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Effects of Ten Different Acupuncture Treatments for Angina Pectoris —A Network Meta-Analysis of Randomized Controlled Trials

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Abstract: ***Objective: To evaluate the clinical effects of different acupuncture treatments on Angina Pectoris. Design: Five databases (PubMed, Embase, Cochrane Library, Web of Science, and OVID) were searched from the earliest available dates to August 1, 2023, and only randomized controlled trials (RCTs) were included. Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to examine methodological quality, and Stata 15.1, Engauge Digitizer 11.3, and Office 2019 were used to process the data. Results: A total of 26 RCTs with 1747 patients were included. The network meta-analysis showed that acupoint application significantly reduced patients' Angina Scores (AS) (surface under the cumulative ranking curve [SUCRA]: 74.1%) and improved patients' Pain Scores (PS) (SUCRA: 100.0%). Cupping significantly improved the patients' laboratory results and other tests (LOT) (SUCRA: 60.0%). Electroacupuncture significantly improved the patients' Quality of Life (QoL) (SUCRA: 54.3%). Acupuncture significantly improved patients' Exercise Tests (ET) (SUCRA: 66.7%) and the Seattle Angina Questionnaire (SAQ) (SUCRA: 93.2%). Auricular acupuncture significantly improved patients' Anxiety and Depression Scores (ADS) (SUCRA, 79.5%). Conclusion: Different acupuncture treatments offer advantages for different aspects of angina pectoris, according to the Ranking Plot of the Network.***

Keywords: Acupuncture, Angina pectoris, Network meta-analysis**.**

1. Introduction

Coronary artery disease (CAD) is a heart disease caused by coronary atherosclerosis, which leads to stenosis or obstruction of the coronary artery lumen or myocardial ischemia and hypoxia. Angina pectoris (AP) is a common coronary artery disease characterized by acute and temporary myocardial ischemia and hypoxia due to insufficient blood supply from the coronary artery and paroxysmal precordial compression. Angina pectoris is divided into stable and unstable angina pectoris. Stable angina pectoris is characterized by compression pain or suffocation of the precordial region. Unstable angina has the same symptoms and is characterized in three ways: (i) resting angina, (ii) new-onset angina, and (iii) crescendo angina [1,2]. According to the World Health Organization (WHO), cardiovascular disease (CVD) is the leading cause of death worldwide. An estimated 17.9 million people died from CVD, representing 31% of all deaths globally. More than three-quarters of these CVD deaths occur in low- and middle-income countries, with China as an example. It is estimated that there are approximately 330 million patients with CVD in China, of which 11.39 million are diagnosed with coronary heart disease. In 2020, CVD mortality in China still ranks first, up to 4.58 million. The mortality rate of urban residents is 126.91/100 000, and that of rural residents is 135.88/100 000 [3]. A higher proportion of economically disadvantaged rural areas is observed in urban areas. For the treatment of angina pectoris, β-blockers, calcium-channel blockers, and short-acting nitrates are still classified as the first choice. Double or triple therapies are often used. The efficacy of these drugs in reducing symptoms of angina pectoris is obvious, but there is no evidence of improvement in survival [4]. Percutaneous coronary intervention (PCI) is also recommended for unstable angina pectoris, and is better than drugs alone. However, PCI itself can lead to irreversible myocardial injury and cardiac dysfunction, which is called myocardial ischemia-reperfusion injury (MIRI) [5].

Acupuncture is a traditional Chinese medicine practice characterized by the insertion of a fine metal needle through the skin of the human body at an acupoint. Modern medical research has found that acupuncture and moxibustion can activate various receptors in the body, among which acupuncture mainly activates various mechanoreceptors [6,7] and moxibustion mainly activates temperature receptors. Both can activate multiple nociceptors. Multiple types of nociceptors mainly connect Aδ-type and C-type fibers [7,8], and their information has two directions at the level of the spinal ganglion: (i) transmission to the associated internal organs via dorsal root reflexes and axonal reflexes, and (ii) the cascade of homeostatic regulation, such as endocrine-immune regulation, is activated at the spinal ganglion, spinal cord, brain, and other levels. In the last few decades, TCM practitioners have made persistent efforts and have published a number of well-designed clinical trials regarding the efficacy of acupuncture in angina pectoris. Holli's trial [9] showed that acceptability scores were significantly higher in the acupuncture group (87.9%) than in the control group (51.7%). Lin, L [10] observed changes in endothelin (ET) and nitric oxide (NO) in electroacupuncture and control groups. After treatment, the results of two groups were control group: 115.619.38 pg/mL (ET), 49.429.39 pg/mL (NO) and electroacupuncture group: 66.2311.20 pg/mL (ET), 54.2321.03 pg/mL (NO). However, it is obvious that there can be limitations to these randomized controlled trails (RCTs) with small patient sample sizes. Therefore, this study aimed to (i) systematically review all observational studies on various acupuncture treatments for angina pectoris and (ii) confirm the effectiveness of acupuncture in the treatment of angina

pectoris.

2. Materials and Methods

2.1 Search Strategy

We systematically searched five electronic databases (PubMed, Embase, Cochrane, Web of Science, and Ovid) from inception to July 1, 2023. The PICOS model was used as the search strategy. PICOS stands for five different components: (P) patients: patients with angina pectoris; (I) intervention: acupuncture; (C) comparison: control group with only standard of care or another type of acupuncture treatment; (O) outcomes: angina pectoris-related tests; (S) study type: RCTs. Using PubMed as an example, Table 1 shows a detailed search strategy (Table 1).

Table 1: Search strategy on PubMed.

