Applications of Ischemic Preconditioning in Enhancing Exercise Performance

Jiayu Wu *

School of Clinical Medicine, Anhui Medical University, Hefei, 230601, China

* Corresponding Author Email: mkmsdk@outlook.com

Abstract. Ischemic preconditioning (IPC) has been proved that it can affect exercise performance, the function of IPC goes beyond simple cardioprotective effect. In terms of resistance motion, IPC can enhance the maximum repetitive power, and relieve muscle fatigue after high-intensity exercise, delaying the accumulation of fatigue-related metabolites. For endurance sports, IPC enhances cardiovascular efficiency by improving heart rate variability and autonomic nerve regulation, accelerating heart rate recovery after exercise, and reducing cardiac pump workload during exercise. Besides, IPC can activate hypoxia adaptation pathway, improve the oxygen utilization rate of skeletal muscle and enhance mitochondrial respiratory capacity. In addition to systematic adaptation, IPC also improves local microcirculation and tissue oxygenation, and enhances antioxidant defense. However, the responses of different groups of people to it show heterogeneity. For example, there are differences in sensitivity among endurance athletes, strength athletes and the elderly in terms of aerobic and anaerobic capacity improvement. Future research needs to clarify its optimal approach in terms of intervention stress, duration and location, and combine clinical trials to verify its application boundaries in different populations. This review examines evidence on ischemic preconditioning, focusing on its roles in autonomic regulation, oxygen utilization, and muscle metabolism, and discusses tailored applications for different populations.

Keywords: Ischemic preconditioning, heart rate variability, hypoxia, exercise.

1. Introduction

Ischemic preconditioning (IPC) refers to the application of a series of non-invasive medical technologies to temporarily and intermittently treat ischemia in local or extensive body parts, putting the body in a transient, non-invasive and reversible ischemic state for reperfusion. In recent years, IPC's potential in the fields of medicine and sports health is gradually becoming evident. It is not only proved to improve myocardial ischemia and promote local oxygenation of the heart, but also reduce ATP consumption and the production of metabolic products during ischemia, protecting muscles [1]. In the field of sports, as a means to enhance athletic performance and promote functional recovery, it has gradually attracted a great deal of attention.

IPC can improve aerobic and anaerobic exercise performance [2]. IPC's effects also show certain differences among different groups. For elite athletes, IPC has been proven that it can enhance the performance of intermittent sprinting and other related events, helping athletes maintain greater endurance and strength during high-intensity exercises [3]. For the general male population, IPC can, to a certain extent, facilitate the recovery of muscle damage after exercise [4]. For elderly women, IPC can enhance grip strength and activity performance [5]. These improvements mainly result from the fact that IPC can enhance the heart's pumping capacity, improve blood circulation, enhance protection for ischemic areas, and increase oxygen utilization efficiency. Through influencing a series of physiological changes, it indirectly affects athletic performance [6]. Furthermore, IPC also enhances the overall functionality of the body by regulating the aerobic system and glycolytic pathways, and this effect is particularly pronounced during the recovery phase after exercise [7]. Recent studies have demonstrated that high-intensity endurance performance improved by 6.9% following IPC conducted under heat stress [8].

Despite sustained interest in ischemic preconditioning, its efficacy for enhancing athletic performance remains contested. Multiple trials have found no meaningful changes in muscle strength or exercise responses following IPC, and recent systematic reviews report effects that are largely

indistinguishable from placebo with at best small improvements in time to exhaustion [9]. Some evidence even suggests that the observed benefits may partly stem from psychological or expectancy effects rather than true physiological adaptations [10]. Moreover, interindividual variability appears substantial. The response to IPC may differ across populations, particularly among the elderly or those with limited physical fitness, where its efficacy has not been consistently verified. The underlying mechanisms through which IPC modulates exercise performance also remain incompletely understood. Clarifying these processes is essential to refine its practical application. This review therefore synthesizes current evidence on the physiological mechanisms of IPC, focusing on its effects on heart rate variability, hypoxia-related signaling, and muscle function. By identifying both the strengths and limitations of existing studies, it aims to provide a foundation for optimizing IPC-based interventions across diverse athletic and clinical contexts.

