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Research the effectiveness of Xiao-xian-xiong-tang for twisted angina in CHD via network pharmacology-molecular interaction

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Corresponding author:
Hui Yu

ywzlp@163.com

Author Affiliation:
Tianjin Ninghe District Hospital.

Yu, H; Zhu, LP; Li, XF; Huang, D.

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INTRODUCTION

Review question / Objective In contemporary medical research, integrating traditional medicines with modern technological approaches, particularly network pharmacology and molecular biology techniques, to delve into the functions and mechanisms of traditional drugs has become a burgeoning research trend. This study aims to explore the effectiveness and underlying molecular mechanisms of the traditional Chinese medicine formula Xiao-xian-xiong-tang in treating twisted angina in coronary heart disease (CHD).

Coronary heart disease, due to its high incidence and mortality rates, has become a global health concern. Angina, a common symptom of CHD, presents significant treatment challenges, particularly in its twisted manifestation due to specific pathological alterations and its episode pattern. Xiao-xian-xiong-tang, a compound of various traditional Chinese herbs, has historically been used to treat cardiothoracic diseases, including angina. However, its mechanisms and clinical efficacy in treating twisted angina within the context of CHD have not been fully validated.

This research will employ network pharmacology methods to organize and analyze the main chemical constituents of Xiao-xian-xiong-tang and their expected biological activities, as well as their potential molecular targets. Additionally, molecular biology technologies, such as molecular docking and signal transduction pathway analysis, will be used to investigate the potential effects of these components at the molecular level on CHD-associated twisted angina.

Through detailed examination of the pharmaceutical ingredients and molecular mechanisms of Xiao-xian-xiong-tang, not only can this provide scientific evidence for the modernization and standardization of traditional Chinese medicine, but it may also offer new therapeutic strategies for treating twisted angina in CHD. This study aims to fill the current research gaps, contributing to the internationalization of Chinese medicine and the advancement of modern medicine.

Condition being studied Coronary heart disease (CHD) poses a major global health challenge, especially as angina, one of its primary symptoms, significantly impacts patient quality of life. Twisted

angina, known for its complex clinical presentation and varied treatment responses, remains a difficult area in clinical research. Historically, the traditional Chinese medicine formula Xiao-xian-xiong-tang has been employed to treat various cardiothoracic conditions, including angina. However, its efficacy and mechanisms under the contemporary medical framework require further investigation.

This study will utilize network pharmacology and molecular interaction techniques to thoroughly analyze the components of Xiao-xian-xiong-tang and their effects on twisted angina in CHD. Network pharmacology, integrating bioinformatics, computational biology, and systems biology, offers a new perspective and methodological approach to the study of traditional Chinese medicines. By constructing a network of interactions between herbal components and disease targets, this method can reveal the characteristics of multi-component, multi-target, and multi-pathway drug effects.

Currently, the research has completed the extraction and analysis of the main active components of Xiao-xian-xiong-tang, identifying several potential bioactive targets. Preliminary molecular docking experiments indicate strong affinity of certain components to these targets, which lays the groundwork for further in-vivo and in-vitro experimental verification.

The ultimate goal of this study is to provide scientific evidence for the clinical application of Xiao-xian-xiong-tang, optimizing treatment protocols for CHD and its complex types of angina. The outcomes of this research are expected to enhance the visibility and acceptance of traditional Chinese medicine in the global treatment of cardiovascular diseases, contributing to the modernization and internationalization of traditional treatment methods.

METHODS

Participant or population The purpose of this study is to investigate the effectiveness of Xiao-xian-xiong-tang on angina pectoris in patients with coronary heart disease (CHD). The patient population includes adult patients diagnosed with CHD and exhibiting angina pectoris. These patients typically experience recurrent angina symptoms that are difficult to manage with conventional treatments. Angina pectoris patients often present a complex clinical picture, characterized by variable pain nature, duration, and poor response to standard medications.

Participants in this study are required to meet the following criteria: 1) aged between 30 and 75 years, regardless of gender; 2) diagnosed with coronary artery disease and exhibiting angina pectoris; 3) symptoms persisting for more than three months; and 4) have not received any other traditional Chinese medicine treatments. Exclusion criteria include: 1) severe heart disease or other serious comorbidities; 2) recent receipt of other interventional treatments; 3) allergy to the ingredients of Xiao-xian-xiong-tang; and 4) inability to comply with the study protocol or poor cooperative attitude.

During the study, patients will be randomized into an experimental group and a control group. The experimental group will receive Xiao-xian-xiong-tang, while the control group will receive conventional symptomatic treatments, including anticoagulants, antiplatelet agents, statins, and cardiac nutrients. The study will conduct regular assessments of patients, including symptom changes, quality of life scores, and electrocardiograms, to systematically evaluate the efficacy and safety of Xiao-xian-xiong-tang.

Participants will be recruited and screened according to ethical standards, and informed consent will be obtained. Patient privacy will be strictly protected, and data security will be ensured throughout the study. Through this research, we aim to provide a scientific basis for the clinical application of Xiao-xian-xiong-tang in the treatment of CHD-related angina pectoris and to further validate its efficacy and safety.