#1	(Angina Pectoris [MeSH Terms]) OR (Angina, Stable [MeSH Terms])
#2	((((((((((((((((((Angina Pectoris) OR (Angina, Stable)) OR (Stenocardia)) OR (Stenocardias)) OR (Angor Pectoris)) OR (Anginas, Stable)) OR (Stable Angina)) OR (Stable Anginas)) OR (Chronic Stable Angina)) OR (Angina, Chronic Stable)) OR (Anginas, Chronic Stable)) OR (Chronic Stable Anginas)) OR (Stable Angina, Chronic)) OR (Stable Anginas, Chronic)) OR (Angina Pectoris, Stable)) OR (Angina Pectori, Stable)) OR (Pectori, Stable Angina)) OR (Pectoris, Stable Angina)) OR (Stable Angina Pectori)) OR (Stable Angina Pectoris)
#3	(#1) OR (#2)
#4	((((Acupuncture[MeSH Terms]) OR (Acupuncture Therapy[MeSH Terms])) OR (Acupuncture, Ear[MeSH Terms])) OR (Moxibustion[MeSH Terms])) OR (Electroacupuncture[MeSH Terms])
#5	((((((((((((((((((((Acupuncture) OR (Acupuncture Therapy)) OR (Acupuncture, Ear)) OR (Moxibustion)) OR (Electroacupuncture)) OR (Pharmacopuncture)) OR (Acupuncture Treatment)) OR (Acupuncture Treatments)) OR (Treatment, Acupuncture)) OR (Therapy, Acupuncture)) OR (Treatment, Pharmacoacupuncture)) OR (Pharmacoacupuncture Therapy)) OR (Therapy, Pharmacoacupuncture)) OR (Acupotomy)) OR (Acupotomies)) OR (Acupunctures, Ear)) OR (Ear Acupunctures)) OR (Auricular Acupuncture)) OR (Ear Acupuncture)) OR (Acupuncture, Auricular)) OR (Acupunctures, Auricular)) OR (Auricular Acupunctures)) OR (Moxabustion)
#6	(#4) OR (#5)
#7	(#3) AND (#6)

2.2 Inclusion Criteria

(1) Studies with angina pectoris as the target disease; (2) experimental group with different acupuncture treatments as an intervention; (3) control group with standard of care treatments or another acupuncture treatment; (4) clinical randomized controlled trial; and (5) studies using at least one of the following outcome indicators: angina scores, laboratory and other tests, exercise tests, anxiety and depression scores, Seattle Angina Questionnaire, and pain scores.

2.3 Exclusion Criteria

(1) papers from conferences, congresses, meeting abstracts, protocols, reviews, systematic reviews, case reports, correspondences, or animal studies, and (2) papers with incomplete or unreported data.

2.4 Study Selection

EndNote X9 was used to manage the references. Two independent investigators (Y.L. and S.L.) screened the titles for duplication, conference/congresses/ meeting abstracts, protocols, reviews, systematic reviews, case reports, correspondences, or animal studies. The two investigators read the abstracts to identify the literature for inclusion and exclusion. The full text of the remaining studies was further identified. During this process, a third investigator (H.F.Q.) supervised the search and adjudicated any disagreement.

2.5 Data Extraction

The extracted data included nine items: (1) author, (2) year of publication, (3) country, (4) study period, (5) sample size, (6) mean age, (7) details of acupuncture treatment, (8) patient, and (9) outcome indicators [11].

2.6 Risk of Bias of Individual Studies

Risk of bias (ROB) was independently assessed by two researchers according to version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) [12]. The five domains were considered as follows: (1) bias arising from the randomization process, (2) bias due to deviations from intended interventions, (3) bias due to missing outcome data, (4) bias in the measurement of the outcome, and (5) bias in the selection of the reported result. Trials were categorized into three levels of RoB: high risk (at least one high-risk concern), medium risk (there exists no high risk and one medium risk concern at least), and low risk (less than five low-risk concerns).

2.7 Data Analysis

In studies where acupuncture was the intervention, all variables were continuous and expressed as means with standard deviation (SD) [13]. Comparisons of continuous variables in the study were reported as mean difference (MD = absolute difference between the means of two groups, defined as the difference in means between the treatment and control groups and calculated using the same scale) or standardized mean difference (SMD =mean difference in outcome between groups/standard deviation of outcome between subjects, used to combine data when trials with different scales) with 95% confidence intervals (CI) and analysis. As there are certainly potential differences across studies, we chose a random-effects model for analysis rather than a fixed-effects model [14].

We used Stata software (version 15.1) and performed NMA aggregation and analysis using Markov chain Monte Carlo simulation chains in a Bayesian-based framework according to the PRISMA NMA instruction manual [15,16]. We used the nodal method to quantify and demonstrate the agreement between indirect and direct comparisons, calculated using the instructions in the Stata software, and if the P-value was > 0.05, the consistency test was passed [17].

The Stata software was used to present and describe the network diagrams of the different acupuncture treatments. In the generated network diagrams, each node represents a different acupuncture treatment or standard-of-care treatment, and the lines connecting the nodes represent direct head-to-head comparisons between different treatments. The size of each node and width of the connecting lines are proportional to the number of studies [18].

The intervention hierarchy was summarized and reported as a P score. The P score is considered a frequentist analog of the surface under the cumulative ranking curve (SUCRA) values and measures the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments. The P score ranges from 0 to 1, where 1 indicates the best treatment with no uncertainty and 0 indicates the worst treatment with no uncertainty. While the P score or SUCRA can be usefully re-expressed as the percentage of effectiveness or acceptability of acupuncture treatments, such scores should be interpreted cautiously unless there are clinically meaningful differences between interventions [19]. To check for the presence of bias due to small-scale studies, which may lead to publication bias in NMA, a network funnel plot was generated and visually inspected for symmetry [20].

