditis by acupuncture. The heterogeneity of the 8 studies was $I^2=94\%$, $P<0.05$, indicating that the data had heterogeneity, and random effects model was adopted. The combined effect size was (SMD=-2.04, 95%CI [-2.86, -1.23]), and the combined effect size test $Z=4.92$, $P<0.00001$. It indicated that acupuncture and moxibustion had advantages over western medicine in reducing TgAb in HT treatment (Figure 6).

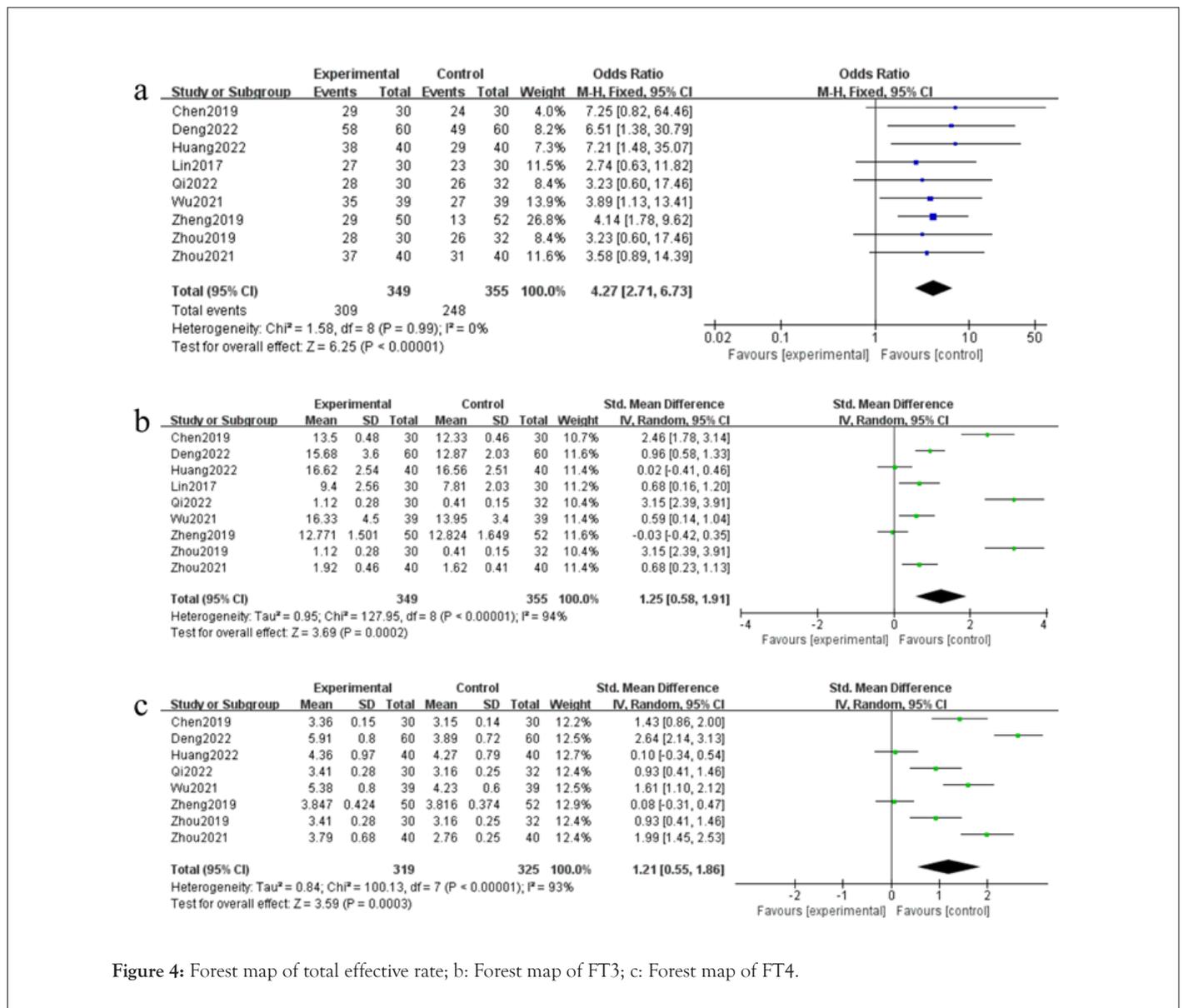


Figure 4: Forest map of total effective rate; b: Forest map of FT3; c: Forest map of FT4.

