MEDS Chinese Medicine (2024)
Clausius Scientific Press, Canada

DOI: 10.23977/medcm.2024.060404
ISSN 2616-1753 Vol. 6 Num. 4

Meta-analysis of the Therapeutic Effect of Traditional Chinese Medicine on Functional Premature Beats Combined with Anxiety and Depression

Na Huang[1,a], Hongsen Du[2], Xianyue He[1], Zhen Ma[2,b,*]

[1]Shaanxi University of Chinese Medicine, Xianyang, Shaanxi Province, 712000, China
[2]Xi'an Hospital of Traditional Chinese Medicine, Xi'an, Shaanxi Province, 710021, China
[a]huang14794746489@163.com, [b]mazhenyisheng@163.com
[*]Corresponding author

Keywords: Traditional Chinese medicine; functional premature beats; anxiety and depression; meta-analysis

Abstract: To explore the therapeutic effect of traditional Chinese medicine on functional premature beats combined with anxiety and depression using meta-analysis. Search for corresponding keywords in CNKI, VIP, Wanfang, CBM, Pubmed, and the Cochrane Library using computers to search for published randomized controlled trials using traditional Chinese medicine for the treatment of functional premature beats combined with anxiety and depression; The time limit is from the establishment of the database to December 2023. Two researchers conducted literature search and screening, and meta-analysis using Revman 5.4. A total of 10 RCTs studies were ultimately included, with a total of 781 patients. Meta-analysis showed that the combination of Chinese and Western medicine in the treatment of functional premature beats combined with anxiety and depression had a clearer therapeutic effect compared to simple Western medicine treatment. However, due to the limited number of included formulas, further clinical validation of the effect is still needed.

1. Introduction

Functional premature beats are a type of arrhythmia with no organic heart disease. Due to their relatively good prognosis, they are also referred to as benign premature beats. The probability of detecting premature beats through a standard ECG is only 1% to 4%. However, dynamic ECG monitoring over 24 or 48 hours reveals that the incidence of premature beats in healthy populations can be as high as 40% to 75%[1]. Clinical manifestations are diverse, including palpitations, chest tightness, shortness of breath, and a feeling of emptiness. The underlying mechanisms are complex, often associated with excessive smoking and drinking, strong tea, coffee, overexertion, and high stress. As the pressures of modern life increase, the incidence of functional premature beats has also gradually risen and trends younger. Studies have found that patients with these conditions often experience anxiety and depression, which can promote sympathetic nerve excitation and trigger abnormal electrical activity in the heart, thus inducing or exacerbating premature beats and creating

a vicious cycle that severely impacts the quality of life of patients. However, there has been no systematic report on the prevalence of functional premature beats combined with anxiety and depression.

In addition, functional premature beats increase the risk of heart-related adverse events[2], thus necessitating appropriate treatment measures. Clinically, the treatment of functional premature beats combined with anxiety and depression often includes antiarrhythmic medications or radiofrequency catheter ablation, combined with psychotropic medications. However, long-term use of antiarrhythmic drugs can lead to other arrhythmias, and radiofrequency ablation has a certain recurrence rate with lower patient acceptance. Psychotropic medications also have many side effects, and their efficacy is often unsatisfactory.

Traditional Chinese Medicine considers functional premature beats to belong to categories such as "palpitations" and "arrhythmias", while anxiety and depression fall under categories such as "stagnation syndrome", "epilepsy syndrome", and "lily disease". Clinical practice indicates that TCM has considerable efficacy in treating premature beats combined with anxiety and depression. This study systematically evaluates the treatment of functional premature beats combined with anxiety and depression using TCM through a meta-analysis, aiming to provide evidence-based support for the clinical application of TCM in this disease.

