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ScienceDirect

Journal of Sport and Health Science 8 (2019) 355−369

www.jshs.org.cn

Review

An overview of ischemic preconditioning in exercise performance: A systematic review

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Received 11 September 2018; revised 29 October 2018; accepted 3 December 2018

Available online 23 January 2019

Abstract

Ischemic preconditioning (IPC) is an attractive method for athletes owing to its potential to enhance exercise performance. However, the effectiveness of the IPC intervention in the field of sports science remains mitigated. The number of cycles of ischemia and reperfusion, as well as the duration of the cycle, varies from one study to another. Thus, the aim of this systematic review was to provide a comprehensive review examining the IPC literature in sports science. A systematic literature search was performed in PubMed (MEDLINE) (from 1946 to May 2018), Web of Science (sport sciences) (from 1945 to May 2018), and EMBASE (from 1974 to May 2018). We included all studies investigating the effects of IPC on exercise performance in human subjects. To assess scientific evidence for each study, this review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. The electronic database search generated 441 potential articles that were screened for eligibility. A total of 52 studies were identified as eligible and valid for this systematic review. The studies included were of high quality, with 48 of the 52 studies having a randomized, controlled trial design. Most studied showed that IPC intervention can be beneficial to exercise performance. However, IPC intervention seems to be more beneficial to healthy subjects who wish to enhance their performance in aerobic exercises than athletes. Thus, this systematic review highlights that a better knowledge of the mechanisms generated by the IPC intervention would make it possible to optimize the protocols according to the characteristics of the subjects with the aim of suggesting to the subjects the best possible experience of IPC intervention.

Keywords: Exercise; Human performance; IPC protocols; Ischemic preconditioning; Sports science

1. Introduction

Ischemic preconditioning (IPC) is an attractive method for athletes due to its relationship with exercise performance. IPC intervention is a noninvasive procedure that involves inducing 3−4 cycles of brief episodes of ischemia (inflation of a blood pressure cuff) and reperfusion (gradual deflation) via a pressure cuff on a skeletal muscle.[1] This intervention was initially developed to decrease the damage caused to internal organs by ischemia and reperfusion.[2] However, it has been speculated that IPC also has an effect on exercise performance, notably by improving muscle oxygenation, vasculature, and blood flow delivery to active tissues and organs.[3]

The mechanisms involved in these athletic improvements are likely related to both metabolic and vascular pathways.[4] As a matter of fact, it is thought that IPC can act through 3 main pathways (i.e., neuronal, humoral, and systemic response).[5−7] The neuronal pathway, which includes the spinal cord and the autonomous and somatosensory nervous systems, is activated by endogenous substances (i.e., adenosine,[8,9] bradykinine,[10] or opioid[11,12]) generated by the stimulated distant organ. These endogenous substances lead to the activation of afferent nerve fibers that transmit the electrical signal to the targeted organ. This signaling leads to protective cellular processes in the targeted organ.[6] The humoral pathway has the same underlying mechanism involving endogenous substances, according to the Hausenloy and Yellon[6] hypothesis. However,

Peer review under responsibility of Shanghai University of Sport.
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https://doi.org/10.1016/j.jshs.2019.01.008
Cite this article: Caru M, Levesque A, Lalonde F, Curnier D. An overview of ischemic preconditioning in exercise performance: A systematic review. *J Sport Health Sci* 2019;8:355−69.

these substances are involved in IPC by their entry into the bloodstream, which causes them to activate their specific receptor upon their arrival in an organ of the central nervous system.[13] This step allows the recruitment of various intracellular pathways of cardioprotection, which are also thought to play a role in exercise performance.[14] The systemic response is a protective response that involves the elimination of inflammation and apoptosis through the stimulation of transient ischemia and reperfusion of an organ or tissue. As a matter of fact, some studies have proven that there is a decrease in the cell membranes of specific adhesion molecules (intracellular adhesion molecule-1, P-selectin) after IPC.[15] Even though the number of studies interested in this type of response is limited, it has been shown that this decrease in inflammation can prevent the exacerbation of ischemic injuries. Thus, through these 3 pathways, it is thought that IPC can be important not only in preventing damage to internal organs following a cardiac episode, but also in athletic performance.

The effectiveness of IPC intervention in the field of sports science remains unclear. Indeed, some studies report significant exercise performance benefits (i.e., time trial performance, maximal oxygen consumption (VO_{2peak}), power output), whereas others demonstrate no effect.[4,16] Also, there does not appear to be a consensus on the optimal procedure to be used for an IPC intervention, which could explain the differences in results between studies. Although many studies seem to be based on the original study of Przyklenk et al.,[17] the number of cycles of ischemia and reperfusion, as well as the duration of the cycle varies from one study to another. Thus, the aim of this systematic review was to provide a comprehensive review examining the IPC literature in sports science.

2. Methods

A systematic literature search was performed by 2 independent reviewers (AL and MC) in PubMed (MEDLINE) (from 1946 to May 2018), Web of Science (sport sciences) (from 1945 to May 2018), and EMBASE (from 1974 to May 2018). The search terms for the inclusion criteria were a combination of database specific MeSH terms and keywords: "remote ischemic preconditioning" OR "remote ischaemic preconditioning" OR "remote preconditioning" OR "remote conditioning" OR "remote ischemic conditioning" OR "remote ischaemic conditioning" OR "transient limb ischemia" OR "muscle ischemia" OR "ischemic preconditioning" AND "performance" OR "sport*" OR "exercise" OR "strength training" OR "running" OR "swimming" OR "cycling" OR "athletes" OR "athletic performance". When it was possible, in the different databases, we added the human filter. Also, the reference lists of all identified studies were scanned manually for additional studies.

2.1. Inclusion and exclusion criteria of studies

We included all studies investigating the effects of IPC on exercise performance in human subjects without any age restriction (age of children $\leq$ 18 and age of adults >19). Journal articles written in a language other than English or French were excluded. During the first analysis by abstract, the conference abstracts, case reports, short communications, systematic reviews, meta-analyses, theses, letters to editor, and protocol papers were excluded due to the inability to evaluate the risk of bias of the individual study. Also, studies with animals or non-healthy subjects were excluded. When the title and the abstract were potentially eligible for inclusion, the full-text was obtained. Studies with a design of randomized, controlled trials, non-randomized controlled trials, and uncontrolled interventions (i.e., pretests and post-tests without controls) were included. The last day of the literature search was June 1, 2018.

2.2. Data extraction and quality analysis

To assess scientific evidence for each study, this review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[18] Two independent researchers (AL and MC) reviewed the articles for eligibility and validity. Data extraction was performed by 1 investigator (AL); when data were lacking in the original article, the authors of the review contacted the original author to obtain additional data. The following data were extracted: characteristics (number, health physical state, sex, and age) of the subjects, IPC sets, ischemia pressure (mmHg), preconditioned limb, time to test, type of exercise, exercise protocol, and findings.

