Clinical Effect of Post-rewarming Fever after Targeted Temperature Management in Cardiac Arrest Patients: A Systematic Review and Meta-Analysis

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Review question / Objective: We aim to investigate the clinical effect of post-rewarming fever (PRF) after targeted temperature management (TTM) in cardiac arrest patients.

Condition being studied: Post-rewarming fever (PRF), or rebound hyperthermia (RH), was observed in many patients who received targeted temperature management (TTM). However, previous studies about the influence of PRF on neurological outcome showed conflicting results. The aim of this systematic review and meta-analysis was to investigate whether the PRF could have an impact on clinically relevant outcomes, including neurological outcome and mortality, in patients suffering from cardiac arrest (CA).

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 April 2022 and was last updated on 09 April 2022 (registration number INPLASY202240052).

INTRODUCTION

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**METHODS**

**Search strategy:** We performed the systematic literature search in the PubMed, EMBASE and CENTRAL databases using the following Medical Subject Headings (MeSH) terms: “heart arrest” AND “targeted temperature management” AND (“fever” OR “hyperthermia”).

**Participant or population:** Adult patients with cardiac arrest who treated with targeted temperature management.

**Intervention:** Post-rewarming fever.

**Comparator:** Post-rewarming normothermia.

**Study designs to be included:** Randomized clinical trials (RCTs) and cohort studies.

**Eligibility criteria:** The studies eligible for the meta-analysis were screened according to the following criteria: (1) the participants of the study were adult patients with cardiac arrest (CA); (2) the study should have a control group treated with targeted temperature management (TTM); (3) the study defined the phenomenon about post-rewarming fever (PRF); (4) the neurological outcome of patients was assessed and/or the mortality was measured in the study; (5) the studies were cohort studies or RCTs; (6) the study papers were written in English.

**Information sources:** PubMed, EMBASE and CENTRAL databases and the References of the previous articles.

**Main outcome(s):** Neurological outcome of cardiac arrest patients.

**Additional outcome(s):** Mortality of cardiac arrest patients.

**Quality assessment / Risk of bias analysis:** Assessment of the risk of bias (ROB) for RCTs was based on the principle of the Cochrane collaborative risk of bias. For non-random studies, we using the Newcastle-Ottawa Scale (NOS) to evaluated ROB.

**Strategy of data synthesis:** I² and P values were applied to assess the heterogeneity of the meta-analysis and the percentage of variability. This was on account of heterogeneity instead of sample error and was assessed as low, moderate, or high when I² was 76%, respectively. Since heterogeneity was high in these studies, a random effects model was employed to determine the merged odds ratios (ORs) and 95% confidence intervals (CIs) for each result.

**Subgroup analysis:** The subgroup analysis is based on the temperature of post-rewarming fever (PRF).

**Sensitivity analysis:** Sensitivity analysis will be conducted through the means of eliminating the included articles one by one to evaluate their impact on the pooled OR and 95% CI.

**Language:** English.

**Country(ies) involved:** China.

**Keywords:** Targeted temperature management; Post-rewarming fever; Neurological outcome; Mortality.

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