2. Mechanisms of Ischemic Preconditioning in Exercise Performance

2.1. Regulation of Heart Rate Variability and Autonomic Function by IPC

Heart rate variability (HRV) represents the fluctuation in the time interval between successive heartbeats (R-R intervals). It primarily reflects the dynamic regulation of cardiac rhythm by the autonomic nervous system and is widely regarded as an indirect marker of sympathetic and vagal modulation, particularly useful for evaluating autonomic adjustments following IPC. Indicators reflecting HRV include time domain variables and frequency domain variables. Time domain variables often involve the standard deviation of all normal R-R intervals (SDNN), which primarily reflects all periodic components responsible for HRV, It is related to the activity functions of the sympathetic and parasympathetic nerves, and is often regarded as the gold standard for HRV time domain measurement. And the percentage of consecutive R-R intervals with a difference exceeding 50 milliseconds (pNN50) is primarily related to vagal nerve activity. And the root mean square of successive R-R interval differences (RMSSD) is the main parameter for evaluating vagal-mediated changes in HRV. Frequency domain variables are quantified by converting the observed variability into Hertz, including low-frequency (LF) and high-frequency (HF) power. LF primarily reflects the activity level of both sympathetic and parasympathetic nerves, while HF primarily reflects the activity level of parasympathetic nerves. LF/HF, on the other hand, reflects the balance between sympathetic and vagal nerves. SD1 represents short-term heart rate variability and baroreceptor activity markers, while SD2 represents long-term heart rate variability and baroreceptor activity markers [11].

Both high- and low-pressure IPC protocols have been shown to improve resistance exercise performance to varying extents, accompanied by alterations in HRV. This suggests that the magnitude of pressure applied during IPC may differentially modulate autonomic activity, thereby influencing subsequent strength performance [12]. A study involving sixteen male participants with at least one year of resistance training experience and demonstrated sensitivity to intervention protocols was conducted. Subjects were randomly assigned to high-pressure IPC (220 mmHg), low-pressure IPC (20 mmHg), or a control group, and performed one-repetition maximum (1RM) tests in upper-body exercises including bench press (BP), front lat pulldown (FLPD), and shoulder press (SP) to assess changes in maximal strength. Concurrently, HRV indices were recorded, time-domain variables (the root mean square of successive R-R interval differences) and frequency-domain parameters (HF, LF, and LF/HF), before IPC and at five-minute intervals up to forty minutes during the intervention. All resistance exercises demonstrated strong reliability, with intraclass correlation coefficients (ICC) ranging from 0.948 to 0.990. Compared to the control group, the maximum intensity of resistance exercises was increased in both the high-pressure IPC and low-pressure IPC groups, suggesting that both high-pressure and low-pressure IPC can enhance resistance exercise performance. Regarding HRV, both high- and low-pressure IPC conditions showed an increase in LF and a reduction in HF at 10, 15, 20, 25, 30, 35, and 40 minutes during the intervention, as well as five minutes after completion. Only the low-pressure IPC group showed an increase in the LF/HF ratio and a decrease in RMSSD during maneuvering compared to the resting value after the same time periods. It can be speculated

that after IPC treatment, sympathetic nerve activity increases while parasympathetic nerve activity decreases, but only low-pressure IPC improves the balance between sympathetic and vagal nerves. This suggests that IPC under high or low pressure may affect the activity changes of the nervous system by influencing relevant indicators reflecting HRV, thereby influencing athletic performance. It is likely that IPC modulates afferent signaling through type III and IV sensory fibers within the autonomic nervous system, facilitating neural activation and consequently enhancing muscle strength. IPC may cause changes in the balance between sympathetic and vagal nerves, particularly leading to an increase in vagal activity and a decrease in sympathetic activity, which affects the performance of resistance exercises [13].