3. Results

3.1. Study selection

A flow chart showing the different phases of this review according to the PRISMA is depicted in Fig. 1. The electronic database search generated 441 potential articles that were screened for eligibility. There were 12 additional records identified through other sources. After the first analysis by title and abstract, 58 full-text articles were assessed. Among these full-text articles, 6 did not meet our inclusion and exclusion criteria (short

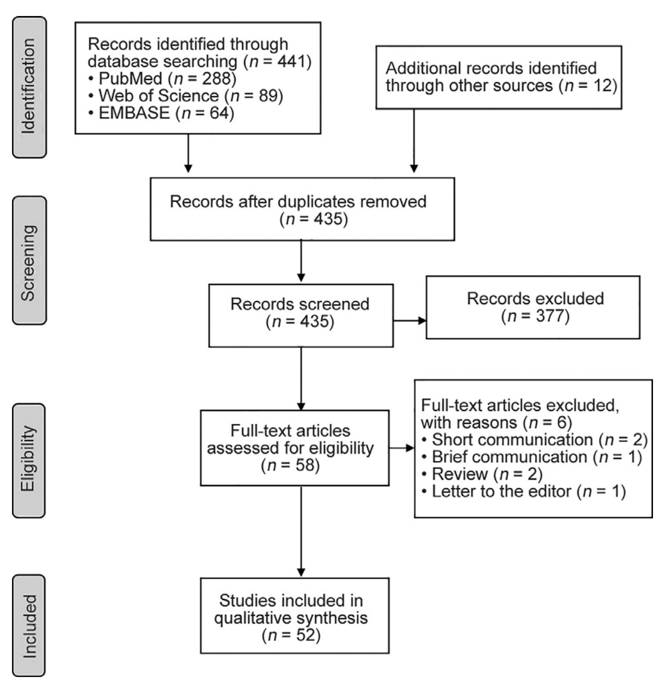

Fig. 1. Literature search and study selection from PRISMA statement.

communication ($n = 2$), brief communication ($n = 1$), reviews ($n = 2$), letter to the editor ($n = 1$)). Finally, a total of 52 studies were identified as eligible and valid for this systematic review.

3.2. Characteristics of included studies

Study characteristics of all 52 included studies are summarized in Table 1. Forty-eight studies were randomized, controlled trials and 4 had a study design that was not available. Among these 48 studies, 44 were crossover trials, 12 were counterbalanced, 11 were single blinded, 2 were double blinded, 3 were controlled, 3 were sham controlled, 2 were placebo and nocebo controlled, and 1 was placebo controlled.

Also, of these 52 articles in this systematic review, 19 investigated cycling performance, 8 investigated flexion strength performance, 6 investigated treadmill performance, 5 investigated sprint performance, 4 investigated swimming performance, 3 investigated handgrip performance, 2 investigated running performance, 2 investigated rowing performance, 1 investigated ascent performance, 1 investigated diving performance, and 1 investigated speed skating performance. Overall, most studies used IPC sets of three 5-min cycles of ischemia followed by 5-min of reperfusion or four 5-min cycles of ischemia followed by 5-min of reperfusion with a pressure cuff inflated to 200 or 220 mmHg. A total of 873 healthy participants, amateur athletes or trained athletes (730 males and 143 females) performed the IPC intervention before exercise performance.

3.3. Effects of IPC on exercise performance

3.3.1. Positive effect of IPC on exercise performance

Out of the 25 articles that found a positive effect of IPC on exercise performance, 2 showed that IPC enhanced performance in 5-km runs, specifically when IPC was administered 1 h before the exercise.[19,20] Ten articles found that IPC had a positive effect on cycling performance. The types of performance studied were incremental maximum cycling,[21,22] time trials,[23,24] aerobic/anaerobic cycling,[25,26] Wingate cycling tests,[27] work-to-work test,[28] short-term cycling,[29] time-to-exhaustion tests,[30] and repeated sprints.[31] Some of these articles attributed IPC to a better maximal power output (W_{max}), total exercise time and total work,[21] a higher VO_2 slow component ($VO_{2\ SC}$),[30] a better central motor drive/output,[30] a better mean power output,[29] an increase in activation of skeletal muscle, and a better critical power.[24] Seven articles found a positive effect of IPC on endurance performances. As a matter of fact, one study found an impact of IPC performance on a rhythmic handgrip exercise.[32] Three studies looked at knee/leg extensions[33–35] and found a positive effect on muscle strength,[33] force production,[34] and number of repetitions.[35] Two other studies found a positive effect of IPC on muscle endurance performance for isometric exercises[36] and biceps curls.[37] Five articles in this systematic review noted a positive effect of IPC on swimming performance. To find this effect, these studies evaluated either time in repeated sprints,[38] a maximal performance,[39] static and dynamic apnea,[40] stroke rates,[41] or performance in a time trial.[42] One study looked at performance of counter movement jump and squat jumps, and found a positive effect of IPC on the concentric and eccentric force produced during these jumps.[43]

3.3.2. No effect of IPC on exercise performance

In this systematic review, 15 articles found no effect of IPC on exercise performance. Out of these articles, 7 looked at running exercises. They found no effect during sprints,[44] submaximal running,[45] short distance running,[46] endurance performance in the heat,[47] time trials,[20] maximal acceleration,[48] and running on a field.[49] Four articles found no effect of IPC during cycling performances, such as submaximal cycling,[3] maximum cycling,[21] cycling at high altitude,[50] and anaerobic cycling.[25] Four articles found no effect of IPC on other performances. These included rugby,[51] rhythmic handgrips,[52] speed skating,[53] and rowing.[54]

3.3.3. Negative effect of IPC on exercise performance

Two articles found a negative effect of IPC on performance. One article was in regard to sprint performance in females.[46] The other article was in regard to anaerobic cycling performance.[55]

3.4. Effects of IPC on performance in altitude

3.4.1. Positive effect of IPC on performance in altitude

Two studies found a positive effect of IPC on performance in altitude. One study found a greater impact of IPC on exercise performance at a simulated altitude of 2400 m than at an altitude of 1200 m.[56] The other study found that IPC improved oxygen saturation during a time trial run in altitude.[57]

3.4.2. No effect of IPC on performance in altitude

One article found that IPC did not have an effect on the presence and severity of acute mountain sickness in altitude. This article also found that IPC had no effect on hypoxic pulmonary vasoconstriction in high altitude.[58]

3.4.3. Negative effect of IPC on performance in altitude

One article stated that IPC attenuated hypoxic pulmonary vasoconstriction during a time trial run in altitude.[57]

3.5. Effects of IPC on blood lactate accumulation during exercise

3.5.1. Positive effect of IPC on blood lactate accumulation during exercise

In this systematic review, 2 studies found that IPC attenuated the accumulation of blood lactate during a 5-km run and a sprint.[19,44] The study that focused on sprints found this result only for females.[44]

3.5.2. No effect of IPC on blood lactate accumulation during exercise

Two studies reported no effect of IPC on blood lactate accumulation during running exercise.[45,49]

3.5.3. Negative effect of IPC on blood lactate accumulation during exercise

One study that looked at swimming performance found that IPC had a negative effect on blood lactate accumulation during this exercise.[41]

Table 1
Summary of the study characteristics and different combinations of IPC before exercise.

