International Journal of EXERCISE SCIENCE

Original Research

The Acute Effects of Ischemic Preconditioning on Short-Duration Cycling: A Randomized Crossover Study

CASSIDY R. NELSON*[1], COLTEN R. BRAND*[2], MATTHEW R. CHITTY*[2], CHAD B. BIRGER‡[3], and SHANE D. SCHOLTEN‡[1]

[1]Department of Exercise and Sports Science, University of Augustana, Sioux Falls, SD, USA; [2]Department of Exercise Science, University of Sioux Falls, Sioux Falls, SD, USA; [3]Department of Economics and Decision Sciences, University of South Dakota, Vermillion, SD, USA

*Denotes undergraduate student author, ‡Denotes professional author

ABSTRACT

International Journal of Exercise Science 16(6): 148-158, 2023. There is recent interest from coaches and athletes regarding IPC as an effective way to generate better competitive outcomes. Regarding cycling specifically, the impact of IPC remains unclear. This study aimed to assess the effectiveness of IPC treatment for improving athletic performance during short-duration cycling. After the exclusion and inclusion criteria, there were 11 volunteers for the 3-minute cycling TT and 13 volunteers for the 6-minute cycling TT. All volunteers were competitive athletes of aerobic sports. The IPC treatment consisted of three alternating cycles of 5 minutes of 100% occlusion followed by 5 minutes of reperfusion to each leg. The sham treatment consisted of three alternating cycles of 1 minute of 100% occlusion followed by 1 minute of reperfusion to each leg. The main finding was that IPC significantly improved (p<0.05) power output during 3-minute (4.22%) and 6-minute (2.29%) cycling TT relative to a sham. Additionally, about one-third of our participants required a tourniquet pressure higher than 220 mmHg to achieve 100% occlusion. These findings indicate ischemic preconditioning, administered bilaterally as three rounds of 5 minutes of total occlusion and ensuing reperfusion 20 minutes before a cycling TT, significantly enhanced average power output.

KEY WORDS: Ergogenic aid, aerobic metabolism, exercise, cardiovascular

INTRODUCTION

Ischemic preconditioning (IPC) may enhance physical performance, thus both coaches and athletes have great interest in the potential of IPC as an effective way to generate better competitive outcomes (4,18). IPC has been shown to improve maximal exercise performance (6,16) and maximal swimming performance (28) in healthy individuals; therefore, IPC could give certain athletes a competitive edge. However, the data showing the effect IPC has on various modes of aerobic performance are inconclusive (1,5,14,19,25). Results may vary due to the type and duration of exercise performed, the treatment time, occlusion pressure, and a

potential placebo effect. With IPC as a novel treatment used to enhance human performance, there is a need to better understand the effectiveness of the various IPC application strategies. Initially thought to be more anaerobic-specific, a recent review of IPC in exercise performance suggests to use IPC for aerobic events as it appears it will be more effective with intense exercise requiring oxygen consumption (4). Mechanisms for how IPC might improve aerobic exercise performance include acute vasodilation and enhanced blood flow (27), enhanced oxygen extraction (15), and reduced lactate accumulation due to enhancements in mitochondria to create adenosine triphosphate (ATP) from aerobic metabolism at greater exercise intensities (16).

Various IPC protocols have been used to assess the effect of IPC on aerobic performance. It has been established that three cycles of five-minute occlusions are as effective as four cycles to produce an ergogenic effect (4). This gives researchers confidence for creating appropriate IPC interventions for exercise performance research. However, various thigh ischemic pressures have been used that range from 200 mmHg to greater than 300 mmHg with 220 mmHg being the most widely used ischemic pressure (4). A potential placebo effect must also be considered, as cuff pressures of 20-50 mmHg are significantly different from and cause no discomfort compared to pressures required for full occlusion. Ischemic pressure and the use of a minimal placebo cuff pressure may be reasons for the varied exercise performance results reported in the literature.

Using prior literature to inform our investigation, we assessed the effectiveness of an IPC protocol that ensured adequate time and cuff pressure to reach muscle hypoxia. We also assessed the IPC effectiveness for improving exercise performance during cycling at three- and six-minute time trials as we hypothesized these aerobic time intervals would be effective to demonstrate an improvement in cycle power output.