Further research indicates that IPC can accelerate heart rate recovery after exercise and enhance athletic performance. To verify the impact of IPC on athletic performance and heart rate during and after the Incremental Cycle Test (ICT), A study involved 18 cyclists, who were divided into three groups: IPC group, sham operation group (SHAM), and control group (Control). Heart rate, power output, and athletic performance were measured during ICT. The results showed that the exercise duration in the IPC group increased by 4.9% ± 4.0%. Meanwhile, the submaximal heart rate, which refers to the maximum heart rate achievable at an exercise intensity lower than the maximum heart rate, decreased from 170 ± 8 bpm to 166 ± 8bpm ($p < 0.05$), and exhibited a faster heart rate recovery. It indicates that IPC may reduce cardiac load during exercise and promote autonomic rebalancing after exercise, and improve cardiac function and accelerate body recovery, thereby playing a positive role in endurance sports [14].

In addition to the traditional airbag compression method, non-occlusive bandaging (NOB) has also been employed as a means of IPC to investigate its impact on HRV. HRV is often used as a prognostic marker for heart disease, reflecting the impact of cardiac autonomic regulation on athletic performance. A study enrolled 30 participants, who were divided into a control group and a NOB group, the results showed that in the NOB group, SDNN increased from 47.69 ± 4.91 milliseconds to 57.53 ± 7.22 milliseconds. Simultaneously, LF, LF/HF, and SD2 increased, while HF decreased. These results indicate that NOB treatment enhances the balance of the sympathetic and vagal nerves. It may indirectly affect athletic performance by improving cardiac autonomic regulation [15]. In summary, both traditional IPC and novel methods such as NOB have demonstrated positive effects on heart rate recovery and HRV. These findings support the view that IPC improves athletic performance through autonomic nervous system regulation, and suggest that future research should further explore the physiological differences and athletic applicability of different IPC protocols.

2.2. Activation of Hypoxia-Related and Antioxidative Pathways

It is known that IPC can cause a reduction in local blood supply, leading to transient local hypoxia. This hypoxic state is not only a signal of injury, but may also initiate a series of molecular level changes that affect the body's athletic performance. It may help to locally adapt to hypoxia during exercise in advance, promote oxygenation in local areas, and improve cardiac and cardiovascular function, thereby enhancing aerobic exercise performance. Early hypoxic adaptation can promote mitochondrial gene expression in the body, increase muscle buffering capacity, and counteract the decrease of erythropoietin in hypoxic environments, thereby accelerating the body's adaptability to exercise [16]. High-altitude areas are characterized by low pressure and low oxygen, which can have a series of impacts on human aerobic activities, by observing the improvement in IPC's adaptability to entering high-altitude areas, we can potentially infer the impact of IPC on hypoxia during exercise. Therefore, the hypoxia pathway triggered by IPC is considered to be one of the important mechanisms for its improvement of aerobic performance.

A study involving seventy-nine healthy adult males was designed to examine whether RIPC could promote early adaptation to high-altitude environments characterized by low pressure and hypoxia, thereby reducing altitude-related discomfort and improving cardiac function and aerobic capacity. The experimental protocol consisted of two sequential phases. In the first phase, heart rate variability and cardiovascular function indices were measured under physiological conditions at low pressure

and low altitude. Participants then underwent graded exercise testing to determine maximal oxygen uptake (VO_2max) and muscle oxygenation (SmO_2), reflecting aerobic capacity and muscle oxygenation efficiency, respectively. Subsequently, RIPC treatment was administered for eight days, with a sham RIPC group serving as the control. The same measurements were repeated under high-altitude conditions to assess whether RIPC treatment enhanced adaptability to hypoxic environments. The second stage is divided into the RIPC treatment group and the sham control group. After 8 days, peripheral blood samples are studied to investigate the physiological effects of RIPC.