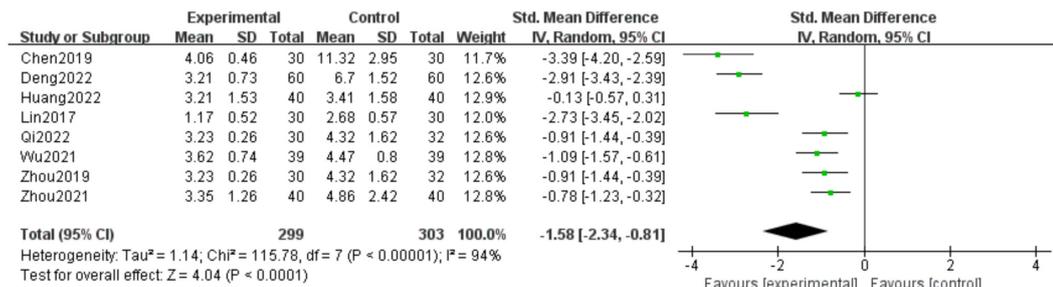


Figure 5: Forest map of TSH.

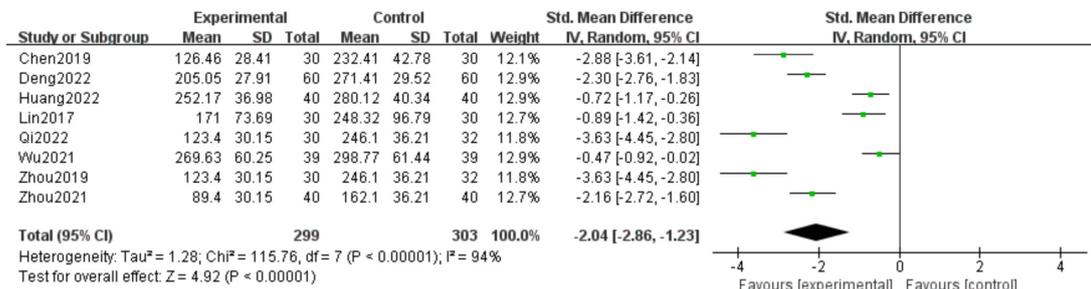


Figure 6: Forest map of TgAb.

TPOAb: A total of 8 studies [24-31] described the TPOAb of acupuncture in the treatment of Hashimoto's thyroiditis. The heterogeneity of 8 studies was $I^2=94\%$, $P<0.05$, indicating that the data had heterogeneity, and random effects model was used. The combined effect size was (SMD=-2.18, 95%CI [-3.04, -1.32]), and the combined effect size test $Z=4.96$, $P<0.00001$. It indicated that acupuncture and moxibustion had advantages over western medicine in reducing TPOAb in HT treatment (Figure 7).

TMAb: A total of one study [31] described TMAb in the treatment of Hashimoto's thyroiditis by acupuncture. The results of meta-analysis (Supplementary Figure S1) showed that the changes of TMAb index in the treatment of HT patients by acupuncture were similar to those in the control group, with no statistical significance ($P=0.54$).

TT4: A total of one study [31] described TT4 in the treatment of Hashimoto's thyroiditis by acupuncture and moxibustion. Meta-analysis results (Supplementary Figure S2) showed that the change of TT4 index in the treatment of HT patients was better than that in the control group, with statistical significance (SMD=0.65, 95%CI [0.13, 1.17], $P=0.01$).

Thyroid volume: A total of 5 studies [23-25, 27, 29] described the thyroid volume in the treatment of Hashimoto's thyroiditis by acupuncture. The heterogeneity of 5 studies was $I^2=22\%$, $P=0.27$, indicating that the data were homogenous and fixed effect model was adopted. The combined effect size was (SMD=-0.93, 95%CI [-1.15, -0.71]) and the combined effect size test $Z=8.13$, $P<0.00001$. It showed that acupuncture and moxibustion had advantages over western medicine in reducing the volume of thyroid gland (Supplementary Figure S3).