METHODS

Participants

Sample-size calculations suggested a sample of 11 participants would provide sufficient statistical power (.80) with alpha 0.05 to detect a 2% power improvement in 3-minute and 6-minute cycle tests. The inclusion criteria include competitive athletes of aerobic sports. The exclusion criteria were: i) any cardiovascular or metabolic disease; ii) use of exogenous drugs, anabolic steroids or other substances that have been shown to enhance exercise performance; or iii) bone, joint, musculoskeletal injury that would affect exercise performance. After the exclusion and inclusion criteria, there were 11 volunteers for the 3-minute cycling time trial (TT) and 13 volunteers for the 6-minute cycling TT. All participants were recruited via word of mouth and gave written informed consent. This research was carried out fully in accordance with the ethical standards of the International Journal of Exercise Science (23) and was approved by the Institutional Review Board of Augustana University (Number SP20.03).

Protocol

The IPC treatment consisted of three alternating cycles of 5 minutes of 100% occlusion followed by 5 minutes of reperfusion to each leg using a Delfi PTS (Delphi Medical Innovations, Vancouver, Canada) unit for blood flow restriction. Particularly, two Delfi PTS units were used simultaneously, one for each lower limb, to hasten the treatment period. Occlusion occurred alternately from right to left lower limbs. The occlusion was performed with blood pressure cuffs that were applied to both of the lower limbs at the sub-inguinal region of the upper thigh (12). Depending on the limb circumference of the participants, either a 24-inch cuff or a 34-inch cuff was utilized for proper fitting per manufacturer recommendations. The Defli PTS unit was chosen due to its non-invasive nature and easy applicability (13). Additionally, it was utilized for IPC treatment due to the fact that it encompasses an internal doppler radar in which it is able to detect the proper restriction of arterial blood flow into the muscle. This method of ischemic preconditioning was chosen as it was suggested by Salvador et al. (2016) future studies utilize doppler flow measurement to ensure there is complete blocking of arterial blood flow (26).The IPC treatment did not employ a uniform pressure for each participant; rather, a personalized tourniquet pressure (PTP) was found, for each participant, by the Delfi PTS unit. For example, one participant's PTP may have been represented by 170 mmHg for full occlusion, whereas another participant's PTP may have been represented by 250 mmHg for full occlusion. Muscle oxygen saturation was measured via near-infrared spectroscopy using a MOXY Muscle Oxygen Monitor (Fortiori Design, Minnesota, USA) by adhering the monitor to the vastus lateralis with real time measurement displayed by a Garmin Edge 1030 (Garmin LTD, USA).

This randomized crossover study consisted of similar but independent time trials of 3-minute and 6-minute cycling TTs. Participants were assigned based on time preference, and each subject served as their own control. All protocols between the IPC and sham treatments in both time trials remained the same as illustrated in Figure 1. Subjects performed a familiarization trial designed to prepare the participant for the sensation of 100% blood flow occlusion and exhaustive cycling TT. The time after treatment to the performance test was not more than 20 minutes. The IPC and sham trials were separated by 4-10 days to allow for recovery and as an adequate washout period from possible prolonged IPC benefits.

The elimination of residual effects was critical, especially when a participant received the IPC treatment prior to the sham treatment. If a participant needed to miss the day of testing, they were rescheduled to a later date within a 4-10 day range from their first treatment trial. All time trials were performed in a controlled laboratory setting. Participants were also instructed to abstain from intense physical activity 48 hours prior to testing, along with caffeine and alcohol 24 hours prior to testing, and to maintain similar diets, levels of rest, and exercise in the days leading up to the tests. All cycling TTs were performed on a Wahoo Kickr (Wahoo Fitness, Georgia, USA) which was calibrated before each test and power output was measured in watts. Immediately following treatment, participants performed a warm-up detailed in Figure 2. Once the participants felt ready, they began their performance test. To ensure near-maximum exertion, participants verbally rated a number for Rate of Perceived Exertion (RPE 6-20).

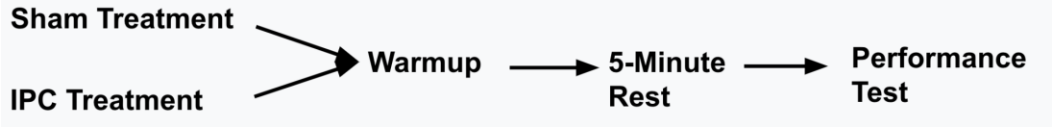

Figure 1. Experimental design of study.