Authors (year)	Subjects	Age (year)	IPC sets	Ischemia pressure (mmHg)	Preconditioned limb	Time to test	Type of exercise	Exercise protocol	Findings
Andreas et al. (2011)[61]	14 healthy male Caucasians	27 ± 7	3 × 5 min	200	Right thigh (unilateral)	4 h or 48 h	Plantar flexion strength	Plantar flexion at half-MVC: every 4 s until exhaustion	IPC participates in recovery by preparing cells to stimulate the cellular metabolism IPC prepares the cellular metabolism for excessive repair tasks
	9 healthy males	27 ± 8	3 × 2 min ischemia + 5 min reperfusion (total of 20 min)	SBP > 30	Right thigh (unilateral)	4 h	Plantar flexion strength	Plantar flexion at isometric MVC: plantar flexion/dorsiflexion contractions: 3 × 5 s	
Bailey et al. (2012)[19]	13 healthy moderately trained males	25 ± 6	4 × 5 min	200	Thigh (bilateral)	45 min	Treadmill	Maximal running test: speed increase by 1 km/h per 2 min to a maximal running speed of 16 km/h and increase of 2% slope every 2 min until exhaustion 45-min rest in supine position Time trial 5 km (treadmill)	IPC in the context of a submaximal incremental running test allows to attenuate the accumulation of blood lactate IPC has a positive effect on running performance in healthy men
Bailey et al. (2012)[63]	13 healthy moderately trained males	25 ± 6	4 × 5 min	220	Thigh (bilateral)	Immediately	Strenuous exercise on treadmill	Maximal running test: 5 × 3 min at 10−14 km/h + 1 km/h and 2% slope every 2 min until exhaustion 45-min rest in supine position Time trial 5 km (treadmill)	IPC prevents a decrease in brachial artery endothelial function usually induced by strenuous exercise
Barbosa et al. (2015)[32]	13 healthy males	25 ± 4	3 × 5 min	200	Thigh (bilateral)	25 min	Rhythmic handgrip	MVC (hand) and handgrip rhythm with 60 cycles/min with target of 45% MVC	IPC allows to delay fatigue and prolongs the time to failure of the task in a handgrip exercise IPC has a positive effect on exercise performance
Beaven et al. (2012)[43]	10 healthy males and 4 healthy females	32 ± 7	2 × 3 min	220	Alternate thigh (unilateral)	0−5 min	Jump/sprint	Squat jump: 3 times with a 90° knee angle followed by CMJ with 6 kg bar resting on posterior deltoids followed by 6 maximal 40-m sprints every 30 s	IPC allows better recovery from maximal effort performed immediately after treatment and 24 h later IPC has a positive effect on concentric and eccentric force in CMJ and squat jumps IPC allows a faster restore of muscle function following a maximal exercise
						24 h	Run/sprint	40-m run: 3 × the submaximal effort at 50%, 70%, and 90% intensity followed by 6 maximal 40-m sprints every 30 s	
Berger et al. (2017)[58]	15 healthy males and 25 healthy females	35 ± 10	4 × 5 min	200	Thigh (bilateral)	30 min	Ascent	Passive ascent from 750 to 3450 m within 2 h	IPC does not have an effect on presence and severity of acute mountain sickness in altitude IPC does not have an effect on hypoxic pulmonary vasoconstriction, which happens in high altitude
Birkelund et al. (2015)[67]	8 healthy males	20−29	4 × 5 min	200	Arm (unilateral)	3 days	Cycling	Warm-up: 3 min with a workload increase from 25 W to 100 W 4 × 2-min exercise periods with heart rate increased to ≥80% of participants maximal pulse	IPC leads to an increase in circulating proopiomelanocortin derivates and metabolic acidosis IPC leads to a decrease in cortisol and ACTH levels

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Table 1 (Continued)

Authors (year)	Subjects	Age (year)	IPC sets	Ischemia pressure (mmHg)	Preconditioned limb	Time to test	Type of exercise	Exercise protocol	Findings
Bunevicius et al. (2016)[59]	24 amateur athletes in track and field	22.5 ± 1.5	Occlusion applied before exercise and removed after each set	120	Groin	30 s	Foot flexor muscle conditioning training	Exercise intensity of 40% MVC: 3 exercises made up of 3 × 8 repetitions for each leg Rest period: 2.5 min between exercises and 30 s between sets	IPC leads to an increase in vascular wall elasticity IPC participates in preventing an increase in HR during exercise but does not increase the myocardium load or have an effect on coronary vascular function IPC leads to lower JT/RR ratio values in an electrocardiography
Caru et al. (2016)[68]	9 male and 8 female amateur triathletes	27.6 ± 6.7	4 × 5 min	SBP < 50	Right arm (unilateral)	5 min	Cycling	2 bouts of constant load exercise tests at 75% and 115% of GET	IPC allows a decrease in the QT interval during moderate to high intensity exercise
Clevidence et al. (2012)[3]	12 male cyclists	26.7 ± 8.6	3 × 5 min for each leg	220	Alternate thighs (unilateral)	5 min	Cycling	5 min at 30%, 50%, and 70% of maximal power followed by exercise at 90% of maximal power until exhaustion	IPC has no effect on aerobic or anaerobic performance in submaximal cycling testing
Cocking et al. (2018)[60]	18 healthy males	32 ± 8	4 × 5 min	220	Arm (bilateral) Thigh (bilateral)	20 min	Rhythmic handgrip	30 min of rhythmic submaximal handgrip exercise at 25% MVC: 30 contraction/relaxation cycles/min	IPC applied to the arm allows for greater brachial artery diameter during exercise IPC applied to the arm has a greater impact on vasculature than IPC applied to the thigh IPC does not have an impact on blood flow during exercise
Cocking et al. (2017)[65]	14 healthy recreational cyclists	29 ± 8	4 × 5 min	220	Alternate between left and right arm and thigh (bilateral)	Immediately	Cycling	1 h cycling time trials (maximum distance achieved)	IPC attenuates the release of high-sensitivity cardiac troponin T IPC does not have an effect on post-exercise NT-proBNP IPC does not have an effect on cardiac function after exercise
Cocking et al. (2018)[23]	12 male cyclists	36 ± 7	4 × 5 min 8 × 5 min 4 × 5 min 4 × 5 min	220	Thigh (bilateral) Thigh (bilateral) Thigh (unilateral) Arm (bilateral)	20 min	Cycling	Warm-up: 10 min consisting of 5 min at 100 W; 2 min at 150 W; 15 s at W_{max}, 30 s at 150 W, repeat × 3; 45 s at 150 W Time trial: 375 kJ at maximum effort	IPC done in accordance with the traditional (4 × 5 min) occlusion/reperfusion cycles provides most benefits to cycling performance
Crisafulli et al. (2011)[21]	17 healthy males	35.2 ± 9.1	3 × 5 min	SBP <50	Thigh (bilateral)	5 min	Cycling	Incremented maximum test: start at 25 W and increase by 25 W/min at 60 rpm until exhaustion Supramaximal test at 130% VO_{2max}	IPC allows a better maximal performance in cycling IPC allows a better W_{max}, total exercise time and total work IPC does not play a role in increasing VO_{2max}