2. Data and Methods

2.1. Data Sources and Literature Search Strategy

Published randomized controlled trials (RCTs) related to TCM treatment of functional premature beats combined with anxiety and depression were searched using computerized databases including China National Knowledge Infrastructure (CNKI), VIP, Wanfang Data, China Biomedical Literature Database (CBM), as well as English databases such as Pubmed and the Cochrane Library. The search strategy was: ((Functional premature beat OR Functional ventricular premature beats) AND (Anxiety OR depression OR emotional disorders OR mental disorders)) AND (Chinese Medicine OR Decoction OR Chinese patent drug OR Tablet OR Pill). The search period was from the inception of the database until December 25, 2023.

2.2. Inclusion Criteria

Study Type: Randomized controlled trials (RCTs);

Participants: Patients diagnosed with functional premature beats along with anxiety, depression, or other mental disorders, with no restrictions on diagnostic criteria;

Intervention Measures: The control group received conventional Western medical treatment, which may or may not include psychological intervention; the treatment group received oral decoctions or patent medicines in addition to the control group’s treatment, or oral Chinese medicine as the primary treatment, with no restrictions on dosage forms.

Outcome Indicators: (1) Total effective rate of clinical symptoms; (2) TCM syndrome score; (3) Efficacy assessed by dynamic ECG, with a reduction in premature beat counts over 24 hours defined as effective if reduced by ≥50%, and ineffective if reduced by <50%; (4) Anxiety scale scores; (5) Depression scale scores.

Exclusion Criteria: (1) Duplicated publications; (2) Presence of severe organic heart disease; (3) Premature beats caused by myocarditis, coronary heart disease, hyperthyroidism, or other heart and systemic diseases; (4) Non-compliance with outcome indicators.

2.3. Literature Screening and Data Extraction

Two researchers independently conducted literature searches and screenings. Data extraction and quality assessment of the literature were performed according to the Cochrane Handbook guidelines, with cross-checking between the two researchers. In cases of disagreement during the screening or extraction process, discussions took place between the two researchers or with a third researcher to reach a consensus.

2.4. Statistical Analysis

Meta-analysis was conducted using the Revman 5.4 statistical software provided by the Cochrane Collaboration, with $\chi 2$ tests for analysis combined with I2 tests for heterogeneity assessment. When $P > 0.1$ and $I2 < 50\%$, indicating low heterogeneity among studies, a fixed-effects model was used; otherwise, when $P \leq 0.1$ and $I2 \geq 50\%$, indicating significant heterogeneity, a random-effects model was chosen, and the sources of heterogeneity were further analyzed. Dichotomous variables were represented by relative risk (RR), while continuous variables were represented by weighted mean difference (WMD), both calculated with a 95% confidence interval (95% CI). A funnel plot was used to analyze potential publication bias.

2.5. Quality Assessment of Included Literature

The Cochrane Collaboration's bias risk assessment tool for randomized controlled trials was used to evaluate the randomization methods, blinding, etc., for the included literature, with assessments categorized as "low risk", "high risk", or "unclear risk". Specific criteria included: (1) Random sequence generation; (2) Random allocation concealment; (3) Blinding of participants and personnel; (4) Blinding of outcome assessors; (5) Incomplete outcome data; (6) Selective reporting; (7) Other biases. The evaluation was conducted independently by two researchers, and in cases of disagreement, a third researcher would join the discussion to reach a resolution.

3. Results

3.1. Literature Search Results

A preliminary search yielded 49 articles, and after screening, 10 RCTs were ultimately included [3-12], all of which were conducted in China. A total of 385 subjects were involved. The literature search and screening process is shown in Figure 1.

