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The effect of ischemic preconditioning on the cardiac autonomic nervous system after exercise: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Completed but not published.

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 17 April 2024 and was last updated on 17 April 2024.

INTRODUCTION

Review question / Objective To systematically assess the impact of ischemic preconditioning intervention on the cardiac autonomic control nerves of athletes during the post-exercise period.

Rationale The state of cardiac autonomic control during and after exercise has been recognized as an important indicator for monitoring exercise training status and adjusting exercise training prescriptions. To systematically assess the impact of ischemic preconditioning intervention on the cardiac autonomic control nerves of athletes during the post-exercise period. Previous research has suggested that high levels of cardiac parasympathetic reactivation in athletes at the end of exercise represent acceptability of higher training intensities and higher-quality training outcomes, as well as faster physiological recovery after training. Because the cardiac autonomic

nervous system is thought to be interconnected with many other physiological systems, the functional status of the autonomic nervous system can provide useful information about the body's overall functional adaptation to training stimuli.

Condition being studied Ischemic preconditioning (IPC) was initially used to reduce prolonged ischemia-reperfusion injury, applied to reduce the area of cardiac injury in myocardial infarction, and is well established in clinical studies. (Eisen, 2004) The exercise field, mainly as a non-invasive intervention to improve athletic performance, has more significant effects in exercise programs targeting the aerobic system for energy supply, and the mechanisms may involve multiple pathways such as neural and somatohumoral.

METHODS

Search strategy The search was conducted by the first author himself in December 2023, and the

search time boundary was set from database creation to December 2023. Search databases include: CNKI, Wikipedia, Web of Science, PubMed and Embase. Search terms are combinations of terms and keywords: ("Ischemic preconditioning" or "remote ischemic preconditioning" or "occlusion preconditioning" or "transient limb ischemia" or "muscle ischemia") AND ("heart rate" or "heart rate recovery" or "heart rate variability" or "parasympathetic" or "cardiac autonomic control") AND ("exercise").

Participant or population The results showed that the beneficial effect of ischemic preconditioning involved healthy amateur athletic participants with less than one year of training, middle-distance runners with some years of training, well-trained road cyclists, runners, triathletes, and elite-level judo athletes.

Intervention Repeated ischemia and reperfusion procedures are performed proximally to the extremities, often using special taping, and typically consist of two to four cycles of 5-minute ischemia and 5-minute reperfusion.

Comparator IPC: ischemic preconditioning; CON: control (no cuff); SHAM: cuff administration with low pressure.

Study designs to be included AMSTAR Literature Quality Assessment Scale, Bias Risk Assessment Chart, Forest plots, Forest plots.

Eligibility criteria The literature search was completed in February 2024 and quality articles were screened based on the following inclusion and exclusion criteria. Inclusion: (1) original studies; (2) completion of at least one exercise or effort test; (3) with recovery effects analysis; (4) experimental design with at least one pair of control vs. control group; (5) exercise experience or athlete subjects. Exclusion: (1) research methodology articles and reviews; (2) articles that do not limit the subjects' exercise level and health status; (3) articles with repetitive or similar content.

Information sources By reading through each study and extracting data from the article. Only variables assessed in more than three studies in total were included in the Meta-analysis, and for the assessment of HRV only two studies were included and therefore excluded. Descriptive information (e.g., sample size, age, training level, IPC treatment procedures, exercise protocols, etc.) and experimental data were used to make data analyses of the images in the text through the article data or by using the Plotdigitizer, and

requesting the authors to give it by email when confronted with missing data in the text.

Main outcome(s) A total of 7 RCTs including 88 subjects were included. The meta-analysis showed that ischemic preconditioning was indeed effectively improving the heart rate short-term recovery (MD = -3.99, 95%CI: -5.93 to -2.05, $p < 0.00001$), and long-term recovery post-exercise (MD = -9.73, 95%CI: -12.74 to -6.73, $p < 0.00001$). There was however no significant effect on resting state heart rate variability (HRV) or peak heart rate (HR peak) (MD = -0.16, 95%CI: -2.46 to 2.14, $p = 0.89$) during the end of exercise.

Quality assessment / Risk of bias analysis

1. Is a pre-design program provided?
2. Is the selection of included studies and data extraction reproducible?
3. Has an extensive and comprehensive literature search been implemented?
4. Has publication status been considered in the inclusion criteria, e.g., gray literature?
5. Is a list of included and excluded studies literature provided?
6. Does it describe the characteristics of the included studies?
7. Is the scientific validity of the included studies evaluated and reported?
8. Is the science of incorporating research appropriately applied to the derivation of conclusions?
9. Is the method of synthetically incorporating the results of the study appropriate?
10. Has the potential for publication bias been assessed?
11. Is a relevant conflict of interest stated?.

Strategy of data synthesis Meta-analysis was applied to short-term HRR, long-term HRR, and Heart Rate peak variables separately using Review Manager version 5.3. The effect sizes of the variables were calculated using pre-intervention versus post-intervention and standard deviation (SD) to determine the significance of the differences, using a significance level of $p \leq 0.05$. The data in the paper involve continuous variables (heart rate), which are commonly expressed as standard error (SE), and the data were transformed using Cochrane Training's Revman Calculator to derive the standard deviation (SD) from the experimental data by means of confidence intervals, p-values, t-values, and standard errors ($SD = SE \cdot \sqrt{N}$). Within-group changes in these variables were determined by calculating the differences before and after the intervention. When it was indeed necessary for the study to have

missing data, the Cochrane Handbook chapter 16.1.3.2 on SD interpolation, the formula given in equation (1) was utilized to estimate SD change, with correlation coefficients (Corr) of 0.80 being taken for each of the IPC groups versus the SHAM/CT group.

Multiple crossover studies were covered in the study, and to estimate the heterogeneity of the crossover studies, the I^2 statistic was used, with $I^2 \leq 25\%$ being low, $I^2 = 20\%-50\%$ being medium, and $I^2 \geq 75\%$ being high.

$SD_{change} = \sqrt{(SD_{baseline}^2 + SD_{final}^2 - 2 \times Corr \times SD_{baseline} \times SD_{final})}$ equation(1).

Subgroup analysis No.

Sensitivity analysis The effects of ischemic preconditioning on short-term heart rate recovery, long-term heart rate recovery, and HRpeak are shown in Figure III. For short-term recovery of heart rate, IPC was associated with a more significant effect size compared with the sham-operated group or control group (CI: (-5.93, -2.05), $p < 0.00001$); heterogeneity between studies was rated as low but not significant ($p = 0.31$, $I^2 = 14\%$). For long-term heart rate recovery, there was also a significant effect size for IPC compared with the sham-operated group or the control group (CI: (-12.74, -6.73), $p < 0.00001$), but there was highly significant heterogeneity between studies ($p = 0.00002$, $I^2 = 80\%$). For HRpeak, there was no significant effect in the IPC group compared to the sham operation or control group (CI: (-2.46, 2.14), $p = 0.89$), and heterogeneity between studies was low and non-significant ($p = 0.94$, $I^2 = 0\%$).

Language restriction No.

Country(ies) involved China.

Keywords intermittent occlusion, cardiac function, parasympathetic nerves, cardiac autonomic control, exercise recovery.

Contributions of each author

Author 1 - Chuan qiu shui Wang - Author I did literature collection, data collection, data analysis, and first draft writing. Author 1 drafted the manuscript.

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