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Table 1 (Continued)

Authors (year)	Subjects	Age (year)	IPC sets	Ischemia pressure (mmHg)	Preconditioned limb	Time to test	Type of exercise	Exercise protocol	Findings
Cruz et al. (2015)[30]	12 recreational cyclists	20−36	4 × 5 min	220	Thigh (bilateral)	90 min	Cycling	Time-to-exhaustion tests: 3 min at baseline followed by a sudden increase (100% of peak power output), until exhaustion or chosen cadence minus 5 rpm for >5 s	IPC leads to a better constant-load performance and a higher $VO_{2\ SC}$ IPC allows to reduce the increase rate in RPE IPC participates in lowering the sensitivity of the body to fatigue signals and allows a better central motor drive/output
Cruz et al. (2016)[29]	15 recreational male cyclists	20−36	4 × 5 min	220	Thigh (bilateral)	33 min	Cycling	Warm-up: 12 min at 90% of subject's individual lactate threshold Seated sprint cycling: 60 s with resistance on pedals at 7.5% of subject's body weight	IPC allows to improve mean power output during short-term cycling performance IPC increases activation of skeletal muscle by modifying anaerobic metabolism and electromyographic responses
de Groot et al. (2010)[22]	12 healthy males and 3 healthy females	27 ± 5	3 × 5 min	220	Thigh (bilateral)	5 min	Cycling	Incremented maximum test: 50 W for 4 min, followed by 100 W for 4 min, followed by 150 W for 4 min and increase by 20 W/min until exhaustion	IPC allows to increase the power output and maximal oxygen consumption during exercise
Ferreira et al. (2016)[38]	23 university swimmers	23.9 ± 0.8	3 × 5 min	220	Thigh (bilateral)	30 min	Swimming	Warm-up: effort of 2−3 on a 0−10 Borg scale for 400 m freestyle swimming, effort of 5−6 for 6 × 50 m with 20 s intervals, effort of 2−3 for 100 m freestyle swimming Repeated sprint swimming: 6 × 50 m sprints at maximal effort every 3 min	IPC has an ergogenic effect owing to a reduction of total time for 6 repeated sprints IPC lead to a better athletic performance in university swimmers
Foster et al. (2014)[57]	12 healthy males and 2 healthy females	42 ± 14	4 × 5 min performed daily for 5 days	about 200	Thigh (unilateral)	Immediately after the 5th day	Running in altitude	Time trial: 12.8 km run with a positive altitude of 782 m (from 3560 m to 4342 m)	IPC allows attenuation of hypoxic pulmonary vasoconstriction IPC improves oxygen saturation in altitude
Foster et al. (2011)[64]	6 male and 2 female experienced cyclists	39.0 ± 9.7	4 × 5 min	SBP < 20	Thigh (unilateral)	90 min	Cycling	Time trial (ergocycle) at 62% of maximal power: complete 100 kJ as quickly as possible in normoxia and hypoxia	IPC attenuates the hypoxic increase in pulmonary artery systolic pressure
Franz et al. (2018)[62]	19 males	24.7 ± 4.0	3 × 5 min	200	Arm (bilateral)	5 min	Eccentric exercise	Bilateral biceps curls: 3 × 10 repetitions using a barbell at 80% of subject's individual concentric 1RM Rest 1 min between sets	IPC leads to a reduction of creatine kinase activity IPC reduces perceived pain and muscle swelling IPC attenuates postexercise decline in the contractile ability of the biceps brachial muscle

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Table 1 (Continued)

Authors (year)	Subjects	Age (year)	IPC sets	Ischemia pressure (mmHg)	Preconditioned limb	Time to test	Type of exercise	Exercise protocol	Findings
Garcia et al. (2017)[51]	8 male amateur rugby players	24 ± 4	3 × 5 min	220	Alternate thigh (unilateral)	1 min	Performance tests	*t* test: 9.14-m run, followed by 4.57 m of side-stepping to the left, followed by 4.57 m of side-stepping to the right, followed by 9.14-m backward run CMJ: 3 standardized jumps at 90° knee flexion with 30 s rest between jumps CJ30: 30 s of maximal continuous jumps	IPC does not lead to an enhanced performance for rugby players IPC does not contribute to short-term recovery after performance
Gibson et al. (2015)[44]	7 males and 9 females	24.1 ± 2.6	3 × 5 min	220	Alternate thigh (unilateral)	11 min	Sprint	Warm-up: 5 min of stationary cycling with 1 kg resistance and at 60 rpm, followed by 2 × 3-s sprints Repeated sprints: 5 × 6-s sprints against 7.5% body mass	IPC has no effect on short maximal efforts IPC has no effect on absolute and relative power, total power, or percentage decrement IPC allows a reduction of blood lactate after exercise in females
Gibson et al. (2013)[46]	16 males and 9 females	22.9 ± 3.2	3 × 5 min	220	Alternate thigh (unilateral)	15 min	Sprint	Warm-up: 10 min of dynamic stretching routines and 2 submaximal 30-m runs 3 maximal sprints: 10, 20, and 30 m timing gates with 1 min of rest between sprints	IPC does not have a significant effect on short distance sprint performance in males IPC has a negative impact on exercise performance in females
Griffin et al. (2018)[24]	12 recreational male athletes	30 ± 6	4 × 5 min	220	Thigh (bilateral)	Immediately	Cycling	Warm-up: 5 min at 90% GET, followed by 5 min of passive recovery Pretest: 3 min of unloaded cycling, followed by 10 s at an increased cadence of ∼110 rpm All-out cycling: 3 min at maximal effort with as high a cadence as possible	IPC allows improvement of critical power without having an effect on W' IPC has an impact on cycling performance during a TT
Griffin et al. (2019)[69]	12 team sports males	22 ± 2	4 × 5 min	220	Arm (bilateral) Thigh (bilateral)	15 min	Sprint	RSE protocol: 3 × (6 × 15 + 15 m) shuttle sprints with passive (standing) recovery between repetitions and passive (seated) recovery between sets	IPC allows an attenuation of fatigue due to a reduced percentage decrement score, independently of the location of the IPC
Hittinger et al. (2015)[50]	15 highly trained male cyclists and triathletes	29.9 ± 6.6	4 × 5 min	SBP < 10−20	Thigh (bilateral)	45 min	Cycling	Two incremental tests (sea level and high altitude): 10-min submaximal exercise at 55% of altitude-specific W_{peak} followed by an increase of 30 W every 2 min until volitional exhaustion	IPC does not have an impact on W_{peak}, cardiovascular hemodynamics and SpO_2 in the context of submaximal and peak exercise