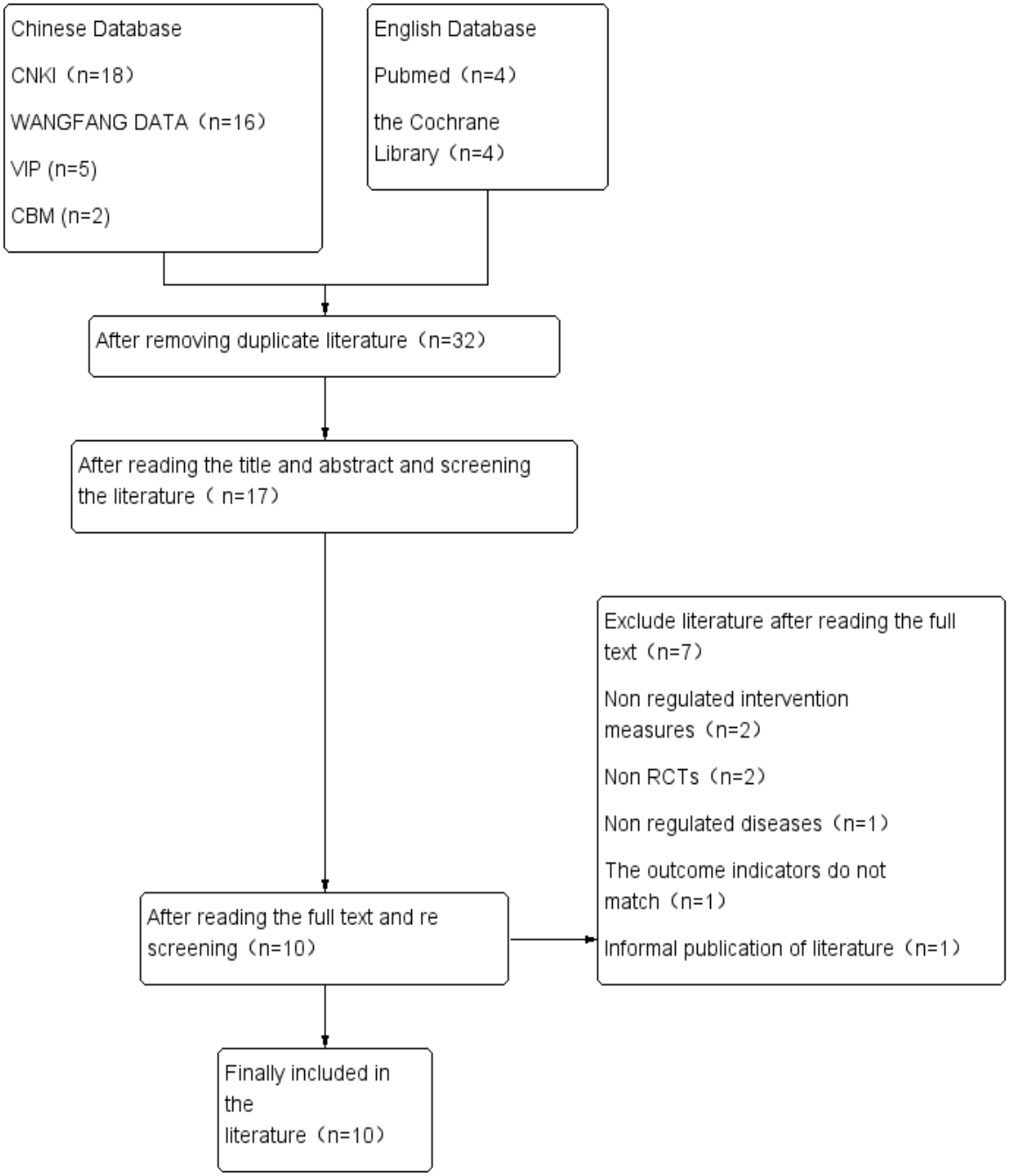

Figure 1: Literature search process

3.2. General Situation and Basic Characteristics of Literature

According to the inclusion and exclusion criteria, a total of 10 articles [3-12] were finally included. The control group was treated with conventional Western medicine, which may or may not include psychological interventions, involving 385 cases in total. The treatment group included patients who received combined Chinese medicine treatment on the basis of the control group, while some were treated mainly with Chinese medicine; there were a total of 396 cases. Other characteristics, such as the intervention measures and the composition of the prescriptions for both groups, can be found in Table 1.