The results demonstrated that participants in the RIPC group exhibited a significantly higher VO_2max (43.97 ± 7.37 ml·kg^{-1}·min^{-1}) than those in the control group (37.52 ± 3.88 ml·kg^{-1}·min^{-1}), suggesting that RIPC enhances aerobic capacity under hypobaric hypoxic conditions. The maximum and minimum values of SmO_2 in the RIPC group both increased, which indicates that the RIPC group can improve oxygenation capacity during hypobaric hypoxia. Meanwhile, under hypobaric hypoxia conditions, the systemic vascular resistance index (SVRI) increased in the RIPC group ($p < 0.05$), pulse pressure variation (PPV%) decreased significantly ($p < 0.05$), the percentage of methemoglobin saturation (SpMet) was significantly reduced, which indicates that under hypobaric hypoxia conditions, RIPC may improve aerobic performance by increasing systemic vascular resistance, reducing pulse pressure variation, and decreasing the percentage of SpMet. Plasma protein mass spectrometry analysis revealed a decrease in thymosin beta 4 (Tβ4) after RIPC. Tβ4 is a protein induced by exercise, primarily serving to protect the cardiovascular system. Meanwhile, plasma heat shock protein 70 (HSP70) decreases. It is known that extracellular HSP70 has a pro-inflammatory tendency, while intracellular HSP70 has an anti-inflammatory tendency, which indicates that RIPC can reduce extracellular HSP70, thereby exerting anti-inflammatory effects during aerobic exercise. Meanwhile, an increase in HSP90 indicates an enhanced tolerance to acute hypobaric hypoxia.

RIPC may improve aerobic exercise by enhancing regional oxygenation through increased aerobic capacity, bolstering cardiac function, and regulating plasma proteins, such as reducing Tβ4 and HSP70, while simultaneously increasing HSP90 [17]. In addition to hemodynamics and protein regulation, IPC also demonstrates potential in anti-oxidative stress at the molecular level. Oxidative stress refers to the state of imbalance between oxidation and antioxidation in the human body, the result is an increase in reactive oxygen species (ROS), either due to excessive production of ROS or a decrease in the ability to eliminate ROS. IPC can enhance anti-ROS levels, thereby reducing ROS. It can increase the activity of antioxidant enzymes such as catalase (CAT) and glutathione peroxidase (GPx), thereby reducing ROS accumulation. IPC can increase the expression of the main factor of redox regulators, the transcription factor Nrf2, and reduce oxidative stress and upregulate HSP70 production to enhance cellular defense. Meanwhile, the mitochondrial respiratory chain is the main source of cellular ROS, IPC can promote the localization of Nrf2 on the outer mitochondrial membrane, thereby protecting the mitochondria [18]. In conclusion, by activating hypoxia-related pathways, IPC not only enhances aerobic capacity and tissue oxygenation at the systemic level, but also achieves multiple protections at the molecular level by regulating plasma proteins and anti-oxidative stress pathways. Collectively, these results highlight that IPC functions as a systemic regulatory process rather than a localized vascular response, integrating hemodynamic, metabolic, and molecular mechanisms to support enhanced endurance capacity and resilience under hypoxic or extreme environmental conditions.

2.3. Modulation of Aerobic and Anaerobic Exercise Capacity

In terms of aerobic exercise, IPC can alleviate exercise fatigue and enhance the oxygen uptake capacity of local muscles. In terms of anaerobic exercise, IPC can increase blood lactate levels, improve athletic performance, and enhance physical function. Maximum accumulated oxygen deficit (MAOD) is the gold standard for measuring human anaerobic metabolism capacity. This provides a basis for evaluating the indirect effects of IPC on aerobic performance. A study involving sixteen male 400-meter runners was conducted, in which participants performed three maximal intensity tests and were assigned to one of three groups: a control group, a local IPC (LIPC) group, and a RIPC

group. Baseline values of maximum accumulated oxygen deficit (MAOD) were first measured, and after seven days, each group underwent IPC treatment followed by a maximal incremental running test. The results indicated that the time taken from the start of exercise to exhaustion was significantly prolonged after IPC treatment, the LIPC group increased by 13.4%, while the RIPC group increased by 13.6% ($p < 0.05$), after IPC MAOD increased ($p < 0.05$), indicating that IPC indirectly improved aerobic endurance by enhancing anaerobic metabolism, allowing the body to delay the onset of fatigue [5].

