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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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Abstract

Aims: The objective of this study is to comprehensively evaluate the influence of ischemic preconditioning intervention on the autonomic control nerves of athletes during the post-exercise period.

Methods: Randomized controlled trials (RCTs) were sourced from PubMed, Web of Science, Embase, Wipo, CNKI, and Cochrane databases, covering the period from inception to December 2023. The quality of the included RCTs was evaluated using the Cochrane Risk Assessment Tool, and a systematic assessment was conducted using RevMan 5.3.

Results: Seven randomized controlled trials (RCTs) involving 88 subjects were included in the analysis. The meta-analysis indicated that ischemic preconditioning significantly improved heart rate during both short-term recoveries (mean difference [MD] = -3.99, 95% confidence interval [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, $p < 0.00001$). However, there was no significant effect observed on resting state heart rate variability (HRV) or peak heart rate (HR peak) at the end of exercise (MD = -0.16, 95% CI: -2.46 to 2.14, $p = 0.89$).

Conclusion: Ischemic preconditioning facilitates the prompt reactivation of cardiac parasympathetic nerves following exercise and enhances both short-term and long-term heart rate recovery. The extent of this recovery effect may be influenced by factors such as the dosage of the intervention, the individual's training level, and the intensity of the exercise performed.

Limitation: Given the limited number of included studies, the small sample size, and the unclear definition of some experimental procedures, it is essential to design more rigorous and comprehensive high-quality randomized controlled trials (RCTs) in the future to investigate the effects of ischemic preconditioning on cardiac autonomic control nerves following exercise.

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

Text box 1. Contributions to the literature
● Ischemic preconditioning accelerates short-term reactivation of the cardiac vagus nerve after exercise, has a significant effect on short-term heart rate recovery, and may be influenced by exercise intensity. ● Ischemic preconditioning does not affect cardiac autonomic control or accelerated sympathetic inhibition during exercise. ● Ischemic preconditioning may have accelerated the ultra-long-term recovery of heart rate through improved energy metabolism. ● Ischemic preconditioning enhances cardiac autonomic control after exercise and has a positive effect on an athlete's adaptation to greater training intensity or recovery. ● Elevated acute heart rate recovery may reduce cardiac risk events after high-dose exercise.

1. Introduction

The assessment of cardiac autonomic control during and post-exercise is recognized as a significant indicator for monitoring an individual's exercise training status and for making necessary adjustments to exercise training prescriptions(Bellenger et al., 2016; Borresen & Lambert, 2008; Buchheit, 2014). Previous research indicates that elevated levels of cardiac parasympathetic reactivation in athletes following exercise may signify their capacity to tolerate higher training intensities, leading to improved training outcomes and more rapid physiological recovery post-exercise(Stanley et al., 2013). The cardiac autonomic nervous system is believed to be intricately linked with various physiological systems. Consequently, the functional status of the autonomic nervous system can yield valuable insights regarding the body's overall adaptation to training stimuli.

In addition to heart rate variability (HRV) during physical exercise, post-exercise heart rate recovery (HRR) serves as an important indicator for assessing the autonomic regulation of cardiac function(Buchheit, Papelier, et al., 2007; Vesterinen et al., 2016). The process of heart rate recovery following exercise is primarily influenced by the coordinated actions of the parasympathetic and sympathetic nervous systems, with a predominant role played by parasympathetic activity(Gourine & Gourine, 2014; Kannankeril et al., 2004). The short-term recovery of heart rate following exercise, characterized by a decline in heart rate from peak levels to below baseline within 60 seconds after stopping, has been shown to reflect the functional capacity of cardiac vagal activity. This measure is significant for predicting mortality risk(Cole et al., 1999). The recovery of heart rate in the short term following a sub-extreme exercise trial demonstrated a significant correlation with an elevated risk of cardiac events among individuals with cardiovascular risk factors(Cole et al., 2000). This could mean that improved cardiac autonomic control after exercise has a positive effect on reducing the

odds of an exercise risk event (i.e., sudden cardiac death) in an exercising population with cardiovascular risk factors or in an exercising population with cured cardiovascular risk(Peçanha et al., 2014).

Ischemic preconditioning (IPC) was initially employed to mitigate prolonged ischemia-reperfusion injury. It has since been utilized to minimize the extent of cardiac damage in patients experiencing myocardial infarction and is well documented in clinical research(Eisen, 2004). Ischemic preconditioning has been employed in the realm of sports primarily as a non-invasive method to enhance athletic performance. It proves to be particularly effective in activities that rely on the aerobic energy system. The underlying mechanisms may involve various pathways, including neural and somatosensory pathways(Caru et al., 2019; de Groot et al., 2010). Among the various neural pathways, the vagal branch of the autonomic nervous system appears to play a significant role in mediating the protective effects associated with ischemic preconditioning(Basalay et al., 2012; Mastitskaya et al., 2012). The effects of ischemic preconditioning on the cardiac vagus nerve in humans at rest have been investigated in several studies, some of which revealed that single-arm ischemic preconditioning enhances indices of heart rate variability associated with vagal control of the heart at rest in healthy men or in patients at cardiovascular risk(Chen et al., 2018; Enko et al., 2011; Morley et al., 2021). Conversely, an alternative study indicated that ischemic preconditioning did not enhance vagal-related metrics of heart rate variability when comparing patients with coronary artery disease to healthy subjects(Zagidullin et al., 2016). We need to further explore the effects of exercise on the cardiac autonomic control system. To this end, a systematic review and meta-analysis were conducted to evaluate the current state and future potential of ischemic preconditioning across different exercise regimens for enhancing cardiac autonomic control, along with its possible mechanisms.