Table 1: Basic characteristics of literature

author	year	Control group	Treatment group	Control group intervention measures	Treatment group intervention measures	course of treatment	Outcome indicators
He QH[3]	2022	42	43	metoprolol tartrate tablets	C + Yiqi Yangyin Anshen decoction	2 weeks	①②③④
Zhang J[4]	2022	30	30	Metoprolol tartrate tablets + placebo	metoprolol tartrate tablets + Yiqi Jianpi recipe	12 weeks	①②③④
Yin T[5]	2021	38	42	mexiletine	C + ShenSongYangXin Capsule + psychotherapy	1 month	①③④
Cai F[6]	2020	31	31	Paroxetine hydrochloride	C + Wenxin decoction	4 weeks	③④
Feng YJ[7]	2020	30	30	metoprolol tartrate tablets	C + Xinkeshu tablets	8 weeks	③④
Guo ZY[8]	2020	68	68	metoprolol tartrate tablets	C + Wuling capsule	4 weeks	③④⑤
Ding YJ[9]	2018	56	56	etoprolol succinate sustained-release tablets + CBT	C + Wenxin Granule	8 weeks	①③④⑤
LI J[10]	2018	30	30	etoprolol succinate sustained-release tablets + alprazolam	C +ShuganDingji Decoction	4 weeks	①②③④
Qin HF[11]	2014	40	46	metoprolol tartrate tablets	ShenSongYangXin Capsule	2 months	①③
Chen YL[12]	2012	20	20	metoprolol tartrate tablets + psychotherapy	Wenxin Jieyu Decoction + psychotherapy	4 weeks	①②③⑤

Outcome measures: ① Total effective rate of clinical symptoms; ② Traditional Chinese Medicine Syndrome Score; ③ Efficacy of dynamic electrocardiogram; ④ Anxiety Scale Score; ⑤ Depression Scale Score

3.3. Assessment of Risk of Bias in Included Studies

The assessment of the risk of bias in the included studies is shown in Figures 2 and 3.