3. Results

3.1 Study and Identification and Selection

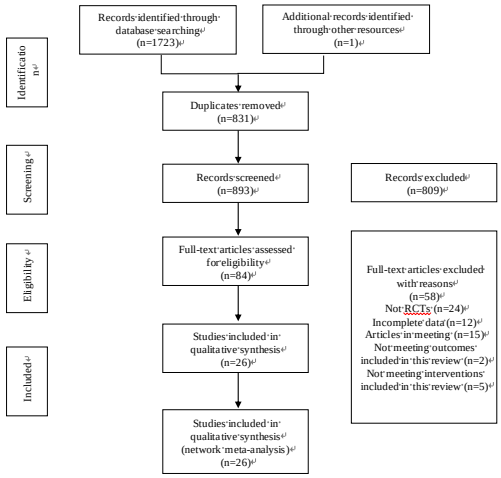

Figure 1: Flow diagram of literature selection

As shown in Figure 1, 1723 publications were retrieved from the electronic database, and one additional publication was manually searched. After eliminating duplicates, the titles and abstracts of the remaining 893 publications were screened and 809 publications were excluded. The remaining 84 publications were read in full text, and 58 publications were excluded (for reasons including non-randomized controlled trials, incomplete data, articles from meetings, and failure to meet the outcomes or interventions included in this review), leaving a final 26 publications to be included in this trial.

3.2 Quality Assessment of the Included Studies

Among the 26 quasi-experimental trials, 17 were defined as low-risk and nine as medium risk. In 16 trials, the lack of double-blinding may have led to systematic differences in the care provided between the experimental and control groups, with deviations from the intended interventions. Details are presented in Supplementary Table 1.

3.3 Characteristics of the Included Studies

A total of 26 randomized controlled trials involving 1747 patients diagnosed with angina pectoris were included. Interventions in the control group included acupoint application (three studies) [21-23], acupoint pressing (two studies)[24,25], acupuncture (13 studies) [9,26-37], acupuncture + cupping (one study) [38], auricular acupuncture (two studies) [39,40], cupping (one study) [41], electroacupuncture (two studies) [10,42], scraping (one study) [43], sparrow pecking method (one study), and needle-embedding therapy(one studies)[44]. Eleven trials reported angina scores as an outcome indicator, 12 trials reported laboratory and other tests as an outcome indicator, seven trails reported exercise tests as an outcome indicator, five trails reported anxiety and depression scores as an outcome indicator, eight trails reported the Seattle Angina Questionnaire as an outcome indicator, and seven trails reported pain scores as an outcome indicator. There were 19 trials from China, two written by the same author from America, two written by the same author from Denmark, and one each from Iran, Japan, and Sweden. The characteristics of the included studies are summarized in Table 2.

Table 2: Characteristics of the trials included in the meta-analysis.

Author	Country	Year	Patient	Age(mean±SD)	Total/male/female	Intervention	Control	Outcome
Zhao, L.	China	2019	angina pectoris	T:62.5±9.9 C:62.6±9.7	T:99/35/64 C:99/39/60	Acupuncture Length of Intervention: 4_weeks Freq: 3_times a week Duration: 30_mins	CON	frequency of angina attacks VAS score Use of rescue medicine Score of SAS Score of SDS 6-Minute walk distance test Seattle Angina Questionnaire
Lin, L.	China	2016	angina pectoris	T:52.9±7.3 C:50.9±6.0	T:45/23/22 C:45/21/24	Acupuncture Length of Intervention: 8_weeks Freq: 1_time a week Duration: 25_mins	CON	vasoactive substances: ET, NO
Ballegaard, S.	Denmark	1986	angina pectoris	T:54±7.5 C:58±7	T:13/12/1 C:13/11/2	Acupuncture Length of Intervention: 3_weeks Freq: 7_times 3_weeks Duration: 20_mins	CON	exercise tests No. of anginal attacks Nitroglycerin consumption
Lan, L.	China	2022	angina pectoris	T:65.20±5.967 C:65.86±7.675	T:15/6/9 C:14/8/6	Acupuncture Length of Intervention: 2_weeks Freq: 5_times a week Duration: 30_mins	CON	Frequency of angina attacks McGill pain score SAS score SDS score
Devon, H. A.	USA	2021	angina pectoris	59±12	24/9/15	Acupuncture Length of Intervention: 5_weeks Freq: 2_times a week	CON	Pain Seattle Angina Questionnaire
Li, X.	China	2015	angina pectoris	T:46.7±7.5 C:44.7±7.25	T:30/9/21 C:21/5/16	Acupuncture Length of Intervention: 30_days Freq: once a day Duration: 30_mins	CON	Dynamic electrocardiogram: duration of myocardial ischemia
Bao, K. J.	China	2016	angina pectoris	T:63±6 C:64±6	T:30/14/16 C:30/12/18	Acupuncture Length of Intervention: 14_days Freq: once a day Duration: 12h	CON	Frequency of angina attack duration of angina attack pain degrees
Tan, X. H.	China	2016	angina pectoris	T:65.58±8.74 C:64.66±8.01	T:33/16/17 C:32/15/17	Acupuncture Length of Intervention: 30_days Freq: once a day Duration: 20_mins	CON	Plasma TXB2 Plasma 6-k-PGF1
Dai, J. Y.	China	1998	angina pectoris	T:59.4±8.5 C:57.4±8.75	T:20/14/6 C:18/12/6	Acupuncture Length of Intervention: 12_days Freq: once a day Duration: 30_mins	CON	blood rheology
Dai, J. Y.	China	1997	angina pectoris	T:62.6±6.7 C:61.5±7.1	T:40/23/17 C:20/11/9	Acupuncture Length of Intervention: 4_weeks Freq: once a day Duration: 24h	CON	Cholesterol level Triglycerides level blood hemorheology
Yin, Lun Hui	China	2009	angina pectoris	T:52.6±4.8 C:52.2±5.0	T:42/24/18 C:38/22/16	Acupuncture Length of Intervention: 30_days Freq: once a day Duration: 30_mins for acupuncture and 10_mins for cupping	CON	exercise tests frequency of anginal attacks duration of angina attack Nitroglycerin consumption
Wang, Y. M.	Sweden	2011	angina pectoris	T:49.2±7.5 C:54.3±9.4	T:58/32/26 C:56/29/27	Duration:5 to 10_mins	CON	onset time of angina pectoris was terminated
Richter, A.	China	1991	angina pectoris	57±9.5	21/19/2	Acupuncture Length of Intervention: 4_weeks Freq: 3_times a week Duration: 30_mins	CON	Chest pain score at maximal workload Maximal workload until onset of chest pain Maximal workload Number of anginal attacks ST-segment depression at maximal comparable workload
Kurono, Y.	Japan	2002	angina pectoris	T:63.9±8.9 C:58.4±12.0	T:10/6/4 C:6/2/4	Duration: 10_mins for acupuncture or 2_mins for sparrow pecking method	Sparrow pecking method	Coronary Diameter
Lan, T.	China	2022	angina pectoris	60.43±5.56	90/58/32	Acupuncture Length of Intervention: 4_weeks Freq: 6_times a week Duration: 20_mins	CON	Hemodynamic indexes Left ventricular parameters Serum myocardial enzymes level Cytokines level