2.Methods

This systematic review, accompanied by a meta-analysis, has been structured in accordance with the conventions found in research articles and adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines

2.1Database search

The literature search was carried out by the first author in December 2023, with a timeframe extending from the inception of the databases up to that date. The databases consulted included CNKI, Wikipedia, Web of Science, PubMed, and Embase. Detailed search strategies are provided in the supplementary material.

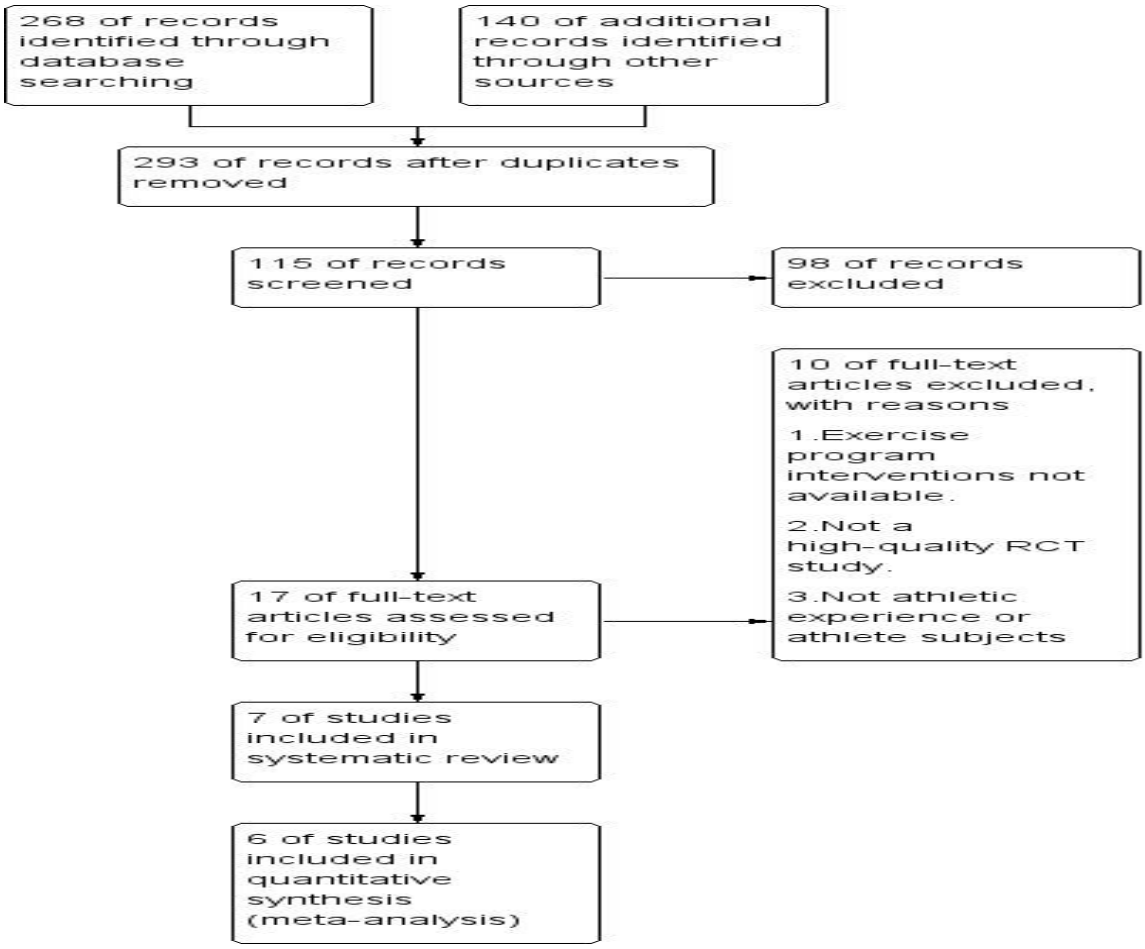
The completion of the literature search occurred in February 2024, during which relevant articles were screened according to specified inclusion and exclusion criteria. The inclusion criteria included: (1) original studies; (2) completion of at least one exercise or effort test; (3) analysis of recovery effects; (4) experimental designs with at least one pair of control groups; and (5) participants with exercise experience or athletes. The exclusion criteria were: (1) methodology articles and reviews; (2) articles that did not specify the subjects' exercise level and health status; and (3) articles containing repetitive or similar content.

