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INPLASY

Tongxinluo Capsule for Acute Myocardial Infarction: A Systematic Review and Meta-analysis

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ADMINISTRATIVE INFORMATION

Support - The State Administration of Traditional Chinese Medicine (No. zyyzdxk-2023259).

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202580092

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 August 2025 and was last updated on 30 August 2025.

INTRODUCTION

Review question / Objective P: Patients with clinically diagnosed AMI in clinical studies; the coronary ligation model and the myocardial ischemia-reperfusion model in animal studies.
I: In clinical trials, the intervention for the test group is GDMT combined with TXL; in animal studies, the intervention for the trail group is TXL at any dose,
C: In clinical trials, the control group receives GDMT or GDMT combined with a placebo; in animal studies, while the control group receives an equivalent volume of non-functional fluids (saline or distilled water) or no treatment.
O: Clinical study outcomes: ①All-cause mortality, cardiovascular mortality, incidence of myocardial reinfarction, incidence of repeat revascularization, incidence of heart failure, incidence of angina pectoris, and incidence of arrhythmias; ② Left ventricular ejection fraction (LVEF); ③Lipid profiles: total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C); ④Inflammatory markers: hypersensitive C-reactive protein (hs-CRP), C-reactive protein (CRP), nitric oxide (NO), and endothelin-1 (ET-1); ⑤ Adverse drug reactions.
Animal study outcomes: ① Myocardial infarction area and no-reflow area; ②Cardiac function: LVEF and left ventricular fractional shortening (LVFS); ③ Constitutive nitric oxide synthase (cNOS) and ET.
S:RCT.

Condition being studied Acute myocardial infarction (AMI) is a leading cause of death worldwide and its incidence is increasing every year, placing a heavy burden on society and becoming a serious health problem. Ischemic heart disease, including AMI, remains the leading cause of cardiovascular mortality worldwide. Reperfusion therapies for AMI, such as percutaneous coronary intervention (PCI) or thrombolysis, can save vulnerable myocardium and reduce the area of myocardial infarction. However, if myocardial

ischemia persists beyond a certain period, reperfusion treatment may worsen myocardial ischemia/reperfusion injury (MIRI). During MIRI, there is extensive infiltration of neutrophils and platelets, then activated neutrophils release oxygen free radicals, proteolytic enzymes, and pro-inflammatory mediators, which directly cause tissue and endothelial damage, leading to lumen occlusion and microvascular dysfunction, thereby reducing myocardial perfusion and resulting in coronary no-reflow phenomenon (NRP) in coronary arteries. Regarding MIRI and NRP, the complex pathological mechanisms and individual variability of the disease pose challenges for effective prevention and treatment strategies in clinical practice. Further research is needed to develop multi-targeted therapeutic agents aimed at improving endothelial function and suppressing inflammatory responses, thereby improving the clinical outcomes of acute myocardial infarction.

METHODS

Participant or population Patients with clinically diagnosed AMI in clinical studies; the coronary ligation model and the myocardial ischemia-reperfusion model in animal studies.

Intervention In clinical trials, the intervention for the test group is GDMT combined with TXL; in animal studies, the intervention for the trail group is TXL at any dose.

Comparator In clinical trials, the control group receives GDMT or GDMT combined with a placebo; in animal studies, while the control group receives an equivalent volume of non-functional fluids (saline or distilled water) or no treatment.

Study designs to be included RCT.

Eligibility criteria Exclusion Criteria: Repeated studies, reviews, clinical protocols, comments, case reports, etc; Studies that include other traditional Chinese medicines or related traditional Chinese medicine interventions apart from TXL; Studies for which research data cannot be obtained even after contacting the original authors. Studies without a control group; Repeatedly published studies; Clinical studies with a sample size of fewer than 50 cases.