Statistical Analysis

The investigators used random block permutations to equally sequence the two treatments. All data were analyzed using R version 3.5.0. A one-way ANOVA was used to statistically analyze the experimental protocols. A Student's T-test was used to analyze the pre-post assessments for the control group. A Shapiro-Wilk test indicated a normal distribution of data. A Tukey post hoc test was run for significant tests. Significance for all comparisons was set at $p < 0.05$.

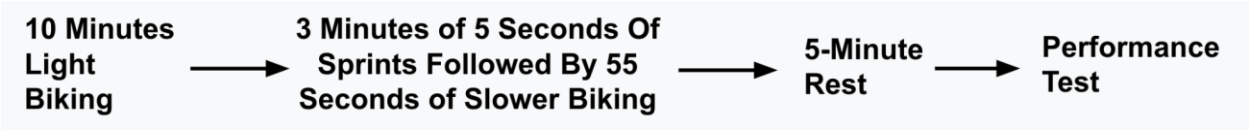

Figure 2. Cycle TT warm-up and cool down.

RESULTS

All participants completed the sham and IPC treatments. The means and standard deviations of the participants' height, weight, and age are detailed in Table 1.

Both the 3-minute and 6-minute cycling TTs (Figure 3) demonstrated greater power output with IPC relative to the sham. In the 3-minute cycling TT, 8 out of 11 participants improved average power output. Similarly, in the 6-minute cycling TT, 10 out of 13 participants improved average power output. Table 2 displays the statistical significance and % improvements for each group.

Illustrated in Figure 4, data from a MOXY Muscle Oxygen Monitor characterizes the sham treatment, as none of our participants reached 0% muscle oxygen saturation. In contrast, the IPC treatment is characterized by a steep decline down to 0% due to 100% occlusion, followed by rapid reperfusion and overcompensation of oxygen saturation.

Displayed in Figure 5 is each participant's PTP. The data show each participant had a unique PTP and 4 (31%) of the 13 participants in the 6-minute time trial had an average PTP of over 220 mmHg. Furthermore, the data in Figure 6 provides evidence supporting the use of PTPs over a universal pressure such as the commonly utilized IPC occlusion pressure of 220 mmHg. A MOXY Muscle Oxygen Monitor showed a participant with a PTP of 276mmHg did not achieve blood flow occlusion when only using a pressure of 220 mmHg. This data indicates that 220 mmHg does not induce 100% occlusion in all participants.

Table 1. Characteristics of participants who completed all conditions in randomized crossover design divided by length of time trial. Both the 3-minute and 6-minute cycling TTs were found to have significant improvement in performance.

	3-minute cycling TT	6-minute cycling TT
Participants (n)	11	13
Males (n)	9	9
Females (n)	2	4
Male Height (cm)	184.0 ± 6.9	183.2 ± 8.8
Female Height (cm)	165.1 ± 3.6	168.3 ± 9.4
Male Weight (kg)	76.1 ± 8.8	83.1 ± 23.1
Female Weight (kg)	61.9 ± 5.5	64.3 ± 8.7
Male Age (yr)	28.3 ± 19.3	25.1 ± 7.3
Female Age (yr)	20.0 ± 0.0	21.3 ± 1.0

Note: Data are presented as mean ± SD.

Table 2. Average performance in time trials

	Sham	IPC	n	*p*-Value	Effect Size (Cohen's d)	Average % improvement
3-minute cycling TT (W)	325.1 ± 67.1	337.6 ± 70.2	11	0.046*	0.18	4.22
6-minute cycling TT (W)	272.0 ± 63.7	278.2 ± 64.5	13	0.032*	0.1	2.29

*A significant difference $p<.05$. Data are presented as mean ± SD.