2.2 Study Selection and Quality Assessment

All articles met the established inclusion and exclusion criteria, leading to a total of 408

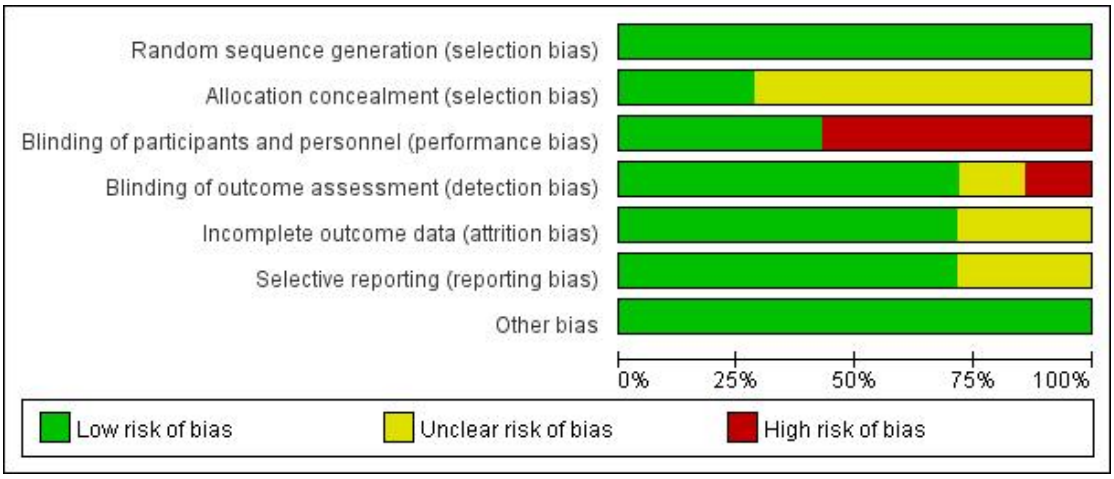
studies identified. Initially, duplicate studies were eliminated. The titles of the remaining studies were reviewed, followed by an examination of the abstracts to ensure they met the criteria. Subsequently, a comprehensive review of each selected article was conducted. (See Figure 1)

Figure 1: Study selection and inclusion procedures

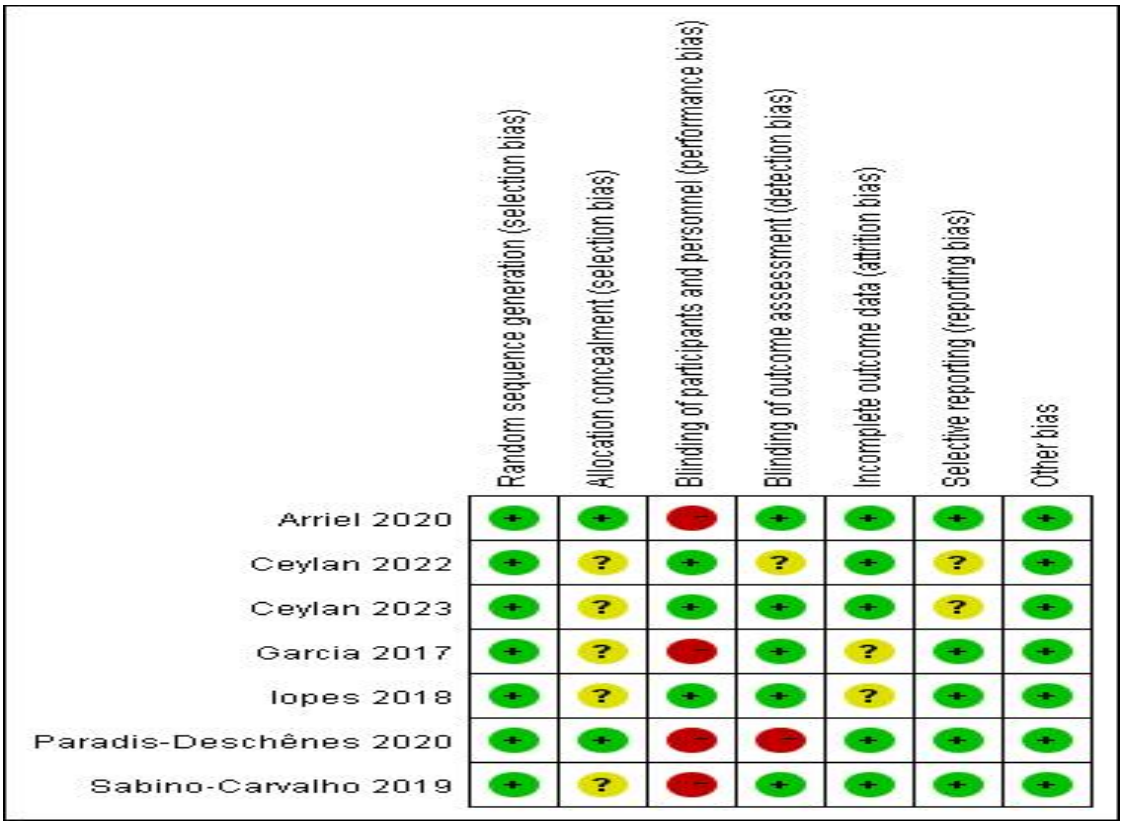


To assess the quality of all the articles in this review, we analyzed the article quality evaluation scale by means of the traditional meta-analysis and AMSTAR Literature Quality Evaluation Form. The Cochrane Risk Assessment Tool was also used to evaluate the risk of bias table for the included articles (Figure I), and the overall quality achieved by each paper was evaluated via common analysis.

