



Efficacy and safety of integrated traditional Chinese medicine and standard Western medicine for patients with acute coronary syndrome: protocol for a systematic review and meta-analysis

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Background: Acute coronary syndrome (ACS), which usually results from the buildup of fatty deposits (plaques) in and on the walls of coronary arteries, remains a major cause of morbidity and mortality worldwide. In the present systematic review, we aim to evaluate the efficacy and safety of adding traditional Chinese medicine (TCM) to standard western medicine to treat patients with ACS.

Methods: A systematic search was carried out in the China National Knowledge Infrastructure (CNKI; Chinese), the Chinese Biomedical Literature Disk Database CBMDisc (Chinese), Wanfang Data (Chinese), PubMed, Embase, and Web of Science for relevant papers up to January 20, 2021. All published randomized controlled trials related to the integration of TCM and Western medicine for ACS will be included. The primary outcome is the effective rate and cardiovascular function index (left ventricular ejection fraction, early peak flow velocity, and thrombolysis in myocardial infarction). The secondary outcome is blood lipid level (total cholesterol, triacylglycerol, low/high density lipoprotein) and the incidence of adverse cardiovascular events. Study selection, data collection, and quality evaluation will be conducted by 2 reviewers independently. Comprehensive meta-analyses together with sensitivity and subgroup analyses will be performed with Stata 15.0 software (StataCorp).

Discussion: The results will provide a high-quality guidance for the current clinical treatment of ACS, and the patients more options to relieve their symptoms. The findings from this study may provide updated evidence concerning the efficacy and safety of TCM for patients with ACS.

Trial registration: This protocol has been registered in the INPLASY platform (<https://inplasy.com/>), and the registration number is INPLASY202140145.

Keywords: Acute coronary syndrome (ACS); traditional Chinese medicine (TCM); systematic review

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Introduction

Acute coronary syndrome (ACS), which usually results from the buildup of fatty deposits (plaques) in and on the walls of coronary arteries, remains a major cause of morbidity and mortality worldwide and is responsible for more than 1 million hospital admissions in America (1). ACS comprises two presentations in clinic: ST elevation myocardial infarction (STEMI) and non-ST elevation acute coronary

syndrome (NSTEMI-ACS), with the latter being further divisible into unstable angina pectoris (UAP) and acute non-STEMI (NSTEMI) (2). ACS has many predisposing factors, including hypertension, smoking, obesity diabetes, etc. The main clinical symptoms mainly include chest tightness and chest pain, and in some serious cases ACS can even lead to heart failure and death (3). Given the above facts, we consider that optimizing the current treatment for

ACS will have important clinical implications.

Percutaneous coronary intervention (PCI), which is a non-surgical procedure that uses a catheter (a thin flexible tube) to place a small structure called a stent to open up blood vessels in the heart, has an immediate effect on revascularization of an infarct related artery (4). It has been widely applied and has significantly improved the prognosis of ACS (5). However, some PCI-related problems, including perioperative myocardial injury, in-stent restenosis, stent thrombosis, no-reflow, and ischemia-reperfusion injury, are difficult to avoid. Over the past three decades, with the development of clinical trials of traditional Chinese medicine (TCM) in China, TCM has been found to have good effects on improving heart function, protecting the myocardium, and treating and preventing arrhythmia and reperfusion injury. In the proposed systematic review, we aim to evaluate the efficacy and safety of adding TCM to standard Western medicine for treating patients with ACS. We present the following article in accordance with the PRISMA-P reporting checklist (available at <http://dx.doi.org/10.21037/apm-21-681>) (6).

Methods

Search strategy

A systematic search will be carried out in the China National Knowledge Infrastructure (CNKI; Chinese), the Chinese Biomedical Literature Disk Database (CBMdisc; Chinese), Wanfang Data (Chinese), PubMed, Embase, and Web of Science for relevant papers up to January 20, 2021. No restrictions will be set on language, sex, race, or course of disease. The search strategy is as follows: [(Acute Coronary Syndrome) or (ST Elevated Myocardial Infarction) or (Non-ST Elevated Myocardial Infarction) or (Angina, Unstable)] and [(Medicine, Chinese Traditional)]. *Table 1* shows the detailed search strategy for PubMed. We will also review the relevant references for additional studies.

Selection criteria

The inclusion criteria include the following: (I) patients older than 18 years; (II) patients treated with conventional Western medicine (control group) and a combination of TCM and Western medicine (experimental group); (III) clear reporting of any of effective rates, cardiovascular function index (including left ventricular ejection fraction,

early peak flow velocity, and thrombolysis in myocardial infarction) blood lipid levels (including total cholesterol, triacylglycerol, and low/high density lipoprotein), or the incidence of adverse cardiovascular events; and (IV) randomized controlled trials (RCTs). The exclusion criteria include the following: (I) reviews, case reports, editorials, or comments; (II) patients in the control group also receiving TCM; (III) patients with severe background diseases or malignant tumors.