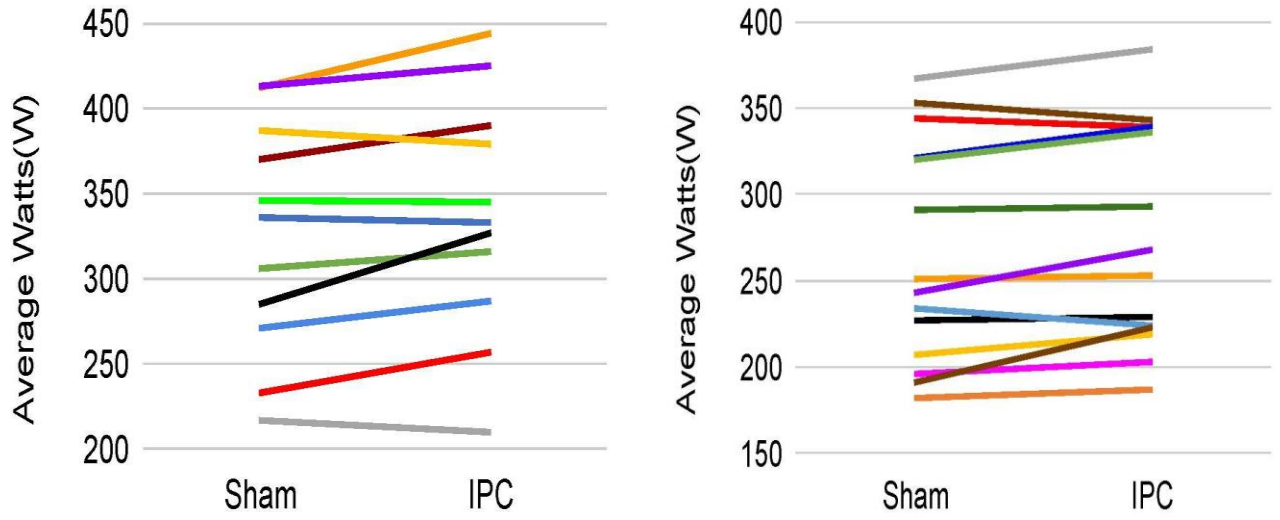

Figure 3. Performance tests. 8 out of 11 participants improved their average watts in the 3-minute cycling TT, 10 out of 13 participants improved their average watts in the 6-minute cycling TT. Each line represents one participant's results. Abbreviations: TT, time trial. Note: Each line represents one participant's results.

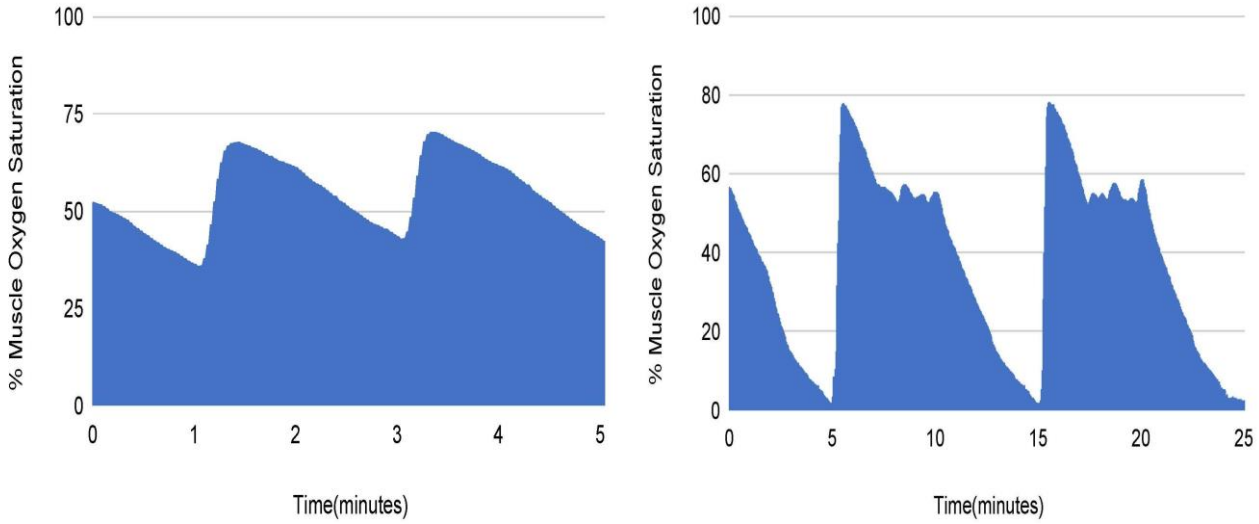

Figure 4. Muscle Oxygen Saturation. A MOXY muscle oxygen monitor was used to assess oxygen saturation levels in the vastus lateralis during IPC and sham treatments. The representative sham treatment does not reach 0% muscle oxygen saturation. The IPC treatment reaches near 0% saturation due to 100% occlusion. Following the occlusion phase a noticeable rapid reperfusion and overcompensation of oxygen saturation in the IPC treatment can be observed.