								T lymphocytes level
Li, D. H.	China	2021	angina pectoris	T:67.03±9.37 C:67.88±8.89	T:59/26/33 C:62/22/40	Acupuncture Length of Intervention: 4_weeks Freq: 3_times a week Duration: 6 to 8h	CON	Frequency of Anginal Attacks Nitroglycerin Consumption VAS Score SAS Score SDS Score Seattle Angina Questionnaire
Ballegaard, S.	Denmark	1990	angina pectoris	T:67±7.25 C:66±6.5	T:24/19/5 C:25/19/6	Acupuncture Length of Intervention: 3_weeks Freq:10_times 3_weeks Duration: 10_mins	CON	exercise test
Mao, X.	China	1993	angina pectoris	T:57.53±8.19 C:54.92±9.24	T:30/21/9 C:30/21/9	Acupuncture Length of Intervention: 10_days Duration: 30_mins	CON	Blood Lipids and Blood Sugar
Liu, W. P.	China	2004	angina pectoris	T:58±34 C:57.3±3.6	T:32/26/6 C:30/25/5	Acupuncture Length of Intervention: 4_weeks Freq: 13_days for treatment, 2_days for rest, and 13_days for treatment Duration: 20_mins	CON	vasoactive substances: NO
Devon, H. A.	USA	2022	angina pectoris	59±12	24/9/15	Acupuncture Length of Intervention: 5_weeks Freq: 2_times a week Duration: 30_mins	CON	Pain Seattle Angina Questionnaire
Wang, M.	China	2015	angina pectoris	T:59±2.75 C:57±3.75	T:15/7/8 C:15/6/9	Acupuncture Length of Intervention: 4_weeks Freq: 3_times a week Duration: 30_mins	CON	Frequency of Anginal Attacks Nitroglycerin Consumption VAS Score SAS Score SDS Score Seattle Angina Questionnaire 6-Minute walk distance test Neutrophile granulocyte Neutrophil/lymphocyte ratio, NLR
Abazari, M.	Iran	2022	angina pectoris	T:49.4±6.99 C:54.4±9.6	T:10/10/0 C:10/10/0	Duration: 5_mins	CON	exercise test SBP DBP Seattle angina questionnaire VAS
Deng, J.	China	2018	angina pectoris	T:57.12±9.78 C:56.49±11.36	T:38/27/11 C:38/22/16	Acupuncture Length of Intervention: 4_weeks Freq: 3_times a week Duration: 24h	CON	Seattle angina questionnaire
Huang, S.	China	2021	angina pectoris	T:66.06±9.11 C:66.22±10.02	T:109/46/63 C:93/45/48	Acupuncture Length of Intervention: 4_weeks Freq: 3_times a week	CON	frequency of angina attacks
Tang, X.	China	2021	angina pectoris	T:56.15±10.51 C:55.27±9.55	T:60/32/28 C:60/36/24	Acupuncture Length of Intervention: 4_weeks Freq: 2_times a week	CON	Frequency of angina attacks Duration of attack Nitroglycerin dosage inflammatory factor blood flow indexes
Zhang, J. Z.	China	2021	angina pectoris	T:62.77±11.08 C:66.85±9.58	T:35/24/11 C:34/21/13	Acupuncture Length of Intervention: 4_weeks Freq: once a week Duration: 5_days	CON	Hamilton Anxiety Scale, HAMA Seattle angina questionnaire

Note: CON, control group with standard of care treatments (no acupuncture treatments); T, experimental group; C, control group; Freq, frequency; VAS, visual analog scale; SAS: Self-rating anxiety scale; SDS: Self-rating depression scale; TXB2, Thromboxane B2; 6-k-PGF1,6-keto-prostaglandin F1, SBP: Systolic blood pressure; DBP, diastolic blood pressure.

3.4 Network Meta-Analysis

The full NMA is shown in Figures 2A, 3A, 4A, 5A, 6A and 7A.

3.4.1 Angina Scores

We tested for consistency and inconsistency in all p-values for indirect and direct comparisons between studies. Most p-values were >0.05, indicating that the effect of consistency between the studies was acceptable. The details are provided in Supplementary Table 2.