Isthmus thickness: A total of 4 studies [23-25, 27] described the isthmus thickness in the treatment of Hashimoto's thyroiditis by acupuncture. The heterogeneity of the 4 studies was $I^2=68\%$, $P=0.03$, indicating that the data had heterogeneity, and the random effects model was adopted. The combined effect size was (SMD=-1.77, 95%CI [-2.29, -1.26]), and the combined effect size test $Z=6.80$, $P<0.00001$. These results indicated that acupuncture and moxibustion had advantages over western medicine in reducing the isthmus thickness (Supplementary Figure S4).

Total scores of TCM syndromes: A total of two studies [23, 28] described the total scores of TCM syndromes in the treatment of Hashimoto's thyroiditis by acupuncture. The heterogeneity of the two studies was $I^2=91\%$, indicating that the data had heterogeneity, and the random effects model was adopted. The combined effect size was (SMD=-1.30, 95%CI [-2.57, -0.03]), and the combined effect size test $Z=2.01$, $P=0.04$. It indicated that acupuncture and moxibustion had advantages over western medicine in reducing the total score of TCM syndromes (Figure 8a).

Publication bias analysis

The "inverted funnel" plot was made to observe and identify whether there was publication bias in the outcome of the total effective rate of acupuncture treatment, and the effect size and standard error were taken as horizontal and vertical coordinates. The results showed that the samples were mostly concentrated at the top of the funnel plot, and the left and right sides were basically symmetrical, indicating that the risk of publication bias was not high (Figure 8b).

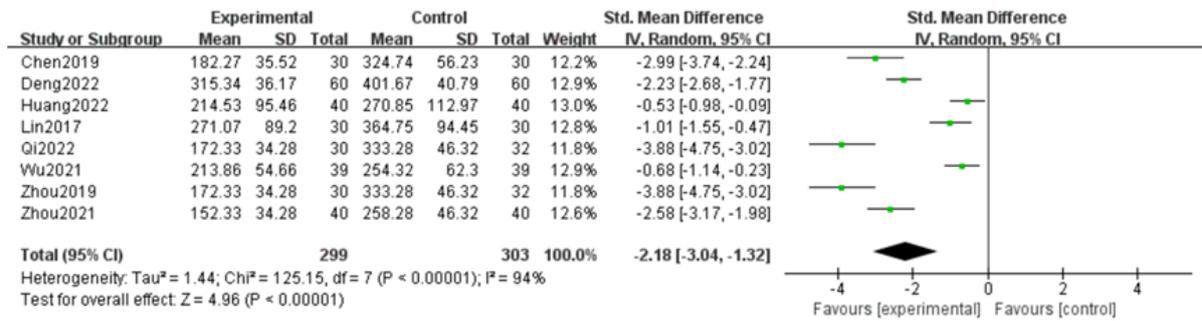


Figure 7: Forest map of TPOAb.

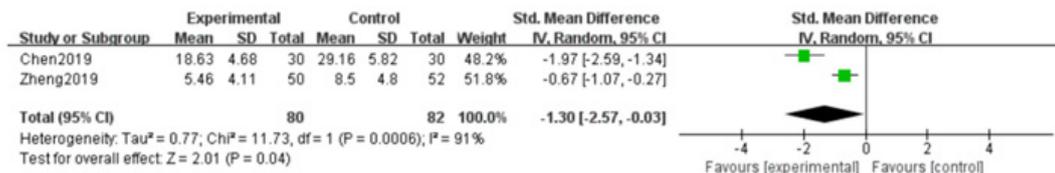


Figure 8a: Forest map of total score of TCM syndromes.

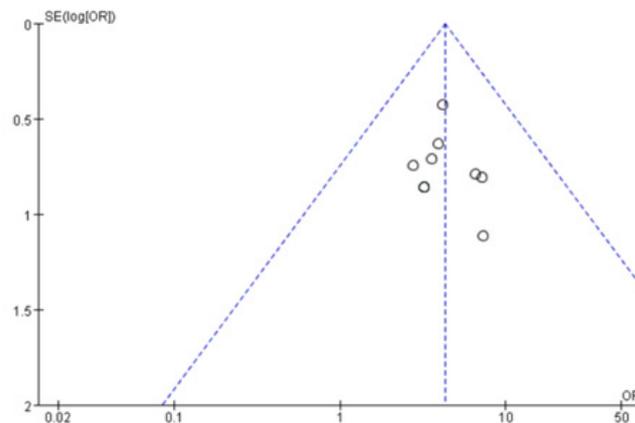


Figure 8b: Funnel plot of total effective rate.