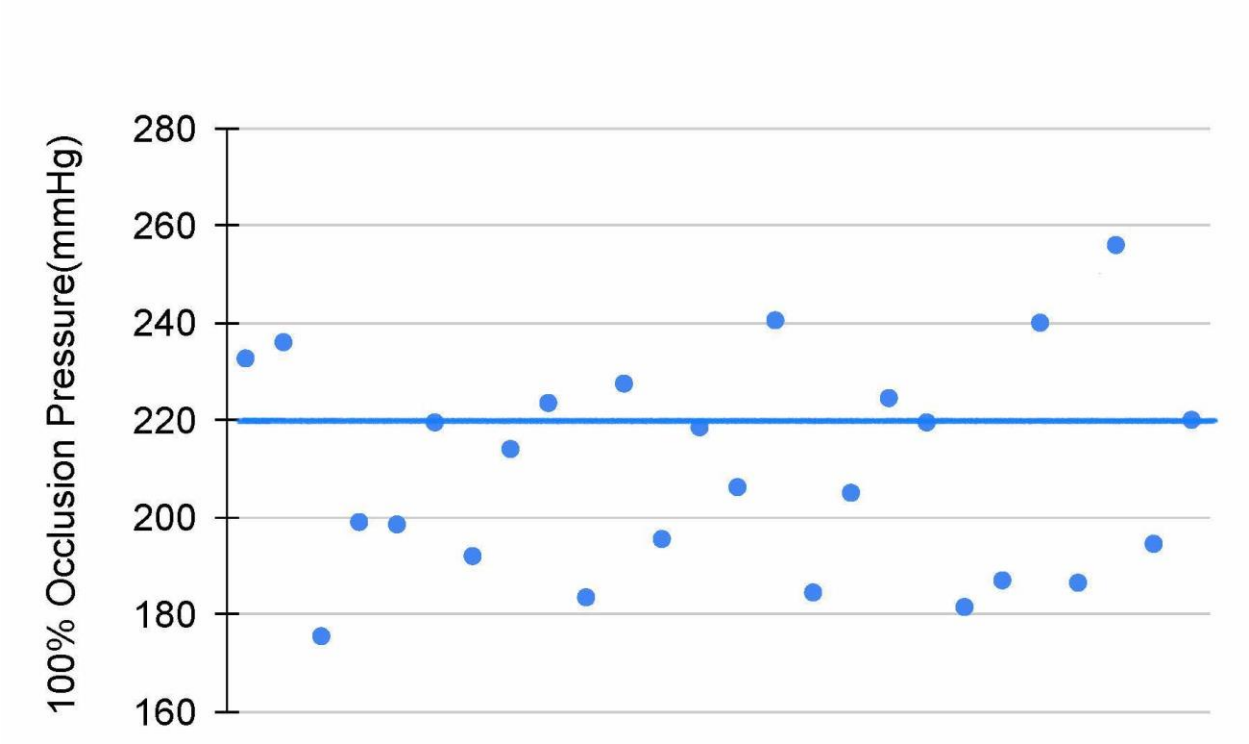

Figure 5. Personal tourniquet pressures of participants of the 6-minute time trial. 30.8% of the limbs had a PTP of over 220mmHg. Each point represents one participant's legs (left and right) from the IPC treatment.