The results of the network meta-analysis showed that compared to the control group's conventional treatments, acupoint application [MD -4.23, 95%CI (-8.12,-0.34)], acupoint pressing [MD -0.98, 95%CI (-4.89,2.94)], acupuncture [MD -2.30, 95%CI (-5.97,1.37)], Acupuncture + Cupping [MD -2.10, 95%CI (-7.91,3.71)], electroacupuncture [MD -4.60, 95%CI (-10.92,1.72)], and scraping [MD -2.99, 95%CI (-8.89,2.90)] were superior to the control group in reducing Angina Scores. The probability ranking of the different acupuncture treatments in terms of reducing Angina Scores was first in the SUCRA for acupoint application (SUCRA:74.1, Figure 2B). A comparison of the two treatments is shown in Figure 8A.

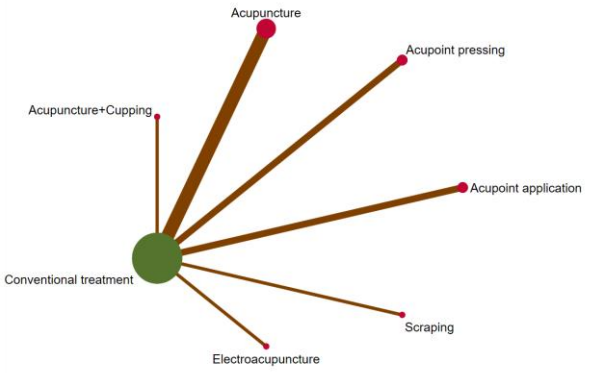

Figure 2A: NMA figure for Angina Scores.

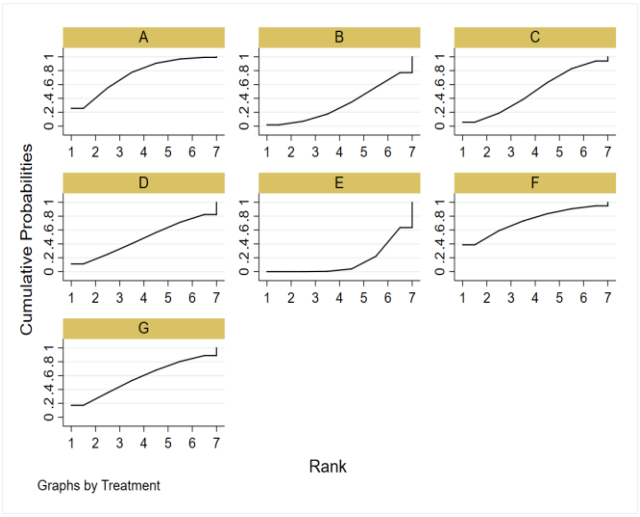

Figure 2B: SUCRA plot for Angina Scores.

3.4.2 Laboratory and other tests (LOT)

We tested for consistency and inconsistency in all p-values for indirect and direct comparisons between studies. Most p-values were >0.05, indicating that the effect of consistency between the studies was acceptable. The details are provided in Supplementary Table 2.

The results of the network meta-analysis showed that compared to the control group's conventional treatments, acupoint application (MD -1.45, 95%CI (-15.76,12.86)], acupuncture [MD -4.44, 95%CI (-14.70,5.83)], auricular acupuncture [MD -0.89, 95%CI (-21.34,19.56)], cupping [MD -6.15, 95%CI (-33.80,21.49)], electroacupuncture [MD -4.41, 95%CI (-20.19,11.36)], scraping [MD -3.76, 95%CI (-18.82,11.30)],and the sparrow pecking method [MD -0.19, 95%CI (-24.73,24.35)] were superior to the control group in reducing LOT. The probability ranking of the different acupuncture treatments in terms of LOT reduction was ranked first in the SUCRA for Cupping (SUCRA:60.0, Figure 3B). A comparison of the two treatments is shown in Figure 8B.

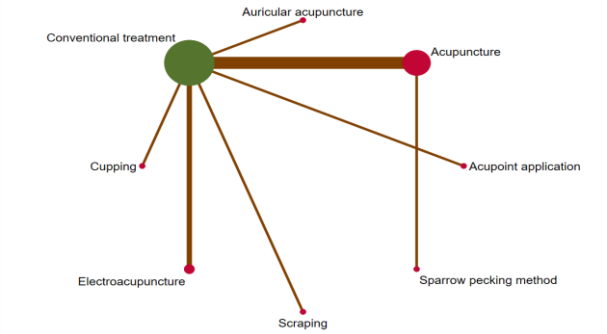

Figure 3A: NMA figure for LOT.

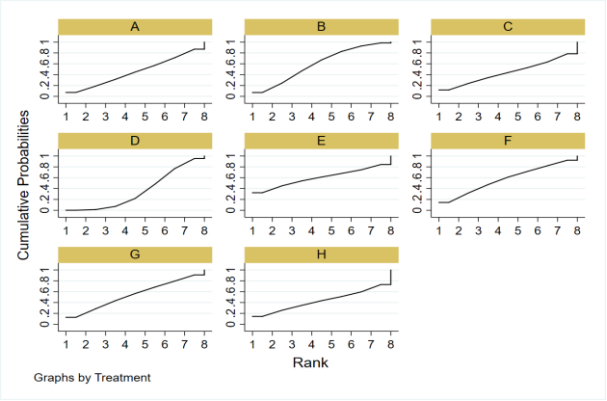

Figure 3B: SUCRA plot for LOT.

3.4.3 Exercise tests

We tested for consistency and inconsistency in all p-values for indirect and direct comparisons between studies. Most p-values were >0.05, indicating that the effect of consistency between the studies was acceptable. The details are provided in Supplementary Table 2.

The results of the network meta-analysis showed that, compared to the control group's conventional treatments, acupuncture [MD 9.70, 95%CI (-6.15,25.55)], Acupuncture + Cupping [MD 10.11, 95%CI (-187.15,207.36)], cupping [MD 3.90, 95%CI (-14.97,22.77)], and electroacupuncture [MD 0.14, 95%CI (-61.42,61.70)] were superior to the control group in improving exercise tests. The probability ranking of the different acupuncture treatments in terms of improving exercise tests was first in the SUCRA for Acupuncture (SUCRA:66.7, Figure 4B). A comparison of the two treatments is shown in Figure 8C.