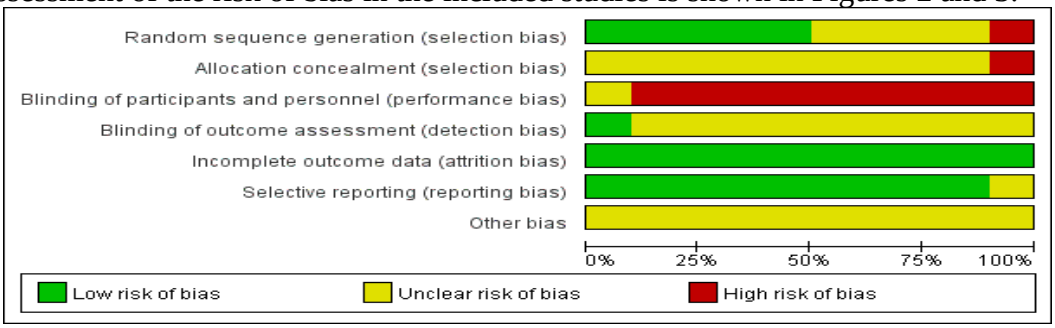

Figure 2: Bias risk assessment results

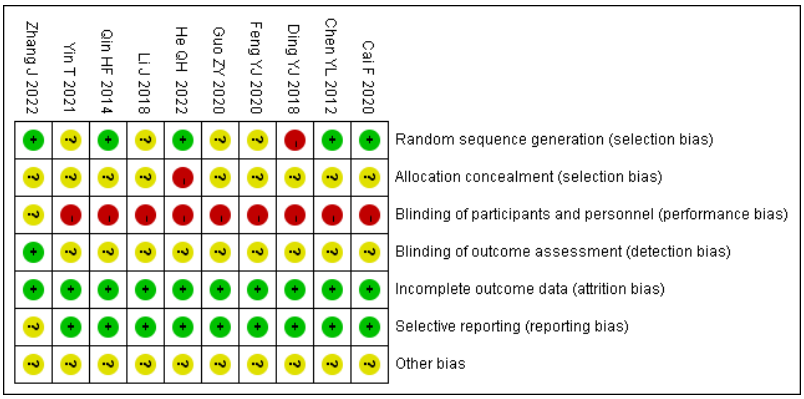

Figure 3: Bias risk assessment results

3.4. Meta-Analysis Results

3.4.1 Overall Clinical Symptom Effective Rate

Seven articles reported the overall effective rate for clinical symptoms. Heterogeneity tests showed mild heterogeneity among studies (P=0.28, I^2=19%). A fixed-effect model was adopted to combine the effect size. The results of the meta-analysis indicated that the overall clinical symptom effective rate in the treatment group was better than that in the control group, and the difference was statistically significant [RR=1.42, 95% CI (1.28, 1.57), P<0.00001]. This suggests that compared to simple Western medicine treatment, combined Chinese medicine treatment or treatment primarily based on Chinese medicine is more effective in improving clinical symptoms of functional premature beats combined with anxiety and depression (as shown in Figure 4).

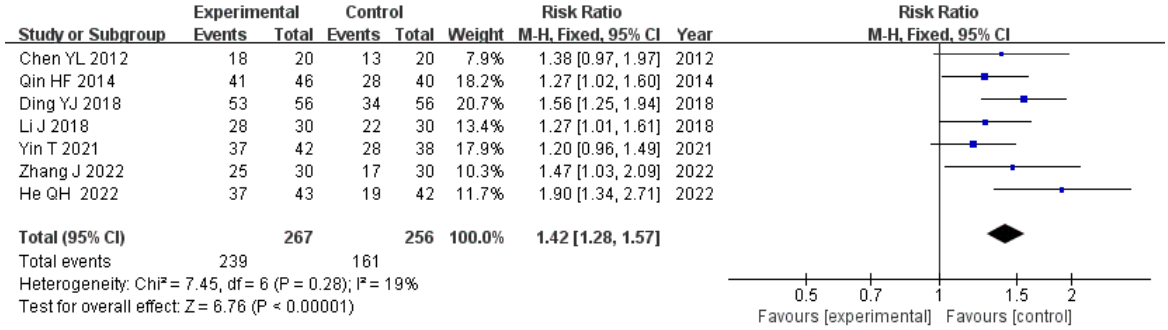

Figure 4: Meta-analysis of overall clinical symptom effective rate

3.4.2 Traditional Chinese Medicine Syndrome Score

Four articles [3, 4, 10, 12] reported on Traditional Chinese Medicine syndrome scores. Heterogeneity tests showed mild heterogeneity among the studies (P=0.16, I^2=42%). A fixed-effect model was adopted to combine the effect size. The meta-analysis results showed that improvement in syndrome scores in the treatment group was better than that in the control group, with a statistically significant difference [MD=-3.92, 95% CI (-4.61, -3.23), P<0.00001] (as shown in Figure 5).

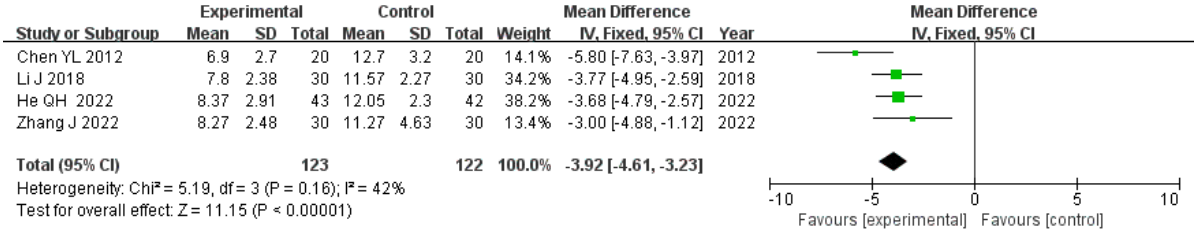

Figure 5: Meta-analysis of traditional Chinese medicine syndrome score

3.4.3 Dynamic Electrocardiogram Efficacy

Eight articles[3,5,7-12] reported on dynamic electrocardiogram efficacy. Heterogeneity tests showed mild heterogeneity among studies (P=0.30, I^2=17%). A fixed-effect model was adopted to combine the effect size. The meta-analysis results indicated that the dynamic electrocardiogram efficacy in the treatment group was better than that in the control group, and the difference was statistically significant [RR=1.19, 95% CI (1.09, 1.30), P<0.0001] (as shown in Figure 6).