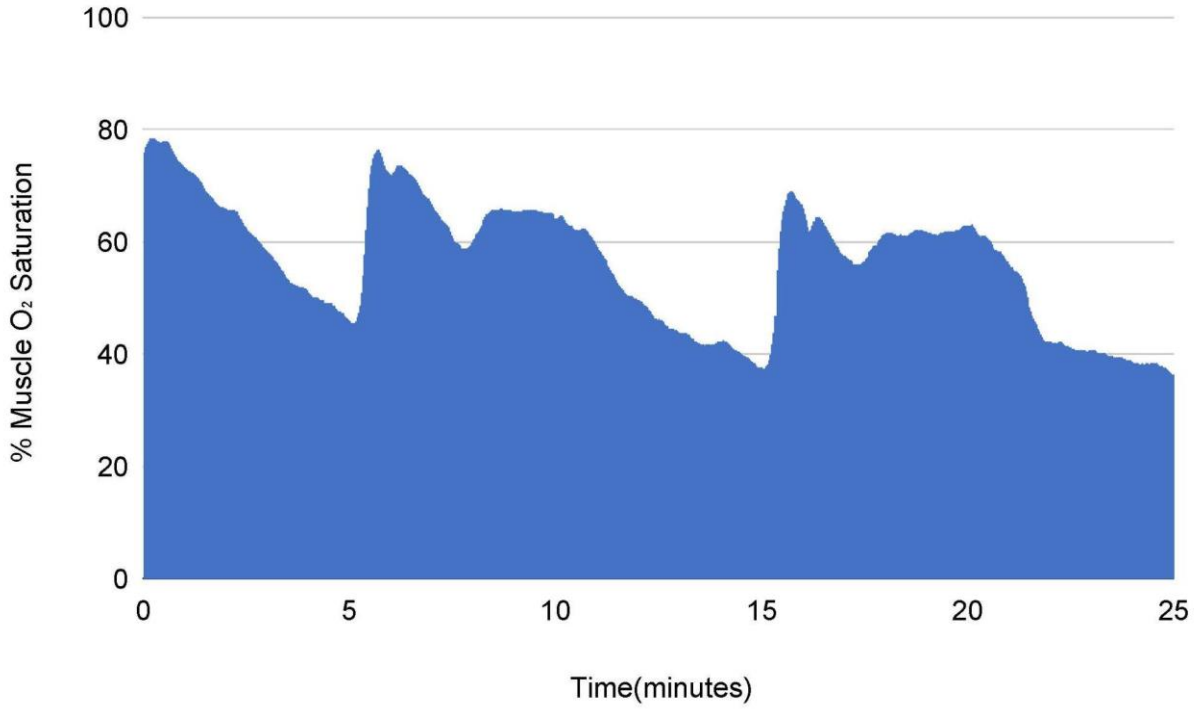

Figure 6. Muscle oxygen saturation at 220mmHg with a PTP of 276mmHg. A participant with a PTP of 276mmHg experiences a negligible decrease in muscle oxygen saturation.

DISCUSSION

There is a broad range of literature regarding the use of IPC to enhance athletic performance. As for the effects of IPC on short-duration cycling, however, the existing literature is inconclusive. There is some data supporting and other data refuting such performance enhancement. Therefore, the purpose of this investigation was specifically to determine whether IPC applied 20 minutes prior to a cycling TT would improve power output. The main finding was that IPC administered as three rounds of 5 minutes of 100% blood flow occlusion and reperfusion significantly improved power output during both 3-minute and 6-minute cycling TTs. These improvements were relative to a sham treatment. The results of this study suggest IPC can be used to an athlete's advantage in short-duration cycling.

A study by Cruz et al., looking at 1-minute cycling TT, found IPC given as four rounds of 5 minutes of occlusion and reperfusion led to a 2.1% improvement relative to the control (7). Additionally, de Groot et al., investigating performance outcomes by incremental maximum cycling tests, found a slighter but still significant improvement of 1.6% (13). Our investigation found more considerable performance improvements, 4.22% (for the 3-minute cycling TT) and 2.29% (for the 6-minute cycling TT), than previous investigations (7,13). For highly trained athletic competitors, differences of less than 0.5% can separate medal and non-medal positions (28).

Most of the existing literature involves three (6,9,11,20,24,25) or four (7,8,10,16–18,22,28) rounds of 5 minutes of blood flow occlusion and subsequent reperfusion. In a systematic review by Caru et al., 21 out of 52 investigations used three rounds of 5-minute IPC, and 30 used four rounds of 5-minute IPC (4). There appears to be no advantage to doing the fourth round over three rounds (26), and perhaps four may be less effective (2). This experiment found three rounds of IPC to elicit significant improvement. It should be noted the time from completion of IPC to test was 15 - 20 minutes. Generally, the time between IPC and exercise test varies from immediately to 72 hours between studies (4). This variation is worth investigating in-depth, as it has been suggested IPC has two windows of opportunity for its benefits: the first opening 5 - 10 minutes after IPC completion and ending within 2-3 hours (3); the second opening occurring about 24 hours post-IPC and lasting up to approximately 72 hours (3,17,21). The current study did not investigate the second window; but, regarding the first window, the improvements in the current investigation support utilizing IPC 20 minutes prior to performance tests.

This study differs most from the existing literature in its use of PTPs. PTPs were found and maintained during the IPC and sham treatments using a Delfi PTS unit for blood flow restriction, which employs an internal doppler radar. In most prior investigations, a universal 220 mmHg was used as the IPC treatment for all participants (1,2,4–10,13,18,22,25,28). However, the current study opted to use PTPs as the investigators were wary 220 mmHg might not be enough pressure to provide 100% occlusion in all participants. We found nearly one-third of our participants needed a tourniquet pressure (as measured by the Delfi PTS unit) higher than the standard 220 mmHg to achieve 100% occlusion.