Figure I: Bias Risk Assessment Chart (A) (B)



(A)



(B)

2.3. Data Analysis

Each study was reviewed, and relevant data were extracted from the articles. Only variables assessed in more than three studies were included in the meta-analysis; consequently, the assessment of heart rate variability (HRV) was excluded since it only featured in two studies. Descriptive information—such as sample size, age, training level, IPC treatment procedures, and exercise protocols—along with experimental data, were utilized to perform data analyses of the images presented in the articles. This was achieved either through the data available in the articles or via Plotdigitizer, and we contacted the authors via email when we encountered missing data. The meta-analysis was conducted separately for short-term heart rate recovery

(HRR), long-term HRR, and peak heart rate variables using Review Manager version 5.3. Effect sizes for the variables were computed by comparing pre-intervention and post-intervention results, along with standard deviations (SD), to determine the significance of the differences, with a significance threshold set at $p \leq 0.05$.

The data presented in the paper consist of continuous variables, specifically heart rate, which are typically expressed as standard error (SE). To derive the standard deviation (SD) from the experimental data, Cochrane Training's RevMan Calculator was employed, utilizing confidence intervals, p-values, t-values, and standard errors $\sqrt{}(S\ D = S * \sqrt{N})$. Within-group changes in these variables were assessed by calculating the differences observed before and after the intervention. In cases where missing data were pertinent to the study, the Cochrane Handbook chapter on SD interpolation provided a formula for estimating SD changes, employing correlation coefficients (Corr) of 0.80 for each of the IPC groups compared to the SHAM/CT group.

The analysis included multiple crossover studies, with the I^2 statistic used to evaluate the heterogeneity of these studies. The thresholds for heterogeneity were defined as low ($I^2 \leq 25\%$), medium ($I^2 = 20\%$-50%), and high ($I^2 \geq 75\%$).

3. Results

The search, screening, and inclusion process identified only seven papers that satisfied our inclusion criteria. However, due to missing data from the Grica literature, only six papers could be incorporated into the meta-analysis(Garcia et al., 2017). Among these 7 studies, 6 studies reported that ischemic preconditioning improved heart rate performance after exercise and was judged to yield better results, and 1 study reported that IPC had no effect of IPC on heart rate recovery. No study results demonstrated a negative effect on heart rate recovery.

Exercise protocols varied between studies, but all induced greater maximal heart rate and exercise fatigue and were used to assess heart rate recovery. The main focus was on lower body exercise, with three studies using similar incremental endurance testing protocols (including running and cycling tests) to induce exercise fatigue and two studies focusing on short-distance sprinting. Two studies involved whole-body explosive movements (judo-specific movements) and the studies did not involve resistance exercise. {See Table 1}

Table 1: Characteristics of the IPC studies

Authors	N	Male	Female	Subjects	Exercise protocols	Analyzing Variables	Is IPC Effective for Heart Rate Recovery?	Other variables analyzed
Garcia (2017)	8	8	0	sub-elite rugby players	rugby-specific exercise protocol	Mean HR(0-60min)	NO	Agility T-test , CMJ, CJ30, PEL
Lopes (2018)	15	15	0	team-sport practitioners	Repeated sprint exercise	HRR(60s)、RMSSD、T30	YES	VO2peak,VCO2peak, RER peak, Lac-
Sabino-Carvalho (2019)	15	11	4	endurance athletes	discontinuous incremental test	HRV, RSA, HRR30S, T30	YES	Lac-
Paradis-Deschênes (2020)	9	9	0	endurance athletes	cycling time trials	HR(30s-120s)	YES	Blood sampling*, SpO2,near-infrared spectroscopy-derived muscle oxygenation parameters*
Arriel (2020)	18	18	0	healthy cyclists	Maximal incremental cycling test	HRR(0s-5min)	YES	Performance*, PO, RPE

Ceylan (2022)	10	10	0	elite judo athletes	special judo fitness test	HR(0s-10min)	YES	Lac-*, oxygen saturation, Systolic blood pressure*
Ceylan (2023)	13	13	0	elite judo athletes	special judo fitness test	HR(1min、30min、60min)	YES	CMJ*,DOMS*

RMSSD:time-domain heart rate variability, T30:HR decay within the first 30s of recovery, RSA: respiratory sinus arrhythmia, CMJ: counter-movement jump； CJ30： 30 s of continuous vertical jumps； PEL: perceived exertion levels; SpO2:arterial O2 saturation; RPE: perceived exertion; PO: power output; DOMS: delayed onset muscle soreness; RER peak: peak respiratory exchange ratio; *, it was influenced by IPC

Table 2 lists the characteristics of the IPC intervention program, including the IPC intervention sets, ischemia pressure, the interval between the IPC intervention and the exercise program, and group settings. On the basis of past research, two experimental procedures should be categorized as post-exercise ischemic conditioning (PEIC), where the IC protocol is performed immediately after exercise. The article itself does not make a strict delineation, which may have affected the results of the analysis. Other studies of ischemia-reperfusion procedures have been performed prior to exercise or between two exercise intervention regimens, usually at intervals of 5-30 minutes, to simulate real sports or game situations.