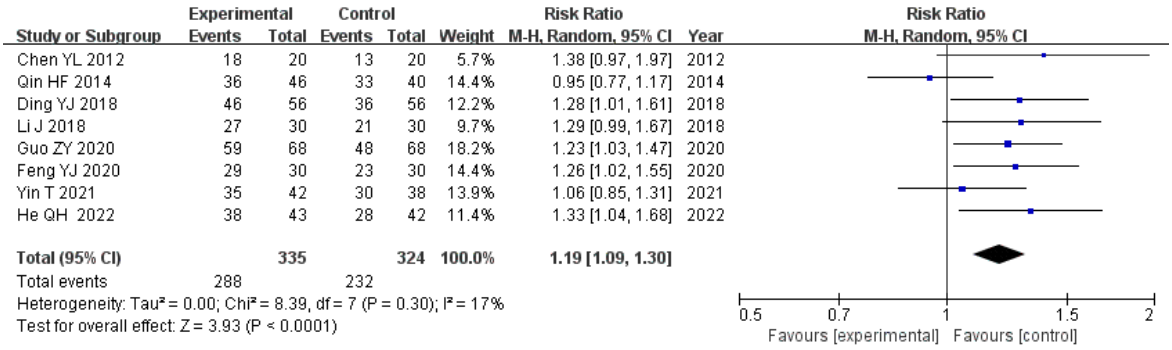

Figure 6: Meta-analysis of dynamic electrocardiogram efficacy

3.4.4 Anxiety Scale Scores

Eight articles [3-10] reported on anxiety scale scores. Heterogeneity tests showed significant heterogeneity among studies (P=0.0002, I^2=76%), and a random-effect model was used. The meta-analysis results indicated that the decrease in anxiety scale scores in the treatment group was better than that in the control group, and the difference was statistically significant [MD=-2.62, 95% CI (-3.47, -1.76), P<0.00001]. Sensitivity analysis showed that the results remained robust, with no directional changes when excluding individual studies (as shown in Figure 7).

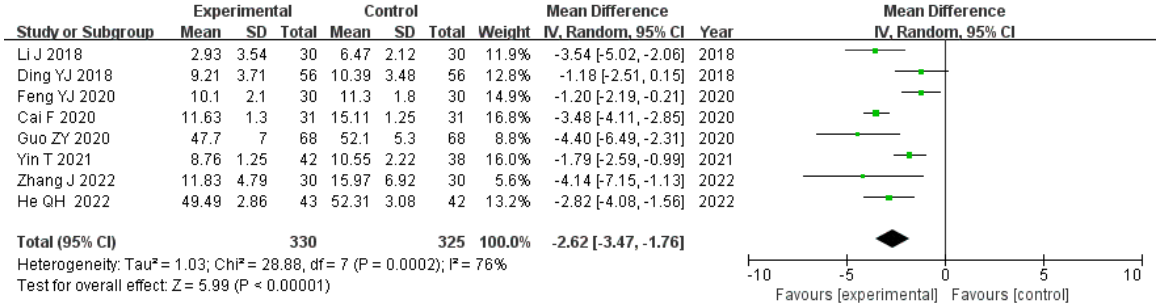

Figure 7: Meta-analysis of anxiety scale score

3.4.5 Depression Scale Scores

Three articles[8,9,12] reported on depression scale scores. Heterogeneity tests showed significant heterogeneity among studies (P=0.003, I^2=83%), and a random-effect model was used. The meta-analysis results indicated that the decrease in depression scale scores in the treatment group was better than that in the control group, and the difference was statistically significant [MD=-3.21, 95% CI (-5.46, -0.96), P=0.005]. Sensitivity analysis showed that the results remained robust, with no directional changes when excluding individual studies (as shown in Figure 8).