PTPs on one individual can vary from leg-to-leg and day-to-day. It is plausible the use of PTP accounts for the improvements seen in the current study being more notable than those observed improvements in prior studies. The universal use of 220 mmHg may also contribute to the discrepancies in whether IPC is effective. Perhaps, 100% occlusion is a key to allowing IPC to be effective. A similar study which did not use a tourniquet pressure of 220 mmHg, rather 50 mmHg above each individuals' systolic blood pressure, found a 4% improvement similar to the improvement seen in the current study's 3-minute cycling TT (6). Based on our findings, future investigations should utilize PTPs to ensure complete occlusion.

Most previous studies inflated pressure cuffs to 10 - 50 mmHg for their shams, but this is a noticeable difference to participants (18). Hence, when a sham of 50 mmHg is used, participants likely know when they are receiving the sham treatment and when they are receiving the IPC treatment, which has historically been 220 mmHg or within 50 mmHg of the systolic blood pressure (4). This is a difficulty that gives rise to the question of whether IPC truly aids athletes or if the improvement is due to a placebo effect (5,22). Potential placebo effects were mitigated in this study by inflating the cuffs to 100% occlusion for both the sham and IPC trials. Participants who asked about the study's goal were told three rounds of 5-minute IPC is known to improve performance outcomes and that the investigation is to determine whether 1x5 minute IPC is as effective. These participants were encouraged to believe both the sham and IPC

treatments would improve their performance. Despite this, the IPC treatment showed improved power output in both time trials compared to the sham treatment.

One possible limitation of the current investigation is that it is nearly impossible to account for every factor that may physiologically impact exercise performance. The quality of sleep a person received the night before each test is a salient example of a physiological factor for which this study did not account. Further, while compliance with diet and exercise was not monitored, investigators encouraged the participants to maintain similar diets, sleep, and exercise the day prior to each lab visit. The authors see the use of PTPs as a strength of this investigation and recommend normalizing the use of PTP in future IPC research. The outcomes of this study are based on 3-minute and 6-minute cycling TTs and cannot necessarily be extended to all aerobic performances. Further research should continue to test other aerobic activities. Finally, future research elucidating the mechanisms behind IPC may lead to a better understanding of how to best harness its potential.

Conclusions: IPC administered bilaterally as three rounds of 5 minutes of total occlusion and ensuing reperfusion before a cycling TT significantly enhances average power output compared to a sham. This benefit is valid for the 3-minute and 6-minute cycling TTs and supports the use of IPC 15-20 minutes preceding short, high-intensity cycling to increase average power output. These results are relevant for athletes wanting to improve their competitive outcomes.

REFERENCES

1. Arriel R, de Souza H, da Mota G, Marocolo M. Declines in exercise performance are prevented 24 hours after post-exercise ischemic conditioning in amateur cyclists. Plos One 13(11): 1–12, 2018.

2. Beaven CM, Cook CJ, Kilduff L, Drawer S, Gill N. Intermittent lower-limb occlusion enhances recovery after strenuous exercise. Appl Physiol Nutr Metab 37(6): 1132–9, 2012.

3. Bolli R. The late phase of preconditioning. Circ Res 87(11): 972–83, 2000.

4. Caru M, Levesque A, Lalonde F, Curnier D. An overview of ischemic preconditioning in exercise performance: A systematic review. J Sport Health Sci 8(4): 355–69, 2019.

5. Cheung CP, Slysz JT, Burr JF. Ischemic preconditioning: Improved cycling performance despite nocebo expectation. Int J Sports Physiol Perform 15(3): 354–60, 2020.

6. Crisafulli A, Tangianu F, Tocco A, Concu O, Mameli G, Mulliri MA, et al. Ischemic preconditioning of the muscle improves maximal exercise performance but not maximal oxygen uptake in humans. J Appl Physiol 111(2): 530–6, 2011.

7. Cruz RS, de Aguiar RA, Turnes T, Salvador AF, Caputo F. Effects of ischemic preconditioning on short-duration cycling performance. Appl Physiol Nutr Metab 41(8): 825–31, 2016.

8. Cruz RS de O, de Aguiar RA, Turnes T, Pereira KL, Caputo F. Effects of ischemic preconditioning on maximal constant-load cycling performance. J Appl Physiol 119(9): 961–7, 2015.

9. Ferreira TN, Sabino-Carvalho JLC, Lopes TR, Ribeiro IC, Succi JE, Da Silva AC, et al. Ischemic preconditioning and repeated sprint swimming: A placebo and nocebo study. Med Sci Sports Exerc 48(10): 1967–75, 2016.