DISCUSSION

TCM considers that this disease belongs to "thyroid nodule," "goiter disease," "consumptive disease," and other categories. Its incidence is mainly related to the emotional disorder, constitution, region, and feeling of the unknown epidemic virus. This disease involves many functional disorders of Zang-fu organs, and the treatment should be based on syndrome differentiation. A thyroid nodule is a disease occurring in the neck due to neck stasis, phlegm, turbidness, and so on, resulting in neck enlargement, and the gain is often benign growth. Traditional Chinese medicine considers Hashimoto's thyroiditis to be within the range of this disease [32]. Therefore, the treatment

should be started by dredging the meridians and collaterals, and acupuncture can be adopted.

The meta-analysis of HT in the previous literature mainly focused on its clinical diagnosis and TCM treatment [33, 34]. Therefore, we conducted the first systematic research and meta-analysis of acupuncture alone in treating Hashimoto's thyroiditis. A total of 9 RCTs were included in this study. In 8 literatures, levothyroxine tablets were used in the control group, and rhatidis was used in 1 study; In 3 literature, acupuncture and moxibustion combined with massage were used in the treatment group; acupuncture alone was used in 3 literatures; 1 paper used warm acupuncture and moxibustion. Acupuncture and moxibustion combined with traditional Chinese medicine prescription treatment. The results

of the meta-analysis showed that acupuncture and moxibustion could significantly improve the level of autoantibodies, thyroid volume, and isthmus thickness in HT patients, and the efficacy of the treatment group was better than that of the control group, with statistical significance. By comparing the levels of FT3, FT4, TSH and TPOAb, and TGAb, it was found that FT3, FT4, TSH and TPOAb, and TGAb in the treatment group were better than those in the control group after treatment. It was confirmed that acupuncture and moxibustion had a better effect on Hashimoto's thyroiditis and were more beneficial in improving the level of thyroid hormone and thyroid-related antibodies in patients. In addition, the safety of the medication showed that only one adverse event was reported in RCTs: An individual patient experienced thrombocytopenia, nausea, and vomiting during the administration of western medicine, and symptoms were relieved after discontinuation of treatment.

The control group was mainly treated with levothyroxine sodium tablets. In the treatment group, the common methods were acupuncture and massage, J-type needle knife, warm acupuncture and moxibustion. The main acupoint are Zusanli (ST36), Yinlingquan (SP9), Yanglingquan (GB34), Sanyinjiao (SP6), Taixi (KI3), Taichong (LR3), Quch (LI11), Waiguan (SJ5), Lieque (LU7), Guanyuan (RN4), Tiantu (RN22), Fenglong (ST40), Hegu (LI4), Ruhui (SJ13), Danzhong (RN17), Zhongwan (RN12), Dazhui (DU14), Shenshu (BL23), Mingmen (DU4), Pishu (BL20). Among them, Taichong (LR3) is the most used, followed by Sanyinjiao (SP6) and Zusanli (ST36). The distribution of these acupoints is in line with the disease position on the top, and the treatment from the bottom and the meridians is the treatment principle where the attending reaches. The Taichong (LR3) acupoint is located in the liver meridian of foot Jueyin, and thyroid disease is mainly related to emotion. Sanyinjiao (SP6) and Zusanli (ST36) are located in the spleen meridian of the foot-Taiyin and the stomach meridian of the foot-Yangming. Thyroid disease is closely related to the region and diet, so selecting these acupoints also aligns with the theoretical knowledge of traditional Chinese medicine of thyroid disease.