Data extraction and quality assessment

Data, including first author's name, year of publication, sample size, sex ratio, average age, background disease, TCM received, duration of treatment, and endpoints reported will be independently collected by 2 reviewers. The quality of enrolled studies will be assessed using version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) (7). A third reviewer will be used to resolve any disagreements.

Statistical analysis

Meta-analyses will be performed if at least two enrolled trials report the corresponding outcomes. Differences will be tested using weighted mean difference (WMD) and relative risk (RR) with 95% confidence interval (CI). Intergroup heterogeneity will be tested using Q test, with $I^2 < 50\%$ and $P > 0.05$ indicating no significant difference. In case of significant heterogeneity, a random-effects model with the DerSimonian-Laird method will be used. Conversely, a fixed-effects model with the Mantel-Haenszel method will be used instead. Potential publication bias will be tested by performing funnel plots. Stability of results will be tested by performing sensitivity analyses through omitting each study sequentially. Finally, subgroup analyses will also be performed. All the above statistical analyses will be performed using Stata version 15.0 software (StataCorp).

Discussion

TCM has been proved to be an effective clinical practice in China, and in recent years, there is growing evidence that hypertension can be effectively controlled by TCM (8). Therefore, we hypothesize that TCM can be also used to treat ACS (9), but unfortunately, no relevant evidence is available now. We believe the proposed systematic review will be the first meta-analysis to evaluate the efficacy

Table 1 Search strategy for the PubMed database

Number	Search items
1	Acute Coronary Syndrome. Mesh.
2	Acute Coronary Syndromes. ti, ab
3	Coronary Syndrome, Acute. ti, ab
4	Coronary Syndromes, Acute. ti, ab
5	Syndrome, Acute Coronary. ti, ab
6	Syndromes, Acute Coronary. ti, ab
7	ST Elevated Myocardial Infarction. Mesh.
8	ST Segment Elevation Myocardial Infarction. ti, ab
9	ST Elevated Myocardial Infarction. ti, ab
10	STEMI. ti, ab
11	Non-ST Elevated Myocardial Infarction. Mesh.
12	Non ST Elevated Myocardial Infarction. ti, ab
13	NSTEMI. ti, ab
14	Non-ST-Elevation Myocardial Infarction. ti, ab
15	Infarction, Non-ST-Elevation Myocardial. ti, ab
16	Infarctions, Non-ST-Elevation Myocardial. ti, ab
17	Myocardial Infarction, Non-ST-Elevation. ti, ab
18	Myocardial Infarctions, Non-ST-Elevation. ti, ab
19	Non ST Elevation Myocardial Infarction. ti, ab
20	Non-ST-Elevation Myocardial Infarctions. ti, ab
21	Angina, Unstable. Mesh.
22	Anginas, Unstable. ti, ab
23	Unstable Anginas. ti, ab
24	Angina Pectoris, Unstable. ti, ab
25	Angina Pectori, Unstable. ti, ab
26	Unstable Angina Pectori. ti, ab
27	Unstable Angina Pectoris. ti, ab
28	Unstable Angina. ti, ab
29	Angina at Rest. ti, ab
30	Angina, Preinfarction. ti, ab
31	Anginas, Preinfarction. ti, ab
32	Preinfarction Angina. ti, ab
33	Preinfarction Anginas. ti, ab
34	Myocardial Preinfarction Syndrome. ti, ab
35	Myocardial Preinfarction Syndromes

Table 1 (continued)**Table 1** (continued)

Number	Search items
36	Preinfarction Syndrome, Myocardial. ti, ab
37	Preinfarction Syndromes, Myocardial. ti, ab
38	Syndrome, Myocardial Preinfarction. ti, ab
39	Syndromes, Myocardial Preinfarction. ti, ab
40	Medicine, Chinese Traditional. Mesh.
41	Traditional Chinese Medicine. ti, ab
42	Chung I Hsueh. ti, ab
43	Hsueh, Chung I. ti, ab
44	Traditional Medicine, Chinese. ti, ab
45	Zhong Yi Xue. ti, ab
46	Chinese Traditional Medicine. ti, ab
47	Chinese Medicine, Traditional. ti, ab
48	Traditional Tongue Diagnosis. ti, ab
49	Tongue Diagnoses, Traditional. ti, ab
50	Tongue Diagnosis, Traditional. ti, ab
51	Traditional Tongue Diagnoses. ti, ab
52	Traditional Tongue Assessment. ti, ab
53	Tongue Assessment, Traditional. ti, ab
54	Traditional Tongue Assessments. ti, ab

and safety of integrated traditional Chinese and Western medicine for ACS patients. Four steps will be strictly implemented to ensure the reliability of results. This review will provide further guidance for the clinical treatment of patients with ACS and offer patients more options to relieve their symptoms.

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Footnote

Reporting Checklist: The authors have completed the PRISMA-P reporting checklist. Available at <http://dx.doi.org/10.21037/apm-21-681>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/apm-21-681>)

[org/10.21037/apm-21-681](https://doi.org/10.21037/apm-21-681)). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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