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Table 1 (Continued)

Authors (year)	Subjects	Age (year)	IPC sets	Ischemia pressure (mmHg)	Preconditioned limb	Time to test	Type of exercise	Exercise protocol	Findings
Incognito et al. (2017)[52]	37 healthy males	24 ± 5	3 × 5 min	200	Left arm (unilateral)	3 min	Rhythmic handgrip	Static handgrip and muscle metaboreflex test: 3 min of baseline, followed by 2 min of 30% MVC SHG with left hand, followed by 3 min of postexercise circulatory occlusion	IPC does not participate in attenuating the central sympathetic outflow directed toward skeletal muscle IPC does not have an effect on pressor response
James et al. (2016)[47]	11 recreational male runners	37 ± 12	4 × 5 min	220	Alternate thigh (bilateral)	10 min	Treadmill	GXT1: submaximal speed protocol with starting speed between 8 and 11 km/h for 3 min followed by 1-min rest during data collection followed by speed increment of 1 km/h until volitional exhaustion (10-min rest) GXT2: same protocol as GXT1, but with starting speed 2 km/h below final speed of GXT1 until volitional exhaustion	IPC does not have any effect on determinants of endurance performance when exercise is performed in the heat
Jean-St-Michel et al. (2011)[39]	8 male and 8 female elite swimmers	18.8 ± 3.3	4 × 5 min	SBP < 15	Arm (unilateral)	about 45 min	Swimming Long-course pool (50 m in length)	7 × 200 m swims at 6-min intervals with target time based on a fixed percentage of swimmer's best time	IPC improves maximal performance for elite swimmers thanks to a modification in skeletal muscle tolerance to maximal exercise due to the release of a humoral protective factor
	8 male and 8 female elite swimmers	19.2 ± 2.9	4 × 5 min	SBP < 15	Arm (unilateral)	about 45 min	Swimming Long-course pool (50 m in length)	Swim at preferred swim length (100 m or 200 m) using best stroke style at 100% effort	
Kaur et al. (2017)[45]	12 male and 6 female habitual runners	27 ± 7	3 × 5 min	220	Thigh (bilateral)	15 min	Treadmill	Stages 1 and 2: velocities = about 2 km/h and about 1 km/h less than stage 3, respectively Stage 3: predetermined self-selected velocity (8.0−16.1 km/h) at 0 incline	IPC has no effect on running performance in the context of submaximal exercise intensities IPC has no influence on blood lactate concentrations
Kido et al. (2015)[28]	15 healthy active males	24 ± 1	3 × 5 min	>300	Thighs (bilateral)	5 min	Cycling	Work-to-work test: gradual increase of the exercise intensity: 3 min at 30 W, 4 min at 90% of GET and 70% of the difference between GET and VO_{2peak} until exhaustion	IPC allows faster muscle deoxygenation and improves exercise endurance
Kjeld et al. (2014)[40]	10 male divers and 1 female diver	18 − 38	4 × 5 min	SBP < 40	Forearm (unilateral)	30 min	Rowing/apnea	Divers: static apnea and dynamic apnea Rowers: time trial 1000 m	IPC plays a significant role in regard to maximal exercise IPC improves performance in static and dynamic apnea
	10 male rowers and 4 female rowers	18 − 35							
Kraus et al. (2015)[73]	6 healthy males and 8 healthy females	22.2 ± 5.3	4 × 5 min	NA	Left arm (unilateral)	15 min	Cycling	4 consecutive 30 s Wingate anaerobic tests at 150 rpm with resistance of 9% body weight with 2 min of rest between tests	IPC allows to improve anaerobic exercise performance in the lower body when applied bilaterally IPC has a positive impact on repeated anaerobic performance
	21 healthy males and 8 healthy females	23.3 ± 3.8			Arm (bilateral)				

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Table 1 (Continued)

Authors (year)	Subjects	Age (year)	IPC sets	Ischemia pressure (mmHg)	Preconditioned limb	Time to test	Type of exercise	Exercise protocol	Findings
Lalonde and Curnier (2015)[25]	8 males and 9 females	28 ± 8	4 × 5 min	SBP < 50	Right arm (unilateral)	5 min	Cycling	Progressive anaerobic test: 6 × 6 s at 0.9, 1.0, 1.1, 1.2, 1.3, and 1.4 Nm/kg of body weight with 2-min active recovery and 3-min passive rest between each test Anaerobic lactic test: 3 Wingate tests: 30-s maximal sprint at 0.8 Nm/kg of body eight for men and 0.77 Nm/kg of body weight for women	IPC does not significantly enhance exercise performance in regard to cycling IPC does not improve anaerobic lactic tests or anaerobic alactic tests IPC allows an increase in power for cycling tests
Lindsay et al. (2017)[26]	13 males and 5 females	23.2 ± 7.1	4 × 5 min performed daily for 7 days	220	Alternate thigh (unilateral)	24 h after the 7th day	Cycling	4 Wingate tests: simulation of Keirin competition: 2000 m velodrome event with final sprint consisting of 625 m (~ 30 s of anaerobic effort)	IPC allows improvement of aerobic and anaerobic exercise performance
Lisboa et al. (2017)[41]	11 male competitive swimmers	20 ± 3	4 × 5 min	220 180	Thigh (bilateral) Arm (unilateral)	1, 2, and 8 h	Swimming	3 × successive 50-m trials in a 50-m swimming pool	IPC plays a role in better swimming performance 2 h and 8 h after administration IPC leads to an increase in blood lactate accumulation and stroke rate
Marocol et al. (2015)[42]	15 amateur swimmers	21.1 ± 3.7	4 × 5 min	220	Alternate arm (unilateral)	5 min	Swimming	Time trial: 100-m front crawl style	IPC applied to the arms improves swimming performance
Marocolo et al. (2016)[37]	21 healthy males	27.3 ± 5.2	4 × 5 min	220	Alternate arm and thigh (unilateral)	4 min	Resistance exercise	Resistance exercise test: elbow flexion biceps curls at load of 12RM	IPC leads to an increased number of repetitions of biceps curls
Marocolo et al. (2016)[35]	13 healthy males	25.9 ± 4.6	4 × 5 min	220	Alternate thigh (unilateral)	8 min	Leg extension	Specific warm-up: 20 repetitions at 60% of predetermined 12RM 3 × maximum sets of the leg extension (2-min rest between sets) with the predetermined 12RM load	IPC leads to a greater number of repetitions in leg extensions
Paixao et al. (2014)[55]	15 amateur cyclists	30.2 ± 7.2	4 × 5 min	250	Alternate thigh (unilateral)	12 min	Cycling	3 Wingate tests: 30 s with load of 0.10 kp/kg with 10 min between tests	IPC has a negative effect on anaerobic performance
Paradis-Deschenes et al. (2017)[33]	9 strength-trained males 8 strength-trained females	25 ± 2 22 ± 1	3 × 5 min	200	Right thigh (unilateral)	18.5 ± 0.1 min	Knee extensions	5 sets of 5 maximum voluntary knee extensions	IPC has a greater impact on muscle strength in males than in females IPC leads to an increased resting blood volume in both sexes IPC increases O_2 extraction in males IPC decreases O_2 extraction in females
Paradis-Deschenes et al. (2016)[34]	10 strength-trained males	25 ± 4	3 × 5 min	200	Right thigh (unilateral)	18 ± 2	Knee extensions	5 sets of 5 maximum voluntary knee extensions	IPC improves force production IPC leads to an increase in muscle perfusion at rest and in recovery periods

