

INPLASY PROTOCOL

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None declared.

Preclinical Evidence of Acupuncture on infarction size of Myocardial ischemia: A Systematic Review and Meta-Analysis of Animal Studies

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Review question / Objective: Whether acupuncture is effective for infarction size on myocardial ischemia rat models.

Condition being studied: Myocardial ischemia is a typical pathological condition of coronary heart disease (CHD), which has been a global issue with high incidence and mortality. Myocardial infarction caused by myocardial ischemia leads to cardiac dysfunction, and the size of myocardial infarction also determines the recovery and prognosis of cardiac function. Acupuncture, a long history of traditional Chinese medicine, is widely used to treat symptoms like thoracalgia and palpitation. Many researches based on rat experiments have shown that acupuncture affects infarction size, cardiac function, myocardial enzyme or arrhythmias severity on myocardial ischemia models; nevertheless, few literatures have systematically reviewed these studies, assessing the risk of bias, quality of evidence, validity of results, and summarizing potential mechanisms. A systematic review of animal studies can benefit future experimental designs, promote the conduct and report of basic researches and provide some guidance to translate the achievements of basic researches to clinical application in acupuncture for myocardial ischemia. Therefore, we will conduct this systematic review and meta analysis to evaluate effects of acupuncture on infarction size on myocardial ischemia rat models.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 June 2022 and was last updated on 10 June 2022 (registration number INPLASY202260044).

INTRODUCTION

Review question / Objective: Whether acupuncture is effective for infarction size on myocardial ischemia rat models.

Rationale: Many experiments on rats existed to illustrate the efficacy of acupuncture on reducing infarction size. The sample size of these experiments is commonly small, and the quality of evidence is unclear. This study will conduct a meta-analysis evaluating acupuncture on

infarction size on myocardial ischemia animal models to provide preclinical evidence for clinical application and reference for future research.

Condition being studied: Myocardial ischemia is a typical pathological condition of coronary heart disease (CHD), which has been a global issue with high incidence and mortality. Myocardial infarction caused by myocardial ischemia leads to cardiac dysfunction, and the size of myocardial infarction also determines the recovery and prognosis of cardiac function. Acupuncture, a long history of traditional Chinese medicine, is widely used to treat symptoms like thoracalgia and palpitation. Many researches based on rat experiments have shown that acupuncture affects infarction size, cardiac function, myocardial enzyme or arrhythmias severity on myocardial ischemia models; nevertheless, few literatures have systematically reviewed these studies, assessing the risk of bias, quality of evidence, validity of results, and summarizing potential mechanisms. A systematic review of animal studies can benefit future experimental designs, promote the conduct and report of basic researches and provide some guidance to translate the achievements of basic researches to clinical application in acupuncture for myocardial ischemia. Therefore, we will conduct this systematic review and meta analysis to evaluate effects of acupuncture on infarction size on myocardial ischemia rat models.

METHODS

Search strategy: The basic search strategy was TU=(“myocardial ischemia” OR “myocardium ischemic” OR “ischemic cardiomyopathy” OR “angina pectoris” OR “angina”) AND (“acupuncture” OR “acupuncture therapy” OR “manual acupuncture” OR “electroacupuncture” OR “acupoints”). Similar Chinese words are used in Chinese database searching strategies. We do not make the detailed search strategy publicly available until the review is complete.

Participant or population: Rat models of myocardial ischemia which induced by medication or left anterior descending coronary artery (LAD) ligature operation.

Intervention: Only electroacupuncture and manual acupuncture will be included. Both pre-treatment and post-treatment can be accepted.

Comparator: Untreated myocardial ischemia rat model group.

Study designs to be included: All controlled studies that examined the effect of acupuncture in rats model of myocardial ischemia will be included.

Eligibility criteria: Inclusion criteria(1) Types of subjects: Rat model of myocardial ischemia induced by medication or coronary artery ligature operation.(2) Types of interventions: Electroacupuncture or manual acupuncture, both pre-treatment and post-treatment are included.(3) Types of controls: Untreated myocardial ischemia model group or blank control group.(4) Types of outcomes:(5) Types of studies: All controlled studies of the effect of acupuncture in rat model of myocardial ischemia with no restrictions on countries or languages.Exclusion criteria(1) Reviews, protocols, case reports, cross-over studies;(2) Studies using rat models merged with another disease;(3) Studies without a control group or only compared different acupuncture prescriptions;(4) Studies that only compared acupuncture with Traditional Chinese Medicine (TCM)/ western medication or compared a combination therapy with either TCM/ western medication.(5) Studies deployed auricular acupuncture, laser acupuncture, transcutaneous electrical acupoint stimulation or other acupuncture techniques.(6) Studies without complete data or for which quantitative data are not available.