Information sources A comprehensive computer-based search was conducted across eight databases (The Cochrane Library, PubMed, Web of Science, Embase, CNKI, WanFang Data, VIP, and SinoMed) and four registries (ClinicalTrials.gov, WHO International Clinical Trials Registry Platform, Chinese Clinical Trial Registry, and International Traditional Medicine Clinical Trial Registry) was conducted to identify randomized controlled trials (RCTs) and animal studies of TXL treatment for AMI.

Main outcome(s) Clinical study outcomes: ①All-cause mortality, cardiovascular mortality, incidence of myocardial reinfarction, incidence of repeat revascularization, incidence of heart failure, incidence of angina pectoris, and incidence of arrhythmias; ② Left ventricular ejection fraction (LVEF); ③Lipid profiles: total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C); ④Inflammatory markers: hypersensitive C-reactive protein (hs-CRP), C-reactive protein (CRP), nitric oxide (NO), and endothelin-1 (ET-1); ⑤ Adverse drug reactions.
Animal study outcomes: ① Myocardial infarction area and no-reflow area; ②Cardiac function: LVEF and left ventricular fractional shortening (LVFS); ③ Constitutive nitric oxide synthase (cNOS) and ET.

Quality assessment / Risk of bias analysis The overall certainty of evidence for each outcome was assessed using the GRADE approach. The initial certainty of evidence from RCTs was considered high but could be downgraded based on five criteria: risk of bias, inconsistency, indirectness, imprecision, and publication bias. Two review authors (Yang Wu, Jingxue Guo) independently made judgments about the certainty of evidence, with disagreements resolved through discussion or by consulting a third author (Xian Wang).
The quality of clinical studies was assessed using the RoB-2 tool, which mainly includes randomization process, deviations from intended interventions, missing outcome data, measurement of outcome, selection of the reported result and overall score. Two reviewers (Yang Wu and Jingxue Guo) independently assessed the quality of the studies. Discrepancies between their assessments were resolved by discussion or consultation with the corresponding author (Xian Wang).
Animal studies were assessed using the risk of bias tool for animal studies developed by the SYstematic Review Centre for Laboratory animal Experimentation (SYRCLE). It consists of 10 main entries, namely randomized series generation, baseline characteristics, allocation concealment, blinding of placement randomization, blinding of investigators, assessment of randomized outcomes, blinding of outcome evaluators, incomplete data, selective outcome reporting, other biases, and total score. Each item is assigned 1 point.

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Strategy of data synthesis Data were extracted from the final included studies by independent reviewers (Yang Wu, Jingxue Guo), including the following information: (i) the name of the first author and the year of publication; (ii) specific information about clinical patients and research animals in each study, including age, sample size, intervention measures, as well as species, quantity, and weight; (iii) the methods of animal model establishment and anesthesia; (iv) outcome indicators including clinical effect, inflammation-related markers, adverse drug reactions, and so on. If multiple observation time points were reported in the study, only the results from the final time point were included.

Subgroup analysis In cases of high heterogeneity in the analysis results, subgroup analysis may be performed to assess the influence of different variables and identify the sources of heterogeneity.Animal experiments can be analyzed by subgroup based on animal species. Clinical trials can be analyzed by subgroups based on the time of medication administration.The animal experiments were analyzed by subgroup based on the species of the animals. The clinical trial was analyzed by subgroups based on the time of medication administration.

Sensitivity analysis In cases of high heterogeneity in the analysis results, sensitivity analysis may be performed to assess the influence of different variables and identify the sources of heterogeneity.

Language restriction The languages of the search were limited to English and Chinese.

Country(ies) involved China.

Keywords Tongxinluo, acute myocardial infarction, meta-analysis, clinical studies, preclinicalstudies.

Contributions of each author

Author 1 - Yang Wu - Study determination and scheme design; Literature screening and data extraction; Data analysis and interpretation; Article writing; Article review and final approval.
Author 2 - Jingxue Guo - Study determination and scheme design; Literature screening and data extraction; Data analysis and interpretation; Article writing; Article review and final approval.
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Author 4 - Xian Wang - Literature screening and data extraction; Article review and final approval.

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