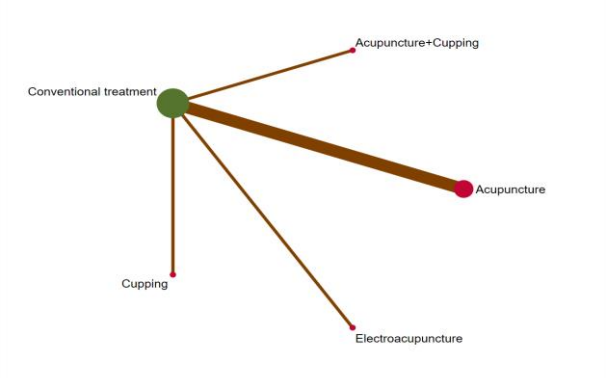

Figure 4A: NMA figure for Exercise tests.

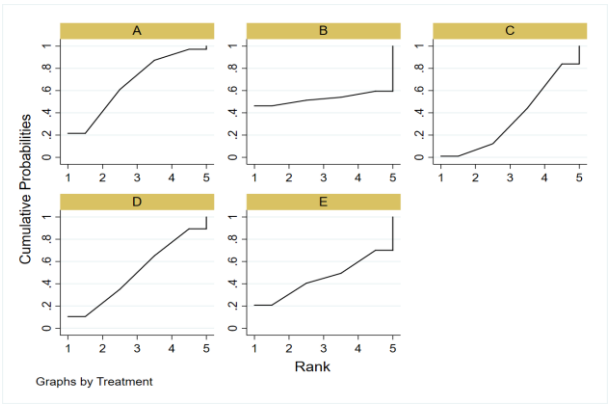

Figure 4B: SUCRA plot for Exercise tests.

3.4.4 Anxiety and Depression Scores (ADS)

We tested for consistency and inconsistency in all p-values for indirect and direct comparisons between studies. Most p-values were >0.05, indicating that the effect of consistency between the studies was acceptable. The details are provided in Supplementary Table 2.

The results of the network meta-analysis showed that compared to the control group's conventional treatments, acupoint application [MD -3.29, 95%CI (-6.77,0.19)], acupuncture [MD -1.59, 95%CI (-4.28,1.09)], auricular acupuncture [MD -3.75, 95%CI (-6.03,-1.46)], and electroacupuncture [MD -0.35, 95%CI (-11.86,11.16)] were superior to the control group in reducing ADS. The probability ranking of the different acupuncture treatments in terms of reducing ADS was first in the SUCRA for Auricular acupuncture (SUCRA:79.5, Figure 5B). A comparison of the two treatments is shown in Figure 8D.

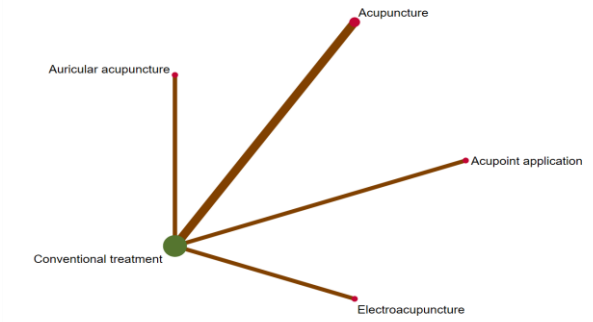

Figure 5A: NMA figure for ADS.

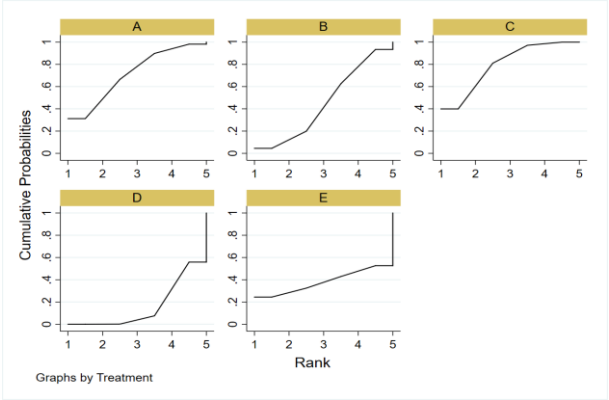

Figure 5B: SUCRA plot for ADS.

3.4.5 Seattle Angina Questionnaire (SAQ)

We tested for consistency and inconsistency in all p-values for indirect and direct comparisons between studies. Most p-values were >0.05, indicating that the effect of consistency between the studies was acceptable. The details are provided in Supplementary Table 2.

The results of the network meta-analysis showed that compared to the control group's conventional treatments, acupoint application [MD 8.34, 95%CI (-6.57,23.25)], acupuncture [MD 19.26, 95%CI (6.90,31.62)], auricular acupuncture [MD 4.40, 95%CI (-12.39,21.19)], cupping [MD 5.10, 95%CI (-11.89,22.09)], electroacupuncture [MD 2.22, 95%CI (-14.48,18.92)], and needle-embedding therapy [MD 1.90, 95%CI (-14.24,18.04)] were superior to the control group in improving SAQ. The probability ranking of the different acupuncture treatments in terms of improving the SAQ was ranked first in the SUCRA for Acupuncture (SUCRA:93.2, Figure 6B). A comparison of the two treatments is shown in Figure 8E.