Table 2: Characteristics of the IPC Intervention Program

Authors	IPC Sets	Ischemia Pressure IPC/SHAM/CT (mmHg)	Time to exercise protocol	Groups	Were Subjects Informed about the Effects of IPC	Experimental design
Garcia (2017)	3×5 min	220/0(CT)	0min	IPC/CON	NO	crossover
Lopes (2018)	3×5 min	220/20(CT)	48h,24h,35min	IPC/CON	NO	Single-blind, randomized, crossover and controlled
Sabino-Carvalho (2019)	4×5 min	220/0/0	17min	IPC/SHAM/CON	YES	randomized, placebo- and sedation-controlled, and crossover
Paradis-	3×5	220/0/0	20min	IPC/NM	NO	Randomized and

Deschênes (2020)	min			ES/AR		crossover
Arriel (2020)	2×5 min	50 mm Hg above systolic arterial pressure/20(SHAM)/0(CT)	5min	IPC/SHAM/CON	NO	Single-blind, placebo-controlled
Ceylan (2022)	3×5 min	220/0(CT)	30min	IPC/CON	YES	Controlled, single-blind, crossover
Ceylan (2023)	3×5 min	50 mm Hg above systolic arterial pressure/20mmHg(PLA)	0min	IPC/SHAM	It was not exposed by the author	Single-blind, placebo-randomized crossover

NMES: neuromuscular electrical stimulation; AR: active recovery; PLA: placebo;

IPC had some favorable effects on the short-term and long-term recovery of heart rate (Tables 3 and 4) but not on the HR peak produced during exercise (Table 3). The definition of long-term heart rate recovery time has not been strictly delineated by any study, which usually uses either 180s of data or 360s of data, with two studies extending long-term heart rate data to 30 and 60 minutes. The undefined time intervals make the rigor of the data and the results of the long-term heart rate recovery analysis in this study somewhat questionable. With respect to the data and results of the studies are concerned, there was only one study in which the long-term heart rate recovery data were better in the CT group than in the IPC group.

Table 3: Comparison of short-term heart rate recovery in IPC and SHAM/CT

Authors	Heart Rate Variables	IPC	SHAM/CT
Lopes(2018)	HRR60s(bpm)	39±11.6	34±11.6
		36±11.6	33±7.4
		38±11.6	34±11.6
Sabino-Carvalho（2019）	HRR30s(bpm)	31±7.4	26±11.6
	70% of maximal effort	31±7.4	26±7.4
Sabino-Carvalho（2019）	HRR30s(bpm)	29±7.4	25±7.4
	75% of maximal effort	29±7.4	24±7.4
Paradis-Deschênes (2020)	HRR60s(bpm)	27±9	33±7

Arriel(2020)	HRR60s(bpm)	53±6	47±5
Ceylan(2022)	HRR60s(bpm)	41±10	29±8
Ceylan(2023)	HRR60s(bpm)	27±8	24±7

Data = mean ± standard deviation

Table 4: Comparison of long-term heart rate recovery in IPC and SHAM/CON

Authors	Heart Rate Variables	IPC	SHAM/CON
Lopes(2018)	HRR Tau(bpm)	78±22	78±15
Arriel(2020)	HRR180s(bpm)	83±7	81±7
Paradis-Deschênes (2020)	HRR120s(bpm)	53±11	58±9
Ceylan(2022)	HRR180s(bpm)	70±8	62±9
Ceylan(2023)	HRR30min(bpm)	100±8	85±7
Ceylan(2023)	HRR60min(bpm)	108±8	91±7

HRR Tau: HR data recorded until 360 s of recovery after set 3 were used to calculate a time constant； Data = mean ± standard deviation

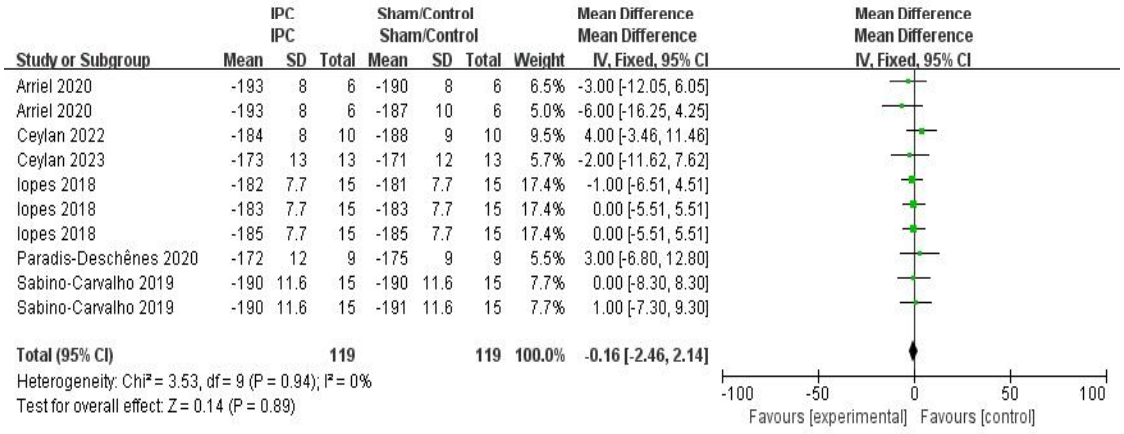
Table 5: Comparison of maximum exercise heart rate (HR peak) between the IPC and SHAM/CON groups