(*continued on next page*)

Table 1 (Continued)

Authors (year)	Subjects	Age (year)	IPC sets	Ischemia pressure (mmHg)	Preconditioned limb	Time to test	Type of exercise	Exercise protocol	Findings
Paradis-Deschenes et al. (2018)[56]	13 trained male road cyclists	27.5 ± 1.6	3 × 5 min	220	Thigh (bilateral)	25.6 ± 0.7	Cycling	Time trial: 5 km in low (F_1O_2 0.180, ~ 1200 m) or moderate (F_1O_2 0.154, ~ 2400 m) simulated altitude	IPC has a greater impact on exercise performance at a simulated altitude of 2400 m than at an altitude of 1200 m
Patterson et al. (2015)[31]	14 healthy males	22.9 ± 3.7	4 × 5 min	220	Thigh (bilateral)	45 min	Cycling	Repeated sprint: 12 × 6 s cycle sprints with resistance at torque factor of 1.0 Nm/kg	IPC leads to a positive effect on peak power output
Richard and Billaut, (2018)[53]	7 male and 2 female elite speed skaters	23.3 ± 2.6	3 × 5 min	SBP < 30	Alternating arms (unilateral)	90 min	Speed skating	Time trials: 2 × 1000 m race on ice on indoor long-track (400 m)	IPC has no effect on self-paced speed skating performance IPC attenuates tissue saturation index and could be linked, at the muscular level, to higher O_2 extraction
Sabino-Carvalho et al. (2017)[66]	14 healthy males 4 healthy females	22.3 ± 0.9 24.0 ± 2.5	4 × 5 min	220	Alternate thigh (unilateral)	NA	Treadmill	Discontinuous incremental test: 6 min of baseline at velocity 1 km/h lower than velocity of ventilatory threshold, followed by 3 min at velocity of 2 km/h higher than baseline velocity, followed by increase of velocity of 1 km/h per stage until volitional exhaustion; each stage is 3 min, followed by a 30-s break Recovery period Supramaximal exercise test: 2 min at 60% of the velocity of last completed stage during the discontinuous incremental test, followed by increase of velocity of 0.5 km/h higher than peak velocity until exhaustion	IPC has no effect on aerobic metabolism parameters IPC leads to a longer time to exhaustion, but possibly because of the placebo effect, because the sham condition has the same results
Seeger et al. (2017)[20]	10 healthy males and 2 healthy females	31 ± 6	4 × 5 min	220	Thigh (bilateral)	1 h 24 h	Treadmill	Warm-up: 5 min Stretching: 5 min Time trial: 5 km as fast as possible	IPC has no effect on exercise performance when it is administered 1 h or 24 h before the exercise IPC administered 1 h before exercise has a greater effect on finish time in 5 km TT than when it is administered 24 h before exercise
Tanaka et al. (2016)[36]	12 healthy males	22 ± 1	3 × 5 min	>300	Thigh (unilateral)	5 min	Muscle endurance	MVC: 3 trials consisting of gradual increase in torque from 0 to maximum over 3 s held for maximum 3 s with 1 min of rest between trials Submaximal fatigue exercise: target torque of 20% MVC until task failure	IPC leads to an enhances muscle endurance performance during a sustained isometric exercise IPC leads to accelerated muscle deoxygenation dynamics IPC enhances local muscle endurance

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Table 1 (Continued)

Authors (year)	Subjects	Age (year)	IPC sets	Ischemia pressure (mmHg)	Preconditioned limb	Time to test	Type of exercise	Exercise protocol	Findings
Thompson et al. (2018)[48]	10 varsity-level male sprinters 8 varsity-level female sprinters	21.7 ± 2.6 20.0 ± 2.6	3 × 5 min	220	Right thigh (unilateral)	15 min	Sprint	4 × 20-m sprints	IPC does not enhance running performance
Tocco et al. (2015)[49]	11 male skilled runners	34.6 ± 8.4	3 × 5 min	50 > SBP	Thigh (bilateral)	5 min	Running	5-km self-paced running tests on an outdoor track	IPC does not improve running performance on a field IPC does not have an effect on ventilatory variables, heart rate and blood lactate accumulation
Turnes et al. (2018)[54]	16 national and regional-level male rowers	24 ± 11	3 × 5 min 3 × 10 min	220	Alternate thigh (unilateral)	30 min	Rowing	2000-m rowing ergometer performance	IPC performed for 5 min or 10 min does not have an effect on rowing ergometer performance

Abbreviations: ACTH = adrenocorticotropic hormone; CMJ = countermovement jumps; GET = gas exchange threshold; GXT = graded exercise test; HR = heart rate; IPC = ischemic preconditioning; JT/RR = distance measured from the J-point up to the end of the T-wave/ distance between two consecutive R waves; MVC = maximal voluntary contraction; NA = not available; NT-proBNP = N-terminal prohormone of brain natriuretic peptide; QT = the time between the start of the Q wave and the end of the T wave; RM = repetition maximal; RPE = ratings of perceived exertion; rpm = revolution per minute; RSE = repeated sprint exercise; SBP = systolic blood pressure; SHG = static hand grip; SpO_2 = saturation of peripheral oxygen; TT = time trial; $VO_{2max/peak}$ = maximum rate of oxygen consumption measured during incremental exercise; $VO_{2\ SC}$ = VO_2 slow component; W = watts; $W_{max/peak}$ = maximum exercise power; W' = calculated as the power-time integral above critical power across the 3 min of work.