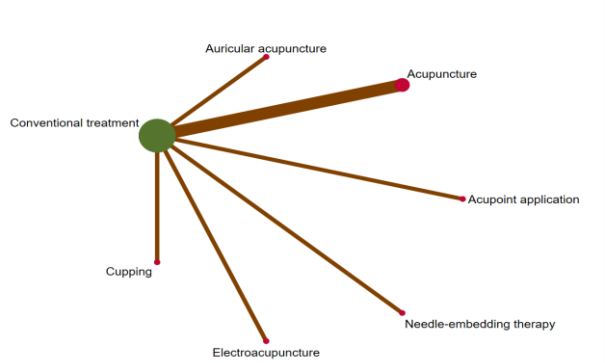

Figure 6A: NMA figure for Angina Scores.

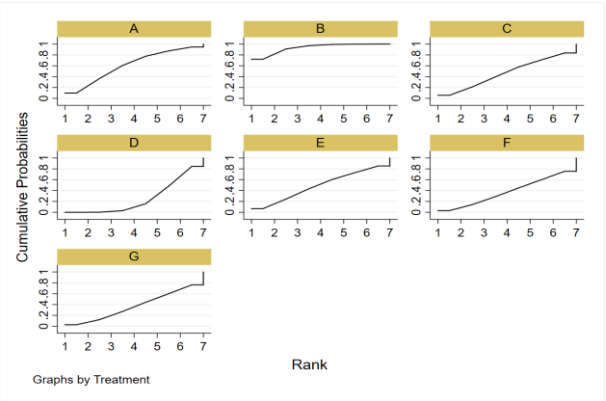

Figure 6B: SUCRA plot for Angina Scores.

3.4.6 Pain Scores

We tested for consistency and inconsistency in all p-values for indirect and direct comparisons between studies. Most p-values were >0.05, indicating that the effect of consistency between the studies was acceptable. The details are provided in Supplementary Table 2.

The results of the network meta-analysis showed that compared to the control group's conventional treatments, acupoint application [MD -11.36, 95%CI (-14.55,-8.18)], acupuncture [MD -0.73, 95%CI (-1.71,0.25)], cupping [MD -2.80, 95%CI (-5.17,-0.43)], and electroacupuncture [MD -1.10, 95%CI (-2.64,0.44)] were superior to the control group in reducing Pain Scores. The probability ranking of the different acupuncture treatments in terms of pain reduction scores was ranked first in the SUCRA for Acupoint application (SUCRA:100.0, Figure 7B). A comparison of the two treatments is shown in Figure 8F.

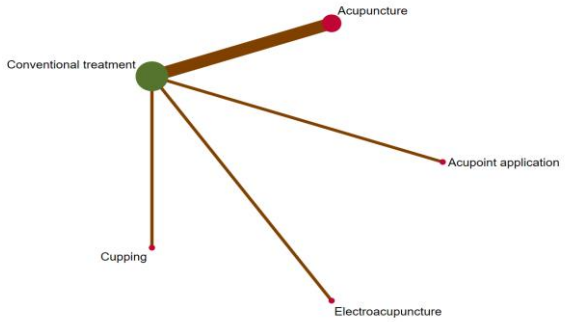

Figure 7A: NMA figure for Pain Scores.

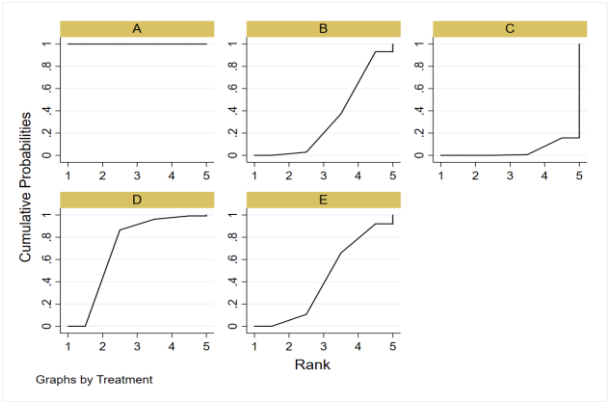

Figure 7B: SUCRA plot for Pain Scores.

3.5 Publication Bias Test

We tested for possible publication bias by constructing separate funnel plots for each outcome indicator. As shown in Figure 6, no significant publication bias was observed in the funnel plots [45].

