INPLASY

Acupuncture at Neiguan (PC6) for Myocardial Ischemia in Animal Models: protective effects and mechanisms — a systematic review protocol

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Corresponding author:
Jun Li

lijun@gzucm.edu.cn

Author Affiliation:
Guangzhou University of Chinese Medicine.

Wang, S; Guo, L; Zhang, Y; Chen, R; Zhong, ML; Tan, CX; Chen, HJ; Li, J; Zeng, RF; Tan, ZP.

ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 January 2026 and was last updated on 22 January 2026.

INTRODUCTION

Review question / Objective Review question/objective: To systematically synthesize evidence from controlled in vivo animal studies on whether acupuncture (manual acupuncture or electroacupuncture) at Neiguan (PC6), alone or combined with other acupoints, exerts cardioprotective effects in models of myocardial ischemia and/or ischemia–reperfusion injury, and to summarize the potential underlying mechanisms and methodological quality.

PICOS: Population: in vivo animal models of myocardial ischemia or ischemia–reperfusion injury (any species, strain, sex). Intervention: acupuncture or electroacupuncture involving PC6 (alone or with other acupoints), with extraction of stimulation parameters (e.g., waveform, frequency, current/voltage, pulse width), timing of intervention, and treatment course. Comparator: blank/no-treatment control, sham acupuncture/sham point, or acupuncture at non-PC6 acupoints. Outcomes: measures of myocardial injury and cardiac function (e.g., infarct size/area at risk, ECG/hemodynamic indices, LVEF/LVFS), plus mechanistic and biomarker outcomes related to inflammation, oxidative stress, mitochondrial function/energy metabolism, cell death/apoptosis signaling, and transcriptional regulation (e.g., CK-MB/troponin, cytokines, SOD/MDA, Nrf2/HO-1, Bcl-2/Bax/caspase pathways). Study design: controlled in vivo animal experiments (randomized where reported). Risk of bias will be assessed using SYRCLE's tool, and findings will be synthesized descriptively given expected heterogeneity.

Condition being studied Myocardial ischemia and ischemia–reperfusion (I/R) injury are major causes of myocardial damage and adverse cardiac outcomes. In preclinical research, myocardial

ischemia and I/R injury are commonly modeled in animals using coronary artery occlusion (temporary or permanent) and related approaches, leading to infarction, impaired cardiac function, electrical instability, inflammation, oxidative stress, mitochondrial dysfunction, and activation of cell-death pathways. This review focuses on myocardial ischemia and/or I/R injury in in vivo animal models and the potential cardioprotective effects and mechanisms of acupuncture at Neiguan (PC6).

METHODS

Participant or population In vivo experimental animals (any species/strain/sex/age) with myocardial ischemia and/or ischemia–reperfusion injury induced by established experimental methods (e.g., coronary artery ligation/occlusion and reperfusion). Studies using ex vivo preparations, isolated organs/cells only, or clinical human participants will be excluded.

Intervention Acupuncture involving Neiguan (PC6), including manual acupuncture and/or electroacupuncture, applied before, during, or after induction of myocardial ischemia/I-R injury. PC6 may be used alone or in combination with other acupoints (data will be extracted to identify the role of PC6). Intervention details to be extracted include acupoints used, needling depth/manipulation, electroacupuncture parameters (e.g., waveform, frequency, intensity/current/voltage, pulse width), timing relative to ischemia/reperfusion, session duration, number of sessions, and treatment course.

Comparator Comparators will include no treatment/blank control, model control, sham acupuncture (e.g., superficial needling, non-acupoint or sham point), non-PC6 acupoint acupuncture/electroacupuncture, or other control conditions as defined by the included studies.

Study designs to be included Controlled in vivo animal experimental studies (parallel-group designs) evaluating manual acupuncture or electroacupuncture at Neiguan (PC6) in myocardial ischemia and/or ischemia–reperfusion models.

Eligibility criteria Inclusion: full-text original in vivo mammalian studies with a controlled comparison; PC6 must be explicitly reported and appropriately located; studies using multiple acupoints are eligible only if PC6 is the primary acupoint and its effect can be distinguished; at least one outcome related to myocardial injury, cardiac function, or cardioprotective effects must be reported.