3.6. *Effects of IPC on metabolism adaptation*

3.6.1. *Positive effect of IPC on metabolism adaptation*

Nine studies in this systematic review found that IPC had a positive effect on certain metabolism adaptations that occur during exercise. Out of the 7 studies that focused on endurance performances, 1 study found that IPC increased vascular wall elasticity and that IPC participated in preventing an increase in heart rate during exercise for foot flexor muscle conditioning training.[59] Another article stated that IPC applied to the arm before rhythmic handgrips allowed for greater brachial artery diameter and had a greater impact on vasculature.[60] One study focused on plantar flexion exercises and found that IPC prepared the cellular metabolism for excessive repair tasks.[61] The next study discovered that IPC led to a decrease in creatine kinase activity during an eccentric exercise.[62] Two studies focused on knee extension exercises. The first found that IPC increased O_2 extraction in males[33] and the second stated that IPC led to accelerated muscle deoxygenation dynamics, which helped with muscular hypertrophy.[36] The last study that looked at endurance exercises found that IPC prevented a decrease in brachial artery endothelial function.[63] One study focused on the effects of IPC on speed skating and discovered that it attenuated the tissue saturation index and could be linked, at the muscular level, to higher O_2 extraction.[53] The last article found that IPC attenuated the hypoxic increase in pulmonary artery systolic pressure during a cycling exercise.[64]

3.6.2. *No effect of IPC on metabolism adaptation*

In this systematic review, 6 studies found that there was no effect of IPC on different metabolism adaptations of the body. Two studies investigated the impact of IPC on rhythmic handgrip performance. The first found that IPC did not have an impact on blood flow.[60] The second stated that IPC did not participate in attenuating the central sympathetic outflow directed toward skeletal muscle.[52] Two other articles focused on the effect of IPC on cycling performance. The first found that IPC did not have an effect on cardiac function after 1-h cycling time trials.[65] The second found that IPC did not have an impact on cardiovascular hemodynamics and saturation of peripheral oxygen in the context of submaximal and peak exercise.[50] Two articles investigated running performance. One study found no effect of IPC on aerobic metabolism parameters,[66] and the other stated that IPC did not have an effect on ventilatory variables and heart rate during running performances on a field.[49]

3.6.3. *Negative effect of IPC on metabolism adaptation*

One study found that IPC decreased O_2 extraction in females during knee extensions.[33]

3.7. *Effects of IPC on blood parameters*

The 2 studies in this systematic review that noted the effects of IPC on blood parameters evaluated cycling performance. The first study found that IPC increased circulating pro-opiomelanocortin derivates and metabolic acidosis. This article also stated that IPC decreased cortisol and adrenocorticotropic hormone levels.[67] The second study found that IPC attenuated the release of high-sensitivity cardiac troponin T after 1 h of cycling time trials.[65]

3.8. Effects of IPC on electrophysiology parameters

Two studies found positive effects of IPC on electrophysiology parameters. One study found that IPC led to a lower JT/RR ratio value (distance measured from the J-point up to the end of the T-wave/distance between two consecutive R waves) in an electrocardiogram during foot flexor muscle conditioning training.[59] The other study found that IPC decreased the QT interval (the time between the start of the Q wave and the end of the T wave; represents ventricular repolarization) during moderate-to-high intensity exercises.[68]

3.9. Effects of IPC on exercise recovery

3.9.1. Positive effect of IPC on exercise recovery

Five studies in this systematic review found positive effects of IPC on exercise recovery. In regard to plantar flexion/knee extension exercises, studies in this systematic review found that IPC prepared cells to stimulate the cellular metabolism,[61] increased the resting blood volume,[33] and increased muscle perfusion at rest and in recovery periods.[34] For eccentric exercises, IPC decreased perceived pain and muscle swelling.[62] This practice also attenuated the postexercise decrease in the contractile ability of the biceps brachii muscle.[62] IPC also had a positive effect on recovery for running exercises. As a matter of fact, one article in this systematic review found that IPC encouraged an easier recovery from maximal jump/sprint efforts[43] and a faster restore of muscle function following a run/sprint exercise.[43]

3.9.2. No effect of IPC on exercise recovery

One article in this systematic review found that IPC had no effect on short-term recovery following a rugby performance.[51]

3.9.3. Unclear effect of UPC on exercise recovery

One article showed that IPC might lead to a longer time to exhaustion for running performance, but this finding could be attributed to the placebo effect, because the sham condition showed the same results.[66]

3.10. Effects of IPC on fatigue

Three studies in this systematic review found positive effects of IPC on the presence of fatigue during performance. The studies looked at rhythmic handgrip exercises,[32] time-to-exhaustion tests,[30] and repeated sprint exercises.[69]

3.11. Effects of IPC on the rating of perceived exertion

One study found that IPC administered before a time-to-exhaustion tests reduced the increase rate in the rating of perceived exertion.[30]

4. Discussion

This systematic review showed an overview of the research done on IPC over the past 28 years. Overall, the studies included were of high quality, with 48 out of 52 studies having a randomized, controlled trial design. The results highlighted in the articles showed the extent to which IPC can be beneficial to exercise performance. Overall, the main finding of this systematic review was that the effects of IPC intervention seemed to be more effective in healthy subjects who wish to enhance their performance in aerobic exercises than in athletes. It is important to note that the first studies about IPC were mainly conducted in healthy subjects, with promising results. However, recent articles studying athletes did not seem to find the same positive effects. This discrepancy could be due to the protocol not being optimized for this population.

4.1. Responders and nonresponders to IPC

In exercise physiology, it has been reported that there are responders and nonresponders to regular physical activity.[70] Indeed, it has been shown in healthy and untrained populations that there is a great interindividual variability in subjects' capacity to improve their cardiac profile in response to regular exercise.[71] It has been hypothesized that the same situation exists for IPC, where there are both responders and nonresponders to the intervention. This finding could explain the variation in hemostatic, endothelial, and inflammatory responses to IPC as a tool to enhance exercise performance. Gene expression could explain this phenomenon.[4,72] The identification of a biomarker aiming to define the optimal preconditioning stimulus remains at the hypothetic stage. However, many studies have been working on elaborating this complex substance.[72]

4.2. Variation in IPC protocols

In this systematic review, there was a lot of variability between studies regarding the IPC protocol. Thus, there did not seem to be a consensus on the optimal procedure to be used for an IPC intervention. Indeed, the number of cycles of ischemia and reperfusion, the duration of the cycles, as well as the period between the time to test and the end of IPC intervention varied from one study to another. Our results showed that the number of cycles of ischemia and reperfusion ranged from 2 cycles[43] to 8 cycles.[23] Also, the duration of occlusion periods ranged from 2 min[61] to 10 min.[54] The majority of studies performed IPC on the day of the test. However, a few studies performed IPC on a daily basis from 5 days[57] to 7 days[26] before the exercise protocol. The time period from the administration of the IPC protocol to the start of the exercise protocol also varied from immediately[24,43,63,65] to 72 h[67] from one study to another. Some studies that explored the second window of protection of IPC[20,43,61,67] reported encouraging results,[43,61,67] whereas others reported results inferior to the first window of protection.[20] Because many different methodologic parameters differed between the studies, the comparison of their results was difficult. As a result, some studies reported no effect of IPC on exercise performance, but this could be due to the IPC protocol not being optimal or to the window of protection not being ideal for the study population.