	IPC	SHAM/CON
Lopes	182±7.7	181±7.7
(2018)	183±7.7	183±7.7
	185±7.7	185±7.7

Sabino-Carvalho (2019)	190±11.6	190±11.6
Sabino-Carvalho (2019)	190±11.6	191±11.6
Paradis-Deschênes (2020)	171±8	175±9
Arriel (2020)	193±8	190±8
Arriel (2020)	193±8	187±10
Ceylan (2022)	184±8	188±9
Ceylan (2023)	173±13	171±12

Data = mean ± standard deviation

The impact of ischemic preconditioning (IPC) on short-term heart rate recovery, long-term heart rate recovery, and peak heart rate (HR peak) is illustrated in Figure III. For short-term heart rate recovery, IPC demonstrated a greater effect size compared to both the sham-operated group and the control group (CI: (-5.93, -2.05), p<0.00001). The heterogeneity among studies was low and not statistically significant (p=0.31, I^2=14%). Regarding long-term heart rate recovery, IPC also showed a significant effect size in comparison to the sham-operated and control groups (CI: (-12.74, -6.73), p<0.00001), although there was considerable

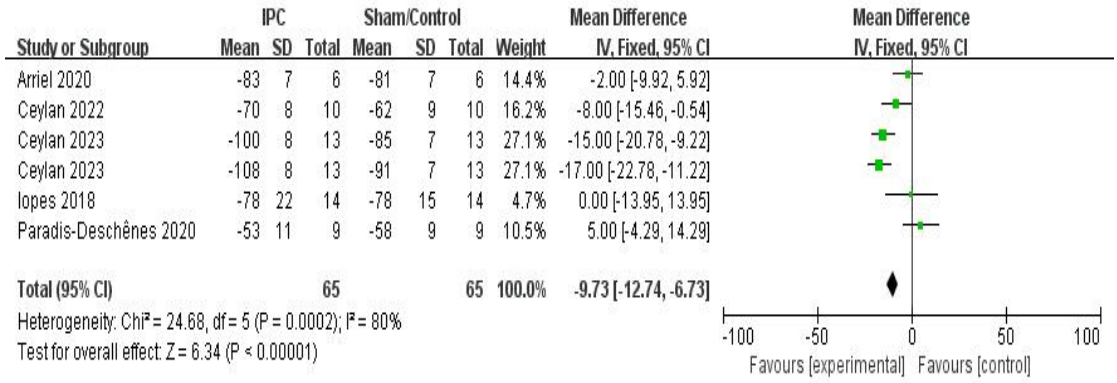


heterogeneity among the studies (p=0.00002, I^2=80%). Conversely, for the HR peak, no significant difference was observed in the IPC group relative to the sham operation or control groups (CI: (-2.46, 2.14), p=0.89), with heterogeneity between studies remaining low and nonsignificant (p=0.94, I^2=0%).

(A)

(B)

Figure III: Plots (A), (B), and (C) present forest plots that illustrate the short-term recovery of heart rate, long-term recovery, and maximal heart rate variables in comparisons between ischemic preconditioning and sham surgery (SHAM) or control (CT) interventions. The horizontal line indicates the 95% confidence interval (CI) for the effect sizes observed in the study, while the diamond at the bottom represents the overall effect as calculated by the fixed-effects model.



(C)

4.Discussion

This study represents the first comprehensive systematic review and meta-analysis examining the effects of ischemic preconditioning on cardiac autonomic regulation following exercise. Our findings indicate that ischemic preconditioning significantly enhances short-term heart rate recovery when compared to long-term heart rate recovery after an exercise protocol. However, it does not demonstrate a significant impact on resting-state heart rate variability or maximum heart rate attained during exercise.

4.1 Quality of thesis

Although the studies all achieved high-quality ratings, some limitations were still identified. The included studies all collected overall data on subject characteristics, including age, height, weight, maximal oxygen uptake, and body mass index, but only two of the studies performed a statistical analysis of the general differences between the groups via the G*power software, reporting exact p values(Arriel et al., 2020; Ceylan et al., 2023). In two studies, the exclusion criteria for subjects were not described, which reduced the reliability of the experimental sample(Ceylan et al., 2023; Lopes et al., 2018). Second, only 2 studies included confidence intervals (CIs) for the main findings to characterize the reliability of the findings(Ceylan & Franchini, 2022; Lopes et al., 2018). IPC has a placebo effect versus a precipitant effect, which is explained by the ability of subjects to perceive pressure band stress sensations to clarify differences between interventions. In addition, whether the subjects were informed of the IPC effect may have allowed them to have positive or negative expectations of IPC, which in turn increased the variability of the results(Sabino-Carvalho et al., 2017). Only two papers have made strict controls for placebo versus sedative effects, allowing for more rigorous

experimental procedures and more credible conclusions(Arriel et al., 2020; Sabino-Carvalho et al., 2019).