Intervention The intervention in the experimental group involved modifications to the Xiao-xian-xiong Tang formula used in the control group.

Comparator The control group received conventional symptomatic treatment, including anticoagulants, antiplatelet agents, statins, and myocardial nutrients.

Study designs to be included Patients with angina pectoris, including those with coronary heart disease, unstable angina pectoris, stable angina pectoris, and other related conditions.The treatment group will receive conventional symptomatic therapy combined with Xiao-xian-xiong-tang, with adjustments in medication as needed.The study must be a randomized controlled trial (RCT), clearly specified with terms such as “randomized,” “randomized controlled,” or “RCT.”

Eligibility criteria Inclusion Criteria

1) Literature comprised exclusively of randomized controlled trials (RCTs);2) Diagnoses of coronary angina adhered to established guideline criteria;3) Each RCT comprising a control group receiving conventional or symptomatic treatments and an

experimental group administered Xiao-xian-xiong Tang.
Exclusion Criteria.
1) Patients experiencing acute exacerbations of angina pectoris due to coronary artery disease are excluded;2) Randomized controlled trials involving multiple intervention strategies are excluded;3)Studies where Xiao-xian-xiong Tang was not employed as the primary therapeutic intervention are excluded;4) Reviews, conference proceedings, and studies conducted on animal models are excluded;5) Duplicate publications of research findings are excluded;6) Literature presenting incomplete or erroneous data is excluded;7) Trials with a total participant count not exceeding 60, with no more than 30 individuals in either the control or the experimental group, are excluded;8) Pilot studies investigating coronary angina in conjunction with other diseases are excluded.

Information sources Literature searches were conducted utilizing databases including CNKI, Wanfang, VIP (CQVIP), SinoMed, the China Clinical Trials Center, the Cochrane Library, Web of Science, EMBASE, PubMed, and the U.S. Clinical Trials Cente.

Main outcome(s) Spanning the period from May 30, 2014 to May 30, 2024. Authors were subsequently contacted for further study details as required for additional disclosures.
Search keywords comprised “coronary heart disease”, “angina”, “stable angina”, “unstable angina”, “small trapping chest soup” and randomized trials denoted by “randomized”, “randomized controlled” and “RCT”.
Initially, a total of 71 papers were selected for review. Upon further screening, 37 papers were identified as duplicates, 7 were categorized as review articles, systematic evaluations, or syntheses, and 8 did not meet the study criteria. Furthermore, studies with a total sample size of 606 or fewer were excluded. After applying these criteria, 13 papers were ultimately included for detailed analysis in this study.

Quality assessment / Risk of bias analysis For this study, Review Manager 5.3 (RevMan 5.3) was employed to assess the quality of the articles. Statistical analyses, including funnel plotting, were conducted using StataMP 18.0. Additionally, Begg’s Test and Egger’s Test were utilized to evaluate publication bias and perform further data analysis.

Strategy of data synthesis Data compilation was executed using Microsoft Excel and included various parameters such as the first author’s name, publication year, study type, treatment duration, randomization status, randomization methodology, total case number, participant details (gender, age, disease duration), lifestyle factors (smoking and alcohol consumption histories), clinical details (angina grading, comorbid conditions, treatment measures), and effectiveness evaluations (clinical efficacy, traditional Chinese medicine (TCM) disease efficacy, and electrocardiogram results).
Additionally, specific data points such as the number of angina episodes, duration, nature, and severity of angina pain, nitroglycerin usage and withdrawal rates, and changes in adipokine resistin were methodically recorded for both the treatment and control groups. Biochemical markers including high-sensitivity C-reactive protein, lipid profiles (cholesterol, triglycerides, HDL, LDL), fibrinogen, blood and plasma viscosity, endothelin-1 (ET-1), nitric oxide (NO), cardiotrophin-1 (CT-1), cytochrome C (Cyt C), soluble Intercellular Adhesion Molecule-1 (sICAM-1), von Willebrand factor (vWF), malondialdehyde (MDA), and superoxide dismutase (SOD) were also thoroughly assessed.

Subgroup analysis Subgroup analyses were not conducted in this study.

Sensitivity analysis Data entry and analysis were conducted using StataMP 18.0 software. This process included generating forest plots and calculating heterogeneity statistics, such as I^2 and P values. Sensitivity analyses were performed using the ‘metainf’ command to identify and exclude studies that significantly influenced overall effect sizes. Subsequent sensitivity validations were carried out to ensure robustness. A fixed-effects model meta-analysis was initially applied. In cases where three or more studies were excluded, the data were further examined using the cut-and-patch method to address potential biases.

Country(ies) involved China/Hospital or university.

Keywords Coronary angina pectoris;Xiao-xian-xiong Tang;Meta-analysis;Network pharmacology; Molecular docking.

Contributions of each author
Author 1 - Hai Yu.
Author 2 - Lingping Zhu.
Author 3 - Xiaofeng Li.
Author 4 - Danni Huang.