Exclusion: in vitro/ex vivo-only studies, human clinical studies, reviews/meta-analyses, case reports, conference abstracts, duplicates, and studies without sufficient methodological or outcome data.

Information sources Electronic databases will be searched from inception to September 2025: PubMed, Embase, Cochrane Library, CNKI, Wanfang Data, Chinese Biomedical Literature Database (CBM), and VIP. We will also hand-search the reference lists of included studies and relevant reviews to identify additional eligible records.

Main outcome(s) Primary outcomes will include measures of myocardial injury severity and cardiac function in animal models, such as:
(1) infarct size (e.g., % of LV or area at risk, TTC/Evans blue or equivalent methods);
(2) cardiac function/hemodynamics (e.g., LVEF, LVFS, LVSP, LVEDP, ±dP/dt);
(3) histopathological injury scores or myocardial structural changes (light microscopy/electron microscopy when reported).
Outcomes will be extracted at the time points reported by the original studies (acute and/or longer-term follow-up).

Quality assessment / Risk of bias analysis Risk of bias in included animal studies will be assessed using SYRCLE's Risk of Bias tool for animal intervention studies. The following domains will be judged as low, high, or unclear risk based on reported information: sequence generation, baseline characteristics, allocation concealment, random housing, blinding of caregivers/investigators, random outcome assessment, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias. Two reviewers will assess risk of bias independently, with disagreements resolved through discussion or consultation with a third reviewer.

Strategy of data synthesis We will provide a structured qualitative (narrative) synthesis of included studies, summarizing study characteristics, animal species, ischemia/I/R models, intervention parameters (manual acupuncture/electroacupuncture details), comparators, and outcomes. Outcomes will be grouped into predefined domains (e.g., myocardial injury/infarct size, cardiac function/hemodynamics, histopathology, biomarkers, and mechanistic pathways) and synthesized by direction and consistency of effects.
If a sufficient number of studies are sufficiently homogeneous regarding species/model,

intervention, comparator, and outcome definitions, a meta-analysis will be considered. Otherwise, results will be summarized descriptively. Mechanistic findings will be synthesized thematically (e.g., inflammation, oxidative stress, mitochondrial function/energy metabolism, cell death/apoptosis signaling, and transcriptional regulation). Potential reporting/publication biases will be discussed qualitatively.

Subgroup analysis Where data permit, we will explore heterogeneity using subgroup analyses according to:
(1) animal species/strain;
(2) model type (myocardial ischemia vs ischemia–reperfusion; method and duration of ischemia/reperfusion);
(3) intervention type (manual acupuncture vs electroacupuncture);
(4) electroacupuncture parameters (e.g., frequency, intensity, waveform), and timing of intervention (preconditioning vs during ischemia vs postconditioning/after reperfusion);
(5) PC6 used alone vs PC6 combined with other acupoints;
(6) study quality/risk of bias (low vs high/unclear).
Subgroup analyses will be conducted only when an adequate number of studies are available within each subgroup.

Sensitivity analysis If quantitative synthesis is feasible, sensitivity analyses will be performed by excluding studies at high risk of bias, excluding studies with unclear key methodological items (e.g., randomization or blinding not reported), and using alternative statistical models (fixed-effect vs random-effects) where appropriate. If meta-analysis is not feasible, we will conduct sensitivity checks qualitatively by comparing conclusions after excluding studies with major methodological concerns (e.g., absence of a defined control group, insufficient reporting of intervention details, or incomplete outcome data).

Country(ies) involved China.

Keywords Myocardial ischemia, ischemia–reperfusion injury, Neiguan (PC6), Electroacupuncture; Animal models, systematic review.

Contributions of each author
Author 1 - Sheng Wang.
Email: sgydwangs@outlook.com
Author 2 - Lin Guo.
Author 3 - Ying Zhang.
Author 4 - Rui Chen.
Author 5 - Minlin Zhong.
Author 6 - Caixia Tan.
Author 7 - Haojie Chen.
Author 8 - Jun Li.
Email: lijun@gzucm.edu.cn
Author 9 - Ruifeng Zeng.
Author 10 - Zhanpeng Tan.