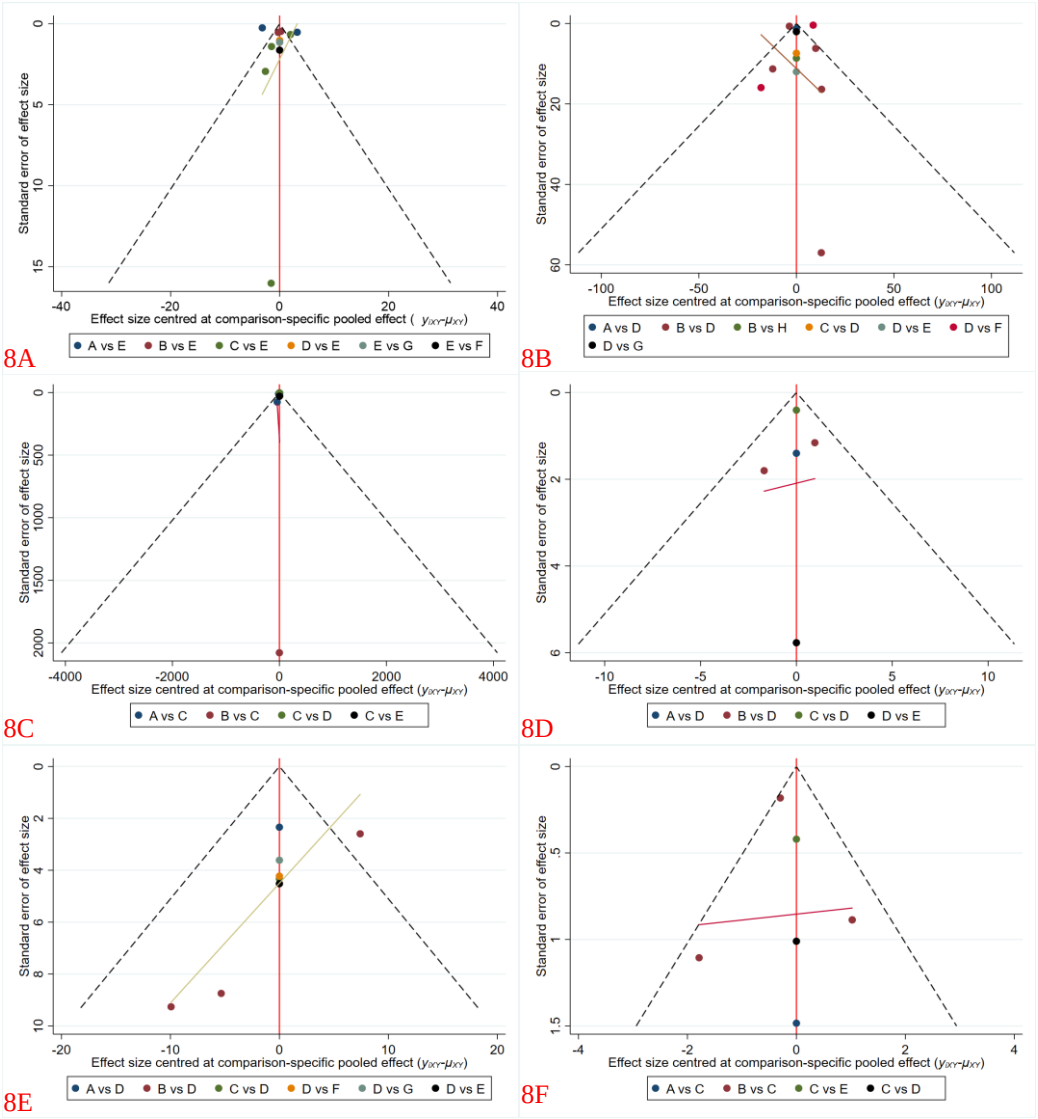

Figure 8: Funnel plot on publication bias. 8A: Angina Scores; 8B: Laboratory and other tests; 8C: Exercise tests; 8D: Anxiety and Depression Scores; 8E: Seattle Angina Questionnaire; 8F: Pain Scores.

4. Discussion

In this trial, we conducted a systematic review and used a network meta-analysis to pool the results of 26 trials with fair and high-quality ratings and to provide joint information of 1747 patients using different acupuncture treatments for angina pectoris. In total, we incorporated 10 different acupuncture treatments: acupoint application, acupoint pressing, Acupuncture, Acupuncture + Cupping, Auricular acupuncture, Cupping, Electroacupuncture, Scraping, Sparrow pecking, and needle embedding. We found that different acupuncture treatments have their own advantages in improving different aspects of angina pectoris, and all acupuncture treatments were significantly effective compared to the usual treatment in the control group. Acupoint application was the most effective method for alleviating angina and pain scores; acupuncture was the most effective method for increasing exercise tests and the Seattle Angina Questionnaire; cupping was the most effective method for improving laboratory and other tests; and auricular acupuncture was the most effective method for easing anxiety and depression symptoms.

The optimal acupuncture treatment regimens for different indicators all have a common feature: a large amount of stimulation, including stimulation range (acupoint application, cupping) and stimulation duration (acupoint application, auricular acupuncture). Studies have shown that the effects of acupuncture are closely related to the amount of stimulation. Wang et al. [46] found the transcription of genes related to neuroplasticity in the spinal cord of rats receiving different numbers of treatments. Wen et al. [46] observed the changes in metabolites in the blood and urine of acute-gouty arthritis rats treated with acupuncture, and found that the metabolite profiles in the blood and urine of rats treated with different numbers of acupuncture were different. In another study [47], researchers used different frequencies of electroacupuncture to stimulate Zusanli (ST36) and Sanyinjiao (SP6) in rats, and the gene transcripts were also different. The treatment effect is not a simple superposition of the treatment amounts, but a stimulation signal composed of different stimulation forms and amounts, thus producing different acupuncture effects. This may explain why acupuncture works best for some aspects of angina pectoris. Other treatments (acupoint pressing, etc.) could result in insufficient stimulation or incorrect stimulation patterns.

Our study had several strengths. It is methodologically

rigorous, using a comprehensive search, robust selection criteria, and detailed data extraction process. This is the first time that a network meta-analysis has been used to explore multiple acupuncture and moxibustion therapies for angina pectoris. This is of great clinical significance, and confirms that acupuncture treatment is significantly superior to the usual treatment. However, several limitations of this network meta-analysis should be considered. First, few trials were included because of the small number of original clinical trials. Second, some acupuncture therapies (moxibustion, etc.) were not included in the study because of the lack of randomized controlled trials. Third, differences in sex, age, race, needle manipulation, and frequency were not considered, which may have affected the experimental results. In fact, there are still many aspects waiting for us to explore in the research on acupuncture in the treatment of angina pectoris. In future research, consideration of the strengths and weaknesses of different acupuncture therapies is needed to guide clinical practice.

5. Conclusions

Based on the Ranking Plot of the Network, we can state that acupuncture treatments surpass the routine treatments for angina pectoris, and different acupuncture treatments show their superiority in different aspects of angina pectoris. More related explorations are needed in the future.

Author Contributions: Y.L. and S.L. had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.
Acquisition, analysis, or interpretation of data: Y.L. and S.L.
Drafting of the manuscript or statistical analysis: Y.L.
Concept and design, critical revision of the manuscript for important intellectual content, or supervision: H.F.Q.

Ethical statement: Not applicable.

Data statement: All relevant data are within the paper.

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Declaration of interest's statement: The authors declare no conflict of interest.

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Supplementary Table 1.