4.3. Variation in IPC methodologic aspects

There was also an inconsistency between studies regarding the limb that was made ischemic. As a matter of fact, some studies performed IPC sets on the thigh, whereas others opted for the arm. One study[23] was interested in these different methodologic aspects. Cocking et al.[23] studied the optimal ischemic preconditioning dose to improve cycling performance. Thus, responses to traditional IPC (4×5 min thigh (bilateral)) were compared with 8×5 min thigh (bilateral), 4×5 min thigh (unilateral) and 4×5 min arms (bilateral). The results of this study reported that traditional IPC (4×5 min) provided most benefits to cycling performance. They also found that applying more dose cycles (8×5 min) had no impact on performance and that unilateral IPC was more effective that bilateral cuffs. Regarding another aspect, de Groot et al.[22] had studied IPC in its beginnings and had shown that with <3 cycles of IPC, the intervention had no clinical interest in sports performance. Also, during a Wingate anaerobic test, Kraus et al.[73] showed an improvement in the mean and maximal power output when the ischemia was applied bilaterally to the arm, rather than a unilateral cuff.

4.4. Variation in types of studies

Beyond the methodologic aspect of IPC for which there is no consensus for the moment, there needs to be consideration for the diversity in the nature of the studies put forward in this systematic review. As a matter of fact, there was a multitude of designs and results addressed by teams of researchers in different fields; such as cycling, sprint, running, swimming, rowing, ascent, skating, flexion strength, handgrip, and so on. The first studies exploring the effects of IPC in sports science focused on maximizing exercise performance, as well as physiological parameters (i.e., power output, maximal oxygen consumption).[19,21,22,64,74] Recently, the results have evolved to highlight the innovative effects of IPC on exercise performance. Indeed, altitude performance has been evaluated,[56–58] along with the effects of IPC on exercise recovery,[33,34,43,51,61,62,66] fatigue,[30,32,69] and rating of perceived exertion.[30] However, research has been reexamined as a result of a lack of evidence to explain the mechanisms responsible for the outcome of IPC.[75] In this regard, there seems to have been some work done by the scientific community. Indeed, the effects of IPC on metabolism adaptations have been studied in numerous studies[33,36,49,50,52,53,59–66] to better understand the observed effects of IPC on sports performance. Also, to our knowledge, this is a point that Incognito et al.[4] and Horiuchi[75] discussed in their systematic review. This approach is directly related to the exploration of a procedure to optimize IPC protocols and, therefore, a consensus.

4.5. Perspectives

Finally, not all studies directly observed a positive effect of IPC on exercise performance. However, they participated in enriching the scientific knowledge on the matter and they provided additional information about IPC, which is currently an unknown therapeutic intervention to the amateur and high-level sports environment. Thus, this section on the perspectives of research on IPC was constructed from the 52 articles of this systematic review and from the perspectives they put forward in their conclusion.

4.5.1. Further research on mechanisms

Many perspectives in the articles of this systematic review focused on defining the different mechanisms observed in each study. Thus, it is possible to conclude that further research should go in a direction that investigates the mechanisms responsible for a decrease in blood lactate concentration during incremental exercise,[19] less damage to skeletal muscle,[62] and positive effects on peak power output during repeated sprint cycling performance.[31] It would also be interesting for the scientific community to know why IPC can lead to an improved blood flow, an improved efficiency of muscular oxygen usage,[43] an attenuation of the normal hypoxic increase of pulmonary artery pressures, and an improvement of oxygen saturation in altitude.[57,64] Future studies should elucidate the cellular and subcellular mechanisms of IPC,[21] better characterize the molecular mechanisms of IPC-induced changes,[68] and define the molecular and biological mechanisms behind the effects of IPC on exercise.[28]

4.5.2. Further research on local factors

Some of the 52 articles in this systematic review noted that further research should find out more about the effect of IPC on local factors, such as working limb flow, oxygen delivery, arteriovenous oxygen difference,[50] energy cost of endurance events,[45] and changes in intramuscular metabolism.[36] These parameters are often forgotten in analyses. Nevertheless, they remain interesting for the reader and they allow a better comprehension of the effects of IPC intervention on local factors.

4.5.3. Further research on variables

There have been some suggestions among the articles included in this systematic review about determining the effects of IPC on different variables. These avenues of research include studying a less healthy population,[57] testing different performance groups,[74] and evaluating different training statuses, types of sport, and risk factors.[3] These parameters have been evaluated recently in other articles, which is shown in our systematic review (Table 1). Nevertheless, it seems essential that researchers continue to investigate the effects of IPC with regard to different sports.

4.5.4. Further research on methods and IPC protocols

A few articles in this systematic review concluded that further research should be done on the methods and protocols associated with the IPC intervention. As a matter of fact, the authors of these articles suggested that there should be further investigation on the differences between the procedures of IPC,[22] the best IPC protocol for the most beneficial effects,[46,48] and the amount of muscle that needs to made ischemic to elicit more performance benefits.[48,50,73] One article in this systematic review focused on these perspectives,[23] as it was argued in the Discussion section. However, there seems to be an increasing need for this type of article to reach a consensus on the best IPC protocol.

4.6. Limitations

No meta-analysis could be conducted because the heterogeneity of the data was too high, which prevented a valid mathematical combination analysis. Indeed, the heterogeneity analysis, measured with Cochran's Q test and the I^2 statistic,[76] revealed an I^2 of 73.47%. Among these important clinical heterogeneities and methodologic heterogeneities, we reported statistical, IPC interventions, outcomes, study participants, and study design heterogeneities. In this sense, the included studies were thought to be too different, either statistically, clinically or in methodologic terms, and thus not suitable for a meta-analysis.

5. Conclusion

It was difficult to compare the results between studies because the characteristics of the participants, IPC protocols and exercise tests differed between studies. Overall, the effects of IPC intervention appeared to be more effective in healthy subjects than in athletes. This finding could be due to the protocol not being optimized for this population. Thus, a better knowledge of the mechanisms generated by the IPC intervention would make it possible to optimize the protocols according to the characteristics of the subjects. We invite researchers to further discuss the mechanisms that may be involved in response to IPC intervention in exercise performance to provide the subjects with the best possible experience of IPC intervention.

Authors' contributions

MC and AL conceived of the study and participated in the design and coordination, performed the literature search and study selection from PRISMA statement, interpreted the data, and contributed to the writing of the manuscript; DC conceived of the study and participated in the design and coordination, and contributed to the writing of the manuscript; MC and FL contributed to the writing of the manuscript. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

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