Regarding anaerobic capacity, different forms of intermittent hypoxia–ischemia conditioning exert distinct effects on muscle oxygenation. A study divided 34 subjects into three groups: one group underwent 3 minutes of IPC (IPC-3), another group underwent 5 minutes of IPC (IPC-5), and one group underwent 7 minutes of IPC (IPC-7). The levels of oxygenated and deoxygenated hemoglobin were assessed using near-infrared spectroscopy, from which total hemoglobin and the tissue saturation index (TSI%) were calculated. Results indicated that TSI% increased following IPC, with the 5-minute protocol producing the most consistent improvement in oxygen saturation and the greatest enhancement in oxygenation capacity in the non-treated limb. It is indicated that IPC can improve muscle oxygenation, enhance anaerobic capacity, and improve microcirculation. Among them, 5-minute IPC is relatively the most effective in improving muscle oxygenation capacity [19]. In summary, IPC improves athletic performance through a dual pathway. On the one hand, it enhances anaerobic metabolism, indirectly prolonging aerobic endurance. On the other hand, it improves local muscle oxygenation and microcirculation, thereby enhancing anaerobic performance. This multidimensional regulatory effect highlights the broad potential of IPC in different modes of exercise.

3. Individual Variability and Mechanistic Uncertainty of IPC

The physiological response to IPC varies considerably among individuals and populations. In elderly women, IPC has been shown to improve grip strength and performance in multiple functional motor tests [8]. Among healthy men, it enhances both aerobic and anaerobic capacity, while in elite athletes, IPC primarily reduces fatigue and accelerates recovery. These findings suggest that IPC exerts beneficial yet heterogeneous effects across demographic groups. However, evidence remains limited for certain populations such as older adults and women, where sample sizes and reproducibility are insufficient. Some studies report no significant changes in muscle capacity or metabolic markers despite marginal improvements in performance [10]. Such inconsistencies may partly arise from individual differences in physiological responsiveness or cognitive perception of the intervention [20]. Therefore, elucidating the underlying mechanisms that mediate these variable outcomes remains a key challenge for future research.

4. Conclusion

The beneficial effects of IPC on athletic performance may be attributed to its mechanisms of influencing heart rate variability, promoting sympathetic-vagal balance, facilitating local muscle oxygenation to adapt to acute hypobaric hypoxia, mitigating inflammatory and oxidative stress, improving cardiac function, and enabling the body to adapt to hypoxic environments during exercise in advance. However, some studies suggest that IPC does not increase muscle strength, and the effects of IPC may be related to the individual's own psychological and physiological responses. Meanwhile, it remains to be investigated whether IPC has different effects on different groups such as ordinary women, elderly groups, and professional athletes, whether IPC methods under different pressures may have opposite effects on the same group, and the safety and universality of IPC application to the human body. The practical value and effectiveness of IPC require further research and confirmation. The mechanism through which IPC exerts its influence still needs to be verified through physiological indicators to exclude any psychological effects. To ensure safe translation into practice,

larger-scale clinical trials integrating physiological markers are needed to disentangle true biological mechanisms from psychological contributions.

References

[1] Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia a delay of lethal cell injury in ischemic myocardium. Circulation, 1986, 74(5): 1124-1136.

[2] Salvador AF, De Aguiar RA, Lisbôa FD, et al. Ischemic preconditioning and exercise performance a systematic review and meta analysis. International Journal of Sports Physiology and Performance, 2016, 11(1): 4-14.