CONCLUSION

This research suggests that acupuncture can improve clinical symptoms, such as thyroid hormone levels, patient autoantibodies, TCM symptoms and other parameters, and thyroid volume. However, there are specific reporting and methodological quality limitations, and future research should improve the management process. In addition, the clinical efficacy of acupuncture for HT needs to be demonstrated in high-quality, large sample randomized controlled trials to generate more evidence-based clinical practice.

LIMITATIONS

This study still has the following deficiencies and limitations: Regarding literature quality, the randomized controlled clinical trials included in this paper have shortcomings such as small sample size, incomplete information, and varying degrees of information loss. All nine studies described whether the random sequence was hidden. Many studies did not explain whether the subjects were blinded, whether the study outcome was blindly evaluated, and did not describe the absence of personnel, so the risk of bias could not be judged. The composition of acupuncture prescriptions, intervention duration, and treatment course differed, and there were differences in efficacy. Many studies

did not mention whether adverse reactions occurred during treatment and the lack of safety evaluation programs.

FUNDING

This study was supported by the China's National Key R&D Program, NO. 2019YFC1709801.

AUTHOR'S CONTRIBUTIONS

Zhili Dou and Lei Zhao contributed equally to this work and share co-first authorship.

CONFLICTS OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

REFERENCES

1. Caturegli P, De Remigis A, Chuang K, Dembele M, Iwama A, Iwama S. Hashimoto's thyroiditis: Celebrating the centennial through the lens of the Johns Hopkins hospital surgical pathology records. *Thyroid*. 2013;23(2):142-150.
2. Ahmed R, Al-Shaikh S, Akhtar M. Hashimoto thyroiditis: A century later. *Adv Anat Pathol*. 2012;19(3):181-186.
3. Teng W, Shan Z, Teng X, Guan H, Li Y, Teng D, et al. Effect of iodine intake on thyroid diseases in China. *N Engl J Med*. 2006;354(26):2783-2793.
4. Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: Clinical and diagnostic criteria. *Autoimmun Rev*. 2014;13(4-5):391-397.
5. Duntas LH, Mantzou E, Koutras DA. Effects of a six month treatment with selenomethionine in patients with autoimmune thyroiditis. *Eur J Endocrinol*. 2003;148(4):389-393.
6. van Zuuren EJ, Albusta AY, Fedorowicz Z, Carter B, Pijl H. Selenium supplementation for Hashimoto's thyroiditis. *Cochrane Database of Systematic Reviews*. *Cochrane Database Syst Rev*. 2013;2013(6):CD010223.
7. Anastasilakis AD, Toulis KA, Nisianakis P, Goulis DG, Kampas L, Valeri RM, et al. Selenomethionine treatment in patients with autoimmune thyroiditis: A prospective, quasi-randomised trial. *Int J Clin Pract*. 2012;66(4):378-383.
8. Yue C, Liu XL. Clinical effect of selenium yeast combined with levothyroxine tablets on Hashimoto's thyroiditis. *Int J Clin Exp*. 2015;14(23):35-37.
9. Lv SY, Wan C, Jin YT. Clinical study on the treatment of Hashimoto's thyroiditis by combination of acupuncture and medicine. *Chin Acupunct Moxibustion Society*. 2019:1240-1243.
10. Chen JS, Chen WK. The mechanism of acupuncture and moxibustion regulating immune function. *Liaoning J Tradit Chin Med*. 2006;33(2):210-211.
11. Zhao S, Gu M, Li S. Research progress on the mechanism of acupuncture and moxibustion in preventing and treating allergic rhinitis. *Shanghai J Acupunct Moxibustion*. 2018;37(6):720-724.