Information sources: Literatures will be searched in the following databases from January 1, 2012 to April 30, 2022: China National Knowledge Infrastructure (CNKI), VIP database for Chinese Technical

Periodicals (VIP), WANFANG database (WF), Chinese biomedical literature service system (SinoMed), Web of Science (WOS), Pubmed and Embase. Moreover, reference lists of eligible studies and previous reviews will also be manually reviewed.

Main outcome(s): The ratio of infarct area to the left ventricle (IS/LV); the ratio of IS to total myocardial area (IS/TA); the ratio of IS to ischemic area at risk (IS/AAR).

Additional outcome(s): (1) Cardiac function: left ventricular ejection fraction (LVEF), left ventricular fractional shortening (LVFS); (2) Myocardial enzymes: CK, CK-MB, LDH, cTnT; (3) Arrhythmia score; (4) ST-segment elevation in electrocardiogram (ECG).

Data management: SX and BY independently extracted and recorded the following details from each study in Excel 2019: (1) basic information: publication year, journal, first author's name; (2) animal model details: animal strain, age, sex, weight, number of rats in each group, model-building method; (3) intervention details: types of acupuncture, pre-treatment or post-treatment, acupoints, depth, electrical stimulator parameters, frequency, duration and course of treatment; (4) outcome measurement details: outcome indexes including mean, standard deviation and p values. For studies that only provide graphical data, we will firstly try to contact the authors for more specific information; if we fail to obtain raw data, software GetData Graph Digitizer will be used to get more accurate quantitative data from the figures. (5) underlying mechanism.

Quality assessment / Risk of bias analysis: Risk of bias assessment: The SYRCLE animal experiment bias risk assessment tool will be applied to evaluate the risk of bias of eligible studies. Studies will be divided into low-bias risk, high-bias risk and unclear-bias risk based on 10 aspects of assessment contents. Two researchers will independently assess the risk of bias whereas any disagreement will be resolved by an intercessor. Quality assessment: Collaborative Approach to Meta-Analysis

and Review of Animal Data from Experimental Studies (CAMARADES) will be used to evaluate the methodological quality of the included studies. Ten aspects of assessment are as follows: (1) peer reviewed publication; (2) control of temperature; (3) random allocation to treatment group; (4) allocation concealment; (5) blinded assessment to outcome; (6) reporting of animals excluded from analysis; (7) precise animal species; (8) sample size calculation; (9) compliance with animal welfare regulations; (10) statement of potential conflict of interests. Two researchers will independently assess the risk of bias whereas any disagreement will be resolved by an intercessor.

Strategy of data synthesis: We used STATA 17.0 to manage the meta analysis. Outcome measures (IS/LV, IS/TA, IS/AAR, LVEF, LVFS, CK, CK-MB, LDH, cTnT and ST-segment elevation in ECG) are continuous data, so we calculated their mean difference (MD) and 95% confidence interval (95% CI) for each MD/SMD. We will assess the heterogeneity between studies using the I² statistics. When I² ≥ 50%, a random-effects model will be used to pool the data, otherwise, a fixed-effects model will be used.

Subgroup analysis: Subgroup analyses about acupoints, different stimulating parameters of electroacupuncture and acupuncture sessions will be conducted to explore the impact of factors potentially influencing the effectiveness of acupuncture on infarction size.

Sensitivity analysis: We will evaluate the robustness of the results using leave-one-out sensitivity analysis.

Language: No restriction on languages.

Country(ies) involved: China.

Other relevant information: No.

Keywords: acupuncture, myocardial ischemia, systematic review, meta-analysis, animals.

Dissemination plans: No.

Contributions of each author:

Author 1 - Xiao Li - Author 1 designed the research plan and wrote the first draft of the manuscript.

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Author 2 - Fayang Ling - Author 2 designed the research plan and wrote the first draft of the manuscript.

Author 3 - Wenchuan Qi - Author 3 designed the research plan and provided statistical expertise.

Author 4 - Sanmei Xu - The author conducted literature search and will do quality assessment in the future.

Author 5 - Bingzun Yin - The author conducted literature search and will do quality assessment in the future.

Author 6 - Zihan Yin - This author provided statistical expertise and software usage guidelines.

Author 7 - Qianhua Zheng - The author is responsible for the collection, management and analysis of outcomes.

Author 8 - Xiang Li - The author is responsible for the collection and management of outcomes.

Author 9 - Fanrong Liang - The author read, provided feedback and approved the final manuscript.