4.2 Analysis of Subjects

Out of a total of 88 subjects, only 4 were female. This limited representation diminishes the impact of ischemic preconditioning on the cardiac autonomic effects observed in female samples. One possible explanation for this underrepresentation is that females may possess inherent protection against ischemic interventions, coupled with the fact that the pool of female professional athletes is significantly smaller than that of their male counterparts, complicating recruitment efforts(Paradis-Deschênes et al., 2017). The findings indicated that the positive effects of ischemic preconditioning were observed in a range of healthy amateur athletic participants, including those with less than one year of training, middle-distance runners with several years of experience, well-trained road cyclists, runners, triathletes, and elite-level judo athletes. Our analysis revealed a beneficial impact of ischemic preconditioning for both participants with limited training years and those with extensive training backgrounds. However, this intervention did not yield any effects for subjects with many training years in rugby. (See Table 6).

Table 6: Analysis of experimental subjects

Authors	Athletes	training duration	Age variable	Other characteristic variables
Garcia (2017)	Amateur Division I rugby union players	≥6 Months Rugby Specialized Training	24±4	Height, weight
Lopes (2018)	Healthy Male	≤1years	25±5	Height, weight
Sabino-Carvalho (2019)	Healthy middle-distance runners	5.0±0.5 years	23±1 （ male ） 24±2 （female）	Maximum Oxygen Intake, Body Fat
Paradis-Deschênes (2020)	Well-trained road cyclist, runner, triathlete	≥2 years	26.4±4.8	Maximum oxygen uptake, body mass index, height, body fat
Arriel (2020)	Healthy Cyclists	≥1 years	28.0±4.6	Weight, body fat, peak power*
Ceylan (2022)	Elite Judo Athletes	9.6±1.9 years	20.0±2.2	Height, body mass index, body fat, defatted weight
Ceylan	Elite Judo Athletes	12.1±0.1 years	18.6±0.9	Body mass index, height, body fat, defatted weight*

(2023)
*:G*power analysis, no difference in general characteristics between groups; Data = mean ± standard deviation

4.3 Exercise programs to induce heart rate variability

The effects of ischemic preconditioning are primarily associated with incremental endurance testing, sprinting, and specialized exercise modalities. Three distinct types of incremental endurance exercise tests—the discontinuous incremental test, the maximal incremental test, and the maximal incremental cycling test—demonstrated beneficial effects on the short-term recovery of heart rate upon completion of these tests(Arriel et al., 2020; Paradis-Deschênes et al., 2020; Sabino-Carvalho et al., 2019). Among the sport-specific programs, the rugby program included short-distance sprinting, serpentine sprinting, and various sprinting drills. In contrast, the judo-specific fitness test (SJFT) emphasized the rapid execution of short-duration back throws. The SJFT is designed to assess the quick completion of back throws within a limited timeframe. The experimental intervention involving the SJFT demonstrated a beneficial effect of intermittent physical conditioning (IPC) on both short-term and long-term heart rate recovery. However, the rugby-specific exercise program showed no impact on heart rate recovery. This discrepancy in findings between Grica and Lopes focused on an exercise program primarily centered on sprinting may be attributed to the more pronounced effect of sprinting on short-term cardiac autonomic control, coupled with its lesser impact on long-term heart rate recovery.

4.4 Effects of IPC on the short-term HRR, long-term HRR, HR peak, and HRV

A strong influence of exercise intensity on the short-term recovery effect on heart rate can be found in studies of various sports, and the recovery effect may gradually decrease with increasing exercise intensity. The possible reason for this is that the higher the exercise intensity, the more excited the cardiac sympathetic nerves are at the end of the exercise, which inhibits the cardiac vagal reactivation effect. For example, in the hyper-extreme repetitive sprint exercise protocol, there was almost no change in the heart rate decay constant in the first 30s. (Del Rosso et al., 2017; Nakamura et al., 2009)Future studies could further analyze the effect of exercise intensity.

In long-term heart rate recovery, either from endurance or sprinting exercise, the recovery data effect was small from 60 s to 360 s. It is speculated that the timing of cardiac vagal reactivation due to ischemic preconditioning was only short-term and did not alter sympathoexcitatory activity during the subsequent recovery time. Significant ultra prolonged heart rate recovery effects were found only in elite judo athletes facing times longer than 10 min. In contrast, ischemic preconditioning had no effect on ultraprolonged heart rate recovery in a study of elite rugby players. It is hypothesized that ultra prolonged heart rate recovery may be associated with improved energy metabolism. Subsequent studies should have a clear definition of the duration of long-term heart rate recovery to improve the quality of the study.

IPC had no impact on the maximal heart rate during exercise, indicating that its primary effect may be on post-exercise vagal control of the heart rather than on autonomic control during exercise. Additionally, no meta-analysis was conducted for heart rate variability due to the limited number of studies available in the literature. IPC does not enhance cardiac vagal

control at rest or improve time-domain heart rate variability following exercise in endurance athletes. This may be attributed to insufficient doses of ischemic preconditioning or the already elevated levels of cardiac vagal control present in endurance athletes, which could render them less responsive or ineffective to such interventions.