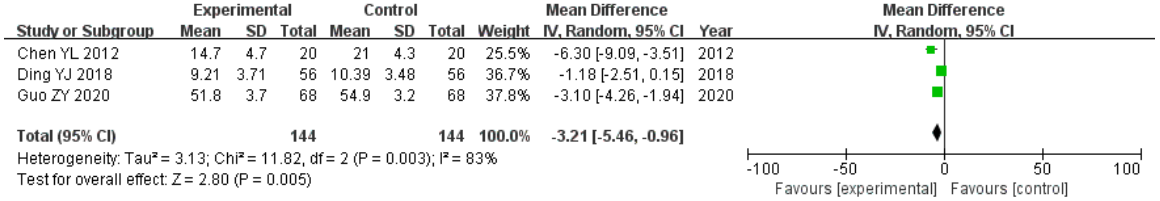

Figure 8: Meta-analysis of depression scale score

3.4.6 Other Results

Two studies[3, 6] reported the effect of the treatment group on sleep, both showing significant

improvement (P < 0.05) in sleep conditions, with increased sleep duration; while the control group showed no significant improvement and had no statistical significance (P > 0.05). Another study[12] pointed out that the traditional Chinese medicine treatment group could improve catecholamine levels in the body, inhibit nerve impulses, and reduce the number of premature ventricular contractions in depressed patients. Scholars[7] compared plasma neuropeptide Y and heart rate variability between the two groups and found that combined Chinese medicine treatment could effectively reduce sympathetic nerve tension and activity, thereby reducing the number of premature ventricular contractions.

3.4.7 Adverse Reactions

A total of seven studies mentioned adverse reactions[3,5-7,9-11], in which three trials[3,7,10] reported no significant adverse reactions, and the other four studies[5,6,9,11] described no statistically significant differences in the incidence of adverse reactions between the two groups (P > 0.05).

4. Discussion

Traditional Chinese medicine holds that "palpitation" and "depression" are both related to the function of the heart spirit, and both conditions can develop when the heart is not nourished and the heart spirit is disturbed. The "Plain Questions Discussing Pain" states, "When one is startled, the heart has no support, the spirit has no home, and there is no certainty in thought, so the qi is disordered." Zhang Jiebing also had the view that "depression always stems from the heart." The main connections between these two conditions are manifested in the relationship between the heart and liver, where in the five elements they are mother and child, and can influence each other; the physiological functions of the heart and liver are related through blood circulation, where the heart governs blood and the liver stores blood, and proper heart qi circulation ensures the liver has blood to store. The heart governs the spirit, and the liver governs the dispersal of qi, so normal liver function allows for the smooth circulation of qi and emotions, thereby nourishing the heart spirit, and they rely on each other, and damage each other in pathology. Therefore, in clinical practice, both heart and liver functions should be improved simultaneously to alleviate premature beats and anxiety and depression symptoms, achieving the effect of treating both heart conditions at the same time[13-14].

The above Meta-analysis shows that for both premature beats and the treatment of anxiety and depression, combined Chinese and Western medicine treatment has clearer efficacy compared to simple Western medicine treatment, and can also improve patient sleep with fewer adverse reactions. The decoctions used in clinical practice mostly aim at benefiting qi and nourishing yin, soothing the liver, calming the heart, and the prescriptions chosen vary from person to person; the commonly used patent medicines are Wenxin Granule and Shensong Yangxin Capsules. The medications often chosen are Danshen, Zhigancao, Suanzaoren, Longgu, Yujin, Xiangfu, Gansong, etc., mostly herbs that benefit qi and calm the spirit, and promote qi circulation and relieve depression.

This study still has the following limitations: (1) all 10 included studies are in Chinese, with general overall quality and possible publication bias; (2) blinding was incomplete or not mentioned in multiple studies; (3) some outcome indicators were included in fewer studies, and the different scales chosen in each study reduced the persuasiveness of the results; (4) there is a lack of large-sample, long-term, high-quality clinical studies.