12. Wang YP, Du XZ, Zhang ZQ. Research progress on immunomodulatory mechanism of acupuncture treatment for rheumatoid arthritis. *Shanghai J Acupunct Moxibustion*. 2017;36(1):108-112.
13. Hu GS, Chen HP, Hou YJ. Immunological observation of moxibustion in treating Hashimoto's thyroiditis. *Shanghai J Acupunct Moxibustion*. 1990;(4):4-7.
14. Zhang YY, Xia Y, You SJ. Analysis of TCM syndromes of 84 cases of Hashimoto's thyroiditis treated with wormwood. *J Liaoning Univ Tradit Chin Medic*. 2013;15(3):95-96.
15. Dong YZ, Zhao JM, Bao CH, Xu HF, Wu RZ, Shi Z, et al. Reflection and prospect on acupuncture-moxibustion in treating Hashimoto's thyroiditis. *J Acupunct Tuina Sci*. 2016;6(14):443-449.
16. Gates A, Gates M, Duarte G, Cary M, Becker M, Prediger B, et al. Evaluation of the reliability, usability, and applicability of AMSTAR, AMSTAR 2, and ROBIS: Protocol for a descriptive analytic study. *Syst Rev*. 2018;7(1):1-7.
17. Pollock M, Fernandes RM, Hartling L. Evaluation of AMSTAR to assess the methodological quality of systematic reviews in overviews of reviews of healthcare interventions. *BMC Med Res Methodol*. 2017;17:1-3.
18. Lu TT, Lu CC, Li MX, Ke LX, Cai H, Yang KH. Reporting and methodological quality of meta-analyses of acupuncture for patients with migraine: A methodological investigation with evidence map. *J Integr Med*. 2022;20(3):213-220.
19. Choi TY, Ang L, Jun JH, Alraek T, Lee MS. Acupuncture and moxibustion for cancer-related fatigue: An overview of systematic reviews and meta-analysis. *Cancers*. 2022;14(10):2347.
20. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011;64(4):383-394.
21. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group*. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Ann Intern Med*. 2009;151(4):264-269.
22. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: A critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ*. 2017;358.
23. Zheng HD. A multicenter randomized controlled study on the treatment of Hashimoto's thyroiditis by moxibustion with herbal cake. *Shanghai Univ Tradit Chin Med*. 2019.
24. Huang T, Zhou Y, Zhang M. Effects of internal administration of Xiaochaihu decoction combined with Danggui Shaoyao powder combined with acupuncture on thyroid function level and immune factors in Hashimoto's thyroiditis patients. *Chin Contemp Med*. 2022;29(11):49-51.
25. Wu R. Analysis of clinical efficacy and safety of acupuncture in the treatment of Hashimoto's thyroiditis with hypothyroidism. *J Tradit Chin Med Eye, Ear, Nose Throat*. 2021;11(4):216-218.
26. Shi WY, Lin ZH, Luo R, Pan J, Zhou WJ, Liu YH, et al. Clinical observation of warm acupuncture combined with yoga posture method in the treatment of periarthritis with frozen period. *Chin Acupunct Moxibustion*. 2019;39(1):33-36.
27. Chen ZA. Clinical observation of acupuncture combined with massage in the treatment of Hashimoto's thyroiditis [D]. *Hubei Univ Tradit Chin Med*, 2019.
28. Danni Z, Hong YL, Qi FJ. Clinical study of "Guben Tongjing" acupuncture combined with bridge bow manipulation in the treatment of Hashimoto's thyroiditis. *World J Integr Tradit Chin West Med*. 2021;16(6):1108-1112+1118.
29. Danni Z, Hong YL, Wang YC. Clinical analysis of acupuncture combined with bridge arch manipulation in the treatment of 62 cases of hashimoto thyroiditis from liver, spleen and kidney. 2019.
30. Deng CM, Wei CG. Clinical randomized controlled trial of J-type acupotomy for Hashimoto's thyroiditis. *Clin Med Pract*. 2022;31(1):18-20+31.
31. Qi FJ, Zuo XH, Gan SY. Clinical study of bridge arch massage combined with acupuncture in treatment of Hashimoto's thyroiditis. *J Hubei Univ Tradit Chin Med*. 2022; 24(01): 100-102.
32. Teng YJ, Zhang Y, Tan ZM. Effect of Tanshinone combined with Utolol on immune function of Hashimoto's thyroiditis with hypothyroidism. *West Chin Med*. 2019;32(3):102-105.
33. Chu P, Wang C, Tai J. Meta-analysis of the value of thyroid peroxidase expression in the diagnosis of Hashimoto's thyroiditis. *Marker Immunoassay Clin Anal*. 2014;21(1):6-11.
34. Chen JD, Zhao Y, Pei X. Meta-analysis of the efficacy of Chinese prescription in treating Hashimoto's thyroiditis. *Chin J Tradit Chin Med*. 2016;34(4):833-837.