An experimental protocol was more specific, directly ignoring the placebo effect by conducting a randomized crossover study of ischemic preconditioning with active recovery versus neuroelectrical stimulation as a means of recovery of athletic performance in endurance athletes. IPC was found to have no significant effect on either acute or long-term recovery of heart rate but reduced the maximal heart rate during exercise. This experimental design may be closer to the "real situation" of athlete recovery than laboratory experiments, but it may have implications for the actual statistical effects on heart rate recovery, raising new questions about the real-life effects of ischemic preconditioning in a competitive setting or after training.(Paradis-Deschênes et al., 2020)

4.5 Possible mechanisms by which IPC affects cardiac autonomic nerves after exercise

Possible hypotheses regarding the mechanism of action of short-term cardiac autonomic control neuro improvement are the mechanism of rapid vagal reactivation and the energy metabolism hypothesis. Previous research that involved blocking vagal and sympathetic receptors has demonstrated that both short-term and long-term heart rate recovery (HRR) primarily depends on the reactivation of cardiac vagal activity following exercise. In contrast, the influence of sympathetic branches appears to be minimal. The energy metabolism hypothesis, on the other hand, is that ischemic preconditioning may reduce post-exercise energy metabolism deficits by increasing the proportion of aerobic metabolism in total exercise energy metabolism expenditure by increasing oxygen uptake and decreasing blood lactate accumulation, decreasing the contribution of anaerobic metabolism during exercise even more, and thus improving heart rate recovery. (Bailey, Jones, et al., 2012; Seeley & Jacobs, 2022)On the basis of the results of the analysis, IPC dominated short-term vagal reactivation and was not accompanied by an improvement in energy metabolism. IPC had less of an effect on long-term sympathoinhibition, and the long-term restorative effect may have been due to an improvement in blood flow and an increase in oxygen uptake.

Cardiac vagal branches were found to play an important role in IPC-mediated protection against ischemia-reperfusion injury in previous animal experiments.(Basalay et al., 2012) The mechanism of vagal activation may involve mainly the neuro-humoral pathway. IPC activation of nociceptive afferent nerves at the intervention site in conjunction with facilitation of the release of circulating substances at the intervention site is involved in direct activation of the cardiac vagus nerve. (Gourine & Gourine, 2014)In contrast, the activation of respiratory coupling, muscle sensory reflexes, metabolite-sensitive afferents, or temperature-sensitive afferents activated by stimulation of the intervening site may affect this neurohumoral pathway. (Buchheit, Laursen, et al., 2007; Peçanha et al., 2017)These results continue to demonstrate the reactivation effect of IPC on the vagus nerve after exercise. Short-term heart rate recovery disproves the postexercise sympathoinhibitory processes and energy metabolism hypotheses. IPC-mediated improvements in cardiac autonomic control during sprint or endurance exercise are not accompanied by changes in energy metabolic indices because they do not alter the HRR or HRV after 60 seconds.

The ultra-long recovery phase of heart rate may be the result of a combination of a sustained decrease in sympathetic activity and an increase in the efficiency of energy metabolism. The metabolic byproduct reduction effect may include both a reduction in metabolic byproduct production and an acceleration of metabolic byproduct removal. First, the enhanced aerobic metabolic function that accompanies exercise cessation activates mitochondria within skeletal muscle, accelerating postexercise oxygen extraction and reducing lactate or hydrogen ion (H+) production. (Kido et al., 2015) Second, ischemic preconditioning has been shown to improve cardiac hemodynamics after strenuous exercise, i.e., to maintain endothelium-dependent vasodilatation, which accelerates blood flow for rapid elimination of metabolic byproducts. The vasodilatory effect involves nitric oxide, an endothelial progenitor cell associated with increased adenosine content. (Bailey, Birk, et al., 2012; Kimura et al., 2007; Ng et al., 2019)Despite the lack of a significant change in heart rate variability observed during the second phase, our study did reveal a noteworthy decrease in lactate levels post-exercise. Consequently, we hypothesize that improved energy metabolism is the predominant physiological mechanism influencing the second stage of recovery.

5. Limitations

Given the limited number of articles included, the small sample size, and the unclear definitions of some experimental procedures, there is a need for more rigorous and comprehensive high-quality randomized controlled trials (RCTs) in the future to investigate the effects of ischemic preconditioning on cardiac autonomic control nerves after exercise.

6. Conclusions

Ischemic preconditioning interventions have been shown to accelerate the rapid recovery of cardiac autonomic control after exercise and are not accompanied by alterations in heart rate variability at rest or in cardiac autonomic control during exercise. The effects act directly through rapid reactivation of the cardiac vagus nerve after exercise, with metabolic effects. This effect may be more effective in endurance sports, judo, and repetitive sprinting. Thus ischemic preconditioning can be used as an effective, non-invasive means of improving athletic performance. It can also be used as a means of recovery between training days or competitions, to increase the intensity of sports training, or to protect against cardiovascular risk events in sports.

Declarations

Authors' contributions

C.W. wrote the main manuscript. J.L. and Y.Y. provided research methodology and supervision. K.W. H.L. and S.L. provided writing supervision and review. All authors reviewed the manuscript.

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Conflict of Interest Statement

The authors report no conflicts of interest.

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