5. Conclusions

In summary, the results of this study suggest that traditional Chinese medicine has a definite clinical effect when combined with Western medicine in treating functional premature beats combined with anxiety and depression, but the results still need verification, and clinical application should still be based on patient conditions and evidence-based evidence. It is hoped that more related research will be conducted in the future to provide more persuasive evidence-based medicine evidence for clinical treatment and medication.

References

[1] Gorenek B, Fisher J D, Kudaiberdieva G, et al. Premature ventricular complexes: diagnostic and therapeutic considerations in clinical practice: A state-of-the-art review by the American College of Cardiology Electrophysiology Council[J]. J Interv Card Electrophysiol,2020,57(1):5~26.

[2] Lee V, Hemingway H, Harb R, et al. The prognostic significance of premature ventricular complexes in adults without clinically apparent heart disease: a meta-analysis and systematic review[J]. Heart,2012,98(17):1290~1298.

[3] He Qunhui. Clinical Observation of Yiqi Yangyin Anshen decoction on the Treatment of Functional Premature Ventricular Contraction (Deficiency of Qi and Yin) with Mild Anxiety[D]. Henan University of Chinese Medicine,2022.

[4] Zhang Jie, Fang Zezhong, Zhang Dong, etc. Therapeutic effect of Yiqi Jianpi recipe on anxiety disorder complicated with functional premature beats[J]. China Modern Doctor,2022,60(15):129~131, 168.

[5] Yin Ting, Zhang Jing, He Shenghu. Study on the efficacy of Shensong Yangxin capsule combined with psychological intervention in the treatment of functional premature ventricular contractions with anxiety[J]. Chinese Community Doctors, 2021,37(30):112~113.

[6] Cai Fei, Zhou Nanhua, Zhang Jie, etc. Observation of the therapeutic effect of integrated traditional Chinese and Western medicine on anxiety with functional ventricular premature contractions[J]. Modern Practical Medicine, 2020, 32(11): 1389~1391.

[7] Feng Yanjing, Li Sufang, Yin Zhiye, etc. The effect of Xinkeshu tablets combined with metoprolol on neuropeptide Y and heart rate variability in young patients with non organic premature ventricular contractions[J]. Chinese Journal of Integrative Medicine on Cardio-/Cerebrovascuiar Disease,2021,19(13):2226~2229.

[8] Guo Zhiying, Li Yufeng, Chen Zhiqiang, etc. Observation of the therapeutic effect of Wuling capsule combined with metoprolol on functional ventricular premature beats related to anxiety and depression[J]. Electronic Journal of Clinical Medical Literature,2020,7(15):158, 181.

[9] Ding Yujun, Duan Shu, Cai Wenyu, etc. The effect of Wenxin granules on anxiety and depression in patients with functional ventricular premature beats[J]. Modern Journal of Integrated Traditional Chinese and Western Medicine, 2018, 27(35):3929~3933.

[10] Li Jie. the Clinical Observation of ShuganDingji Decoction in the Treatment of Functional Ventricular Premature Beat With Anxiety [D]. Shandong University of Traditional Chinese Medicine,2018.

[11] Qin Haifeng, Liu Xincan, Guo Jiao. Treatment of 46 Cases of Functional Premature Beats with Physical Symptoms with Shensong Yangxin Capsules[J]. Traditional Chinese Medicinal Research,2014,27(12):18~19.

[12] Chen Yongliang, Liu Jianhe, Zhou Xiaoming, etc. Clinical Observation on the Treatment of 40 Cases of Functional Ventricular Premature Contraction with Depression with Wenxin Jieyu Decoction[J]. Guiding Journal of Traditional Chinese Medicine and Pharmacy,2012,18(8):45~48.

[13] Varatharajah Y, Chen H, Trotter A, & Iyer R. K. A Dynamic Human-in-the-loop Recommender System for Evidence-based Clinical Staging of COVID-19. In HealthRecSys@ RecSys, 2020, 21-22.

[14] Chen H, Varatharajah Y, de Ramirez S. S,Arnold P, Frankenberger C, Hota B, & Iyer R. A retrospective longitudinal study of COVID-19 as seen by a large urban hospital in Chicago. medRxiv, 2020, 11.