

INPLASY PROTOCOL

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None declared.

Traditional Chinese Medicine in treatment of Coronary Artery Disease with Anxiety or Depression: a network meta-analysis

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Review question / Objective: To compare the clinical efficacy of different traditional Chinese medicine (TCM) in the treatment of coronary artery disease (CAD) combined with anxiety or depression. **Condition being studied:** Coronary artery disease (CAD) is a leading cause of death in the world, the incidence of depression and anxiety in CAD patients is as high as 14% ~ 47% and 20% respectively, which is significantly higher than that in the general population. Moreover, evidences have shown that depression and anxiety are risk factors for the development of CAD, with depression an established independent risk factor of CAD, both are strongly associated with poor cardiac outcomes. Anxiolytics and antidepressants are common treatment for anxiety and depression. However, the use of anxiolytics and antidepressants in CAD patients is controversial. Some of anxiolytics and antidepressants, such as the selective serotonin reuptake inhibitors (SSRIs), are concerned about their cardiovascular related side effects. Studies shown that most of anxiolytics and antidepressants may interact with a variety of drugs for cardiovascular diseases, increasing clinical uncertainty. Some anxiolytics and antidepressants are cardiotoxic, which may cause certain damage to the cardiovascular system in patients with mental anxiety and depression, such as traditional tricyclic antidepressants, which have been proved to be highly cardiotoxic in studies. Evidence shown that traditional Chinese medicine (TCM) can effectively and safely alleviate the anxiety and depression in patients with CAD.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 April 2021 and was last updated on 14 November 2021 (registration number INPLASY202140124).

INTRODUCTION

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coronary artery disease (CAD) combined with anxiety or depression.

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death in the world, the incidence of depression and anxiety in CAD patients is as high as 14% ~ 47% and 20% respectively, which is significantly higher than that in the general population. Moreover, evidences have shown that depression and anxiety are risk factors for the development of CAD, with depression an established independent risk factor of CAD, both are strongly associated with poor cardiac outcomes. Anxiolytics and antidepressants are common treatment for anxiety and depression. However, the use of anxiolytics and antidepressants in CAD patients is controversial. Some of anxiolytics and antidepressants, such as the selective serotonin reuptake inhibitors (SSRIs), are concerned about their cardiovascular related side effects. Studies shown that most of anxiolytics and antidepressants may interact with a variety of drugs for cardiovascular diseases, increasing clinical uncertainty. Some anxiolytics and antidepressants are cardiotoxic, which may cause certain damage to the cardiovascular system in patients with mental anxiety and depression, such as traditional tricyclic antidepressants, which have been proved to be highly cardiotoxic in studies. Evidence shown that traditional Chinese medicine (TCM) can effectively and safely alleviate the anxiety and depression in patients with CAD.

METHODS

Search strategy: PubMed: (Coronary Heart Disease OR Coronary Diseases OR Ischemia, Myocardial OR Acute Coronary Syndrome OR Myocardial Infarction OR Angina Pectoris OR Stenocardia) AND (Depressions OR Depressive Symptoms OR Emotional Depression or Angst or Nervousness or Hypervigilance or Anxiousness or Social Anxiety) AND (wendan decoction OR yixinshu OR jieyuzhitong OR xinkeshu OR shuganjieyu OR Chaihu Longgu Muli decoction).

Participant or population: Patients with a definite diagnosis of coronary

atherosclerotic heart disease with anxiety or depression.

Intervention: The intervention group was additionally treated with TCM preparation on the basis of the control group, including Wendan decoction, Yixinshu capsule, Jieyu Zhitong prescription, Xinkeshu tablet, Shugan Jieyu decoction or Chaihu Longgu Muli decoction.

Comparator: The control groups received standard treatment, including CAD secondary prophylactic drugs and anti-anxiety and depression drugs.

Study designs to be included: Randomized Controlled Trial or Controlled Clinical Trial, Clinical Trial.

Eligibility criteria: Inclusion criteria: 1) Patients with a definite diagnosis of coronary atherosclerotic heart disease with anxiety or depression. Age is 18 years to 80 years. 2) Sufficient sample size is required ($N \geq 20$) Exclusion criteria: 1) Repeated research; 2) the intervention is not a single traditional Chinese medicine preparation; 3) HAMA and HAMD scores at baseline were not recorded.

Information sources: The two authors will be independent to extract data from each study (PubMed, Cochrane Library, EMBASE, Web of Science, CINAHL, CNKI, WanFang, CBM, published from inception to 30st November 2020, the use of standardized data extraction, including research characteristics (such as the first author's name, year of publication, random method, randomized, blinded, lost to follow-up and hidden exit), the study of the characteristics of the object (included in the number of cases, for example) and outcomes measure (HAMA and HAMD). At the end of the intervention, the results of intentionality analysis (ITT) will be extracted preferentially.

Main outcome(s): Hamilton Anxiety Scale (HAMA) score and Hamilton Depression Scale (HAMD) score.

Additional outcome(s): Adverse reactions(ADRs), SAQ (seattle angina questionnaire) which consisted of five aspects: AS (anginal stability), AF(the frequency of angina) ,PL(physical limitation), TS(Treatment satisfaction), DC(Disease cognitive).

Quality assessment / Risk of bias analysis: The risk of bias in the included studies was assessed using the Cochrane Handbook 5.1.0 RCT Risk of Bias Assessment Tool. Specific criteria: 1. Whether random method is adopted; 2. Whether allocation concealment is adopted; 3. Whether the participants and implementors are blind; 4, Whether the measurement results are blind, 5. Data integrity, 6. Whether there is selective reporting, 7. Each outcome was classified as low-risk, unclear, or high-risk for the presence of other biases. At the same time, the modified Jadad scale was used to evaluate the methodological quality of the included literatures. The specific criteria are shown in Attachment 1. Two evaluators will independently evaluate the quality. In case of disagreement, the third party will intervene to discuss and solve the problem.

Strategy of data synthesis: The bias of variance size parameter of heterogeneity (I^2) estimated from the NMA model using R V5.4 software was used to evaluate the statistical heterogeneity among studies. GEMTC14.3 based on the Bayesian framework was used for mesh meta-analysis, and the Markov chain Monte Carlo fitting consistency model was used for Bayesian inference. Four chains were set initially, and the number of iterations was set as 50 000 times. The first 20 000 times were used for annealing to eliminate the influence of initial values. The last 30 000 times were used for sampling, and PSRF was used to reflect the convergence degree of the model. When PSRF was close to or equal to 1, it indicated that the data had good convergence, and the consistency model was used for mesh meta-analysis. The surface area under the cumulative ranking curve (SUCRA) of different interventions was calculated by STATA15. The quality of evidence will be

evaluated using Grade Pro 3.6 software for the quality of treatment effect evaluation through NMA.

Subgroup analysis: None.

Sensitivity analysis: When the heterogeneity of each study was large, the observation difference of low-quality studies were excluded, and the results of the network meta-analysis were compared with the consistent model and the non-consistent model.

Language: Chinese.

Country(ies) involved: China.

Keywords: Traditional Chinese Medicine, Coronary Atherosclerotic Heart Disease, Anxiety and Depression, Network Meta-analysis.

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