10. Franz A, Behringer M, Harmsen J-F, Mayer C, Krauspe Rüd, Zilkens C, et al. Ischemic preconditioning blunts muscle damage responses induced by eccentric exercise. Med Sci Sports Exerc 50(1): 109–15, 2018.

11. Gibson N, White J, Neish M, Murray A. Effect of Ischemic preconditioning on land-based sprinting in team-sport athletes. Int J Sports Physiol Perform 8(6): 671–6, 2013.

12. Griffin PJ, Ferguson RA, Gissane C, Bailey SJ, Patterson SD. Ischemic preconditioning enhances critical power during a 3 minute all-out cycling test. J Sports Sci 36(9): 1038–43, 2018.

13. de Groot PCE, Thijssen DHJ, Sanchez M, Ellenkamp R, Hopman MTE. Ischemic preconditioning improves maximal performance in humans. Eur J Appl Physiol 108(1): 141–6, 2010.

14. Hittinger EA, Maher JL, Nash MS, Perry AC, Signorile JF, Kressler J, et al. Ischemic preconditioning does not improve peak exercise capacity at sea level or simulated high altitude in trained male cyclists. Appl Physiol Nutr Metab 40(1): 65–71, 2015.

15. Horiuchi M, Endo J, H. J. Thijssen D. Impact of ischemic preconditioning on functional sympatholysis during handgrip exercise in humans. Physiol Rep 3(2): 1–9, 2015.

16. Jean-St-Michel E, Manlhiot C, Li J, Tropak M, Michelsen MM, Schmidt MR, et al. Remote preconditioning improves maximal performance in highly trained athletes. Med Sci Sports Exerc 43(7): 1280–6, 2011.

17. Kuzuya T, Hoshida S, Yamashita N, Fuji H, Oe H, Hori M, et al. Delayed effects of sublethal ischemia on the acquisition of tolerance to ischemia. Circ Res 72(6): 1293–9, 1993.

18. Lalonde F, Curnier DY. Can anaerobic performance be improved by remote ischemic preconditioning? J Strength Cond Res 29(1): 80–5, 2015.

19. Lindner T, Scholten S, Halverson J, Baumgarten K, Birger C, Nowotny B. The acute effects of ischemic preconditioning on power and sprint performance. S D Med 74(5): 210–9, 2021.

20. Loukogeorgakis SP, Panagiotidou AT, Broadhead MW, Donald A, Deanfield JE, MacAllister RJ. Remote ischemic preconditioning provides early and late protection against endothelial ischemia-reperfusion injury in humans. J Am Coll Cardiol 46(3): 450–6, 2005.

21. Marber MS, Latchman DS, Walker JM, Yellon DM. Cardiac stress protein elevation 24 hours after brief ischemia or heat stress is associated with resistance to myocardial infarction. Circulation 88(3): 1264–72, 1993.

22. Marocolo M, Willardson JM, Marocolo IC, da Mota GR, Simão R, Maior AS. Ischemic preconditioning and

placebo intervention improves resistance exercise performance. J Strength Cond Res 30(5): 1462–9, 2016.

23. Navalta JW, Stone WJ, Lyons TS. Ethical issues relating to scientific discovery in exercise science. Int J Exerc Sci 12(1): 1–8, 2019.

24. Paradis-Deschênes P, Joanisse DR, Billaut F. Ischemic preconditioning increases muscle perfusion, oxygen uptake, and force in strength-trained athletes. Appl Physiol Nutr Metab 41(9): 938–44, 2016.

25. Richard P, Billaut F. Time-trial performance in elite speed skaters after remote ischemic preconditioning. Int J Sports Physiol Perform 13(10): 1308–16, 2018.

26. Salvador AF, De Aguiar RA, Lisbôa FD, Pereira KL, de O. Cruz RS, Caputo F. Ischemic Preconditioning and Exercise Performance: A Systematic Review and Meta-Analysis. Int J Sports Physiol Perform 11(1): 4–14, 2016.

27. Tapuria N, Kumar Y, Habib MM, Amara MA, Seifalian AM, Davidson BR. Remote ischemic preconditioning: A novel protective method from ischemia reperfusion injury—A review. J Surg Res 150(2): 304–30, 2008.

28. Williams N, Russell M, Cook CJ, Kilduff LP. Effect of ischemic preconditioning on maximal swimming performance. J Strength Cond Res 35(1): 221–6, 2021.