[3] Cheng CF, Kuo YH, Hsu WC, et al. Local and remote ischemic preconditioning improves sprint interval exercise performance in team sport athletes. International Journal of Environmental Research and Public Health, 2021, 18(20): 10653.

[4] Patterson SD, Swan R, Page W, et al. The effect of acute and repeated ischemic preconditioning on recovery following exercise induced muscle damage. Journal of Science and Medicine in Sport, 2021, 24(7): 709-714.

[5] Telles LGDS, Billaut F, Cunha G, et al. Ischemic preconditioning improves handgrip strength and functional capacity in active elderly women. International Journal of Environmental Research and Public Health, 2022, 19(11): 6628.

[6] Su Y, Li W. Research progress on the impact of remote ischemic preconditioning on sports performance and its physiological mechanisms. Chinese Sports Technology, 2024, 60(10): 31-39.

[7] Chen Y, Yang J, Muradov O, et al. Effect of ischemic preconditioning on maximum accumulated oxygen deficit in 400 meter runners. European Journal of Sport Science, 2023, 23(5): 789-796.

[8] Wang A, Hurr C. Effect of ischemic preconditioning on endurance running performance in the heat. Journal of Sports Science and Medicine, 2024, 23(4): 799-811.

[9] Incognito AV, Burr JF, Millar PJ. The effects of ischemic preconditioning on human exercise performance. Sports Medicine, 2016, 46(4): 531–544.

[10] Valenzuela PL, Martín Candilejo R, Sánchez Martínez G, et al. Ischemic preconditioning and muscle force capabilities. Journal of Strength and Conditioning Research, 2021, 35(8): 2187-2192.

[11] Souza HLR, Oliveira GT, Meireles A, et al. Does ischemic preconditioning enhance sports performance more than placebo or no intervention a systematic review with meta analysis. Journal of Sport and Health Science, 2025, 14: 101010.

[12] Telles LG, Billaut F, de Souza Ribeiro A, et al. Ischemic preconditioning with high and low pressure enhances maximum strength and modulates heart rate variability. International Journal of Environmental Research and Public Health, 2022, 19(13): 7655.

[13] Gardner RN, Sabino Carvalho JL, Kim J, et al. Two weeks of remote ischaemic preconditioning alters sympathovagal balance in healthy humans. Experimental Physiology, 2020, 105(9): 1500-1506.

[14] Zhong Z, Dong H, Wu Y, et al. Remote ischemic preconditioning enhances aerobic performance by accelerating regional oxygenation and improving cardiac function during acute hypobaric hypoxia exposure. Frontiers in Physiology, 2022, 13: 950086.

[15] Koch SE, Martin E, Verma A, et al. Tefillin use induces preconditioning associated changes in heart rate variability. PLoS One, 2023, 18(1): e0280216.

[16] Arriel RA, Meireles A, Hohl R, et al. Ischemic preconditioning improves performance and accelerates the heart rate recovery. The Journal of Sports Medicine and Physical Fitness, 2020, 60(9): 1209-1215.

[17] Mujika I, Sharma AP, Stellingwerff T. Contemporary periodization of altitude training for elite endurance athletes a narrative review. Sports Medicine, 2019, 49(11): 1651-1669.

[18] Liu J, Gu Y, Guo M, et al. Neuroprotective effects and mechanisms of ischemic or hypoxic preconditioning on neurological diseases. CNS Neuroscience and Therapeutics, 2021, 27(8): 869-882.

[19] Marocolo M, Arriel RA, Guedes G, et al. Evaluating local muscle oxygen saturation ischemic preconditioning protocols and the myth of overcompensation. Journal of Human Kinetics, 2024, 95: 71-82.

[20] Marocolo M, da Mota GR, Simim MA, et al. Myths and facts about the effects of ischemic preconditioning on performance. International Journal of Sports Medicine, 2016, 37(2): 87-96.