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Whole-body Cryotherapy as a Recovery Technique after Exercise: A Review of the Literature

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ABSTRACT

This review aims to evaluate the current body of literature investigating the effect of whole body cryotherapy on recovery after exercise. A systematic search was conducted to investigate the effect of whole body cryotherapy (WBC, exposure to temperatures between −110 to −190 °C) on markers of recovery after damaging exercise in healthy, physically active subjects. Of the 16 eligible articles extracted, ten induced muscle damage using controlled exercise in a laboratory setting, while six induced damage during sport-specific training. Results indicated that muscle pain was reduced in 80 % of studies following WBC. Two applied studies found recovery of athletic capacity and performance with WBC improved, variables of this nature were also improved in 71 % of studies using controlled exercise. Further benefits of WBC treatment included reduction of systemic inflammation and lower concentrations of markers for muscle cell damage. These results suggest that WBC may improve recovery from muscle damage, with multiple exposures more consistently exhibiting improvements in recovery from pain, loss of muscle function, and markers of inflammation and damage. The diversity in muscle damage protocols, exposure timing with regards to exercise, as well as temperatures, duration and frequencies of exposure, make specific recommendations preliminary at present.

Introduction

In the days following unaccustomed intense training or competition, athletes often experience a dull aching pain, stiffness, tenderness and prolonged loss of muscle strength, which can last for up to 5–7 days [4, 18]. For athletes engaged in strenuous training cycles or competing on multiple days, experiencing reduced force generating capacity for such a length of time can be detrimental to performance. Although it is not yet clear what mechanisms specifically trigger these symptoms, they may result from exercise-induced muscle damage (EIMD). More specifically this damage may involve eccentric contractions, which force high loads on fewer muscle units, predisposing these cells to greater structural damage [5, 6, 11, 16]. It is established that structural muscle cell damage is followed by a sustained reduction in optimal force production, the delayed onset of muscle soreness (DOMS), and an acute inflammatory response [3, 5, 6, 23]. Local and systemic inflammation occurs due to ultra-structural damage of muscle fiber units after intense, repetitive or unaccustomed exercise [11, 26]. This inflammatory response is part of the natural process of the muscle tissue after injury, mobilizing leukocytes that contribute to clearing and regenerating the damaged tissue [24]. The time taken to return to cellular homeostasis and peak functional capacity after

EIMD may be related to the recovery of both the cells directly damaged by exercise, and those neighboring cells that may be damaged as part of the inflammatory response [26].

It has been proposed that cold therapies aid recovery following EIMD through a dampening of the inflammatory response and through an analgesic effect [1, 9]. A novel form of cold therapy, Whole Body Cryotherapy (WBC) has gained popularity with athletes after its initial introduction as an anti-inflammatory therapy treatment in chronic inflammatory conditions [20, 30]. A typical session of WBC involves the participant standing in a chamber that fills with a safe, but extremely cold gas, maintained at temperatures of between −110 °C and −190 °C for at least two and a maximum of five minutes [1, 8]. The interest in this therapy stems from studies that suggest that the extreme temperature of WBC may magnify the effect of cold therapies such as cold water immersion (CWI), thus potentially shortening recovery time. Cold therapies have been shown to reduce pain and the inflammatory response [1], and it has been proposed that WBC can further restrict the inflammatory response and accelerate the recovery of both the structural integrity and functionality of muscle following EIMD [1, 20, 26, 30].

Despite the gain in popularity of WBC, there remains little evidence for its efficacy, and little guidance regarding the application of optimal WBC protocols for optimizing recovery from strenuous exercise. The inconclusive nature of information is partly due to various exercise and WBC modalities, temperatures, timing in relation to exercise, and frequencies [1, 7]. This is also due to the fact that the relationships between EIMD, the subsequent inflammatory processes and effect on muscle performance are not yet fully understood. Thus, it is difficult to confirm which aspects of the recovery process are affected by WBC. In general, studies investigate the effect of WBC on muscle or athletic performance, as well as on indirect markers of muscle damage including muscle enzyme creatine kinase (CK), and systemic markers of inflammatory response such as cortisol and cytokines. Measurement of cytokines often include the pro-inflammatory interleukin-8 and -1β, tumor necrosis factor-α (TNF-α); anti-inflammatory interleukin-10 and -1ra; and the inflammation regulator interleukin-6. IL-6 increases in circulation during inflammatory responses [28], but when released from muscle tissue during exercise, it has been proposed to also increase circulating IL-1ra, IL-10, and cortisol that all form part of the anti-inflammatory process after muscle damage [20, 25, 28]. The measurement of inflammation markers is important given the hypothesis that WBC may influence the mechanisms of the inflammatory process during recovery. It is suggested that WBC dampens the inflammatory response [1] and reduces edema formation following EIMD. IL-6 is identified as a myokine, which is released from contracting muscles into the circulatory system during exercise. It cannot be excluded that muscle contractions elicited as shivering thermogenesis in response to cold exposure may contribute to changes in blood IL-6 concentration. However, it is likely that this effect would be small in comparison to the exercise-induced increases.

This review will evaluate the current body of literature examining the effects of WBC on recovery of athletic performance following exercise, including a systematic search for relevant articles, and a narrative evaluation. Specifically, we focused on articles that included at least one variable that has been associated with performance loss due to EIMD. This included athletic performance parameters, maximal voluntary contraction measurements, pain and blood concentration of CK, cortisol and cytokines. We aim to provide evidence-based suggestions on the optimal use of WBC treatment for effective muscle recovery from EIMD, with specific focus on athletic performance, pain and systemic inflammation.

Methods

A systematic search of the literature was conducted according to PRISMA guidelines on six databases in August 2015 and repeated for currency before submission in November 2016. The databases searched were Cinhal, Medline, Web of Science, SportDiscus, PubMed and Scopus. Twenty-one key words and phrases were used in combination (Boolean logic [AND, and OR]), these included "whole body cryotherapy" OR "cryogenic chamber therapy" OR cryotherapy OR cryostimulation OR cryo * AND "pain measurement" OR "delayed onset muscle soreness" OR "creatine kinase" OR "muscle fatigue" OR cytokine OR "muscle damage" OR "muscle function (loss of)" OR immun * OR inflam * OR "maximal voluntary contraction" OR "Isometric contraction" OR "muscle torque" AND exercise OR running (run *) OR "eccentric exercise" OR athlete * . Three independent researchers (CR, CC and KE) then used specific inclusion criteria to extract articles for analysis following the CONSORT search strategy template (▶ **Fig. 1**). Any differences or discrepancies in the selection of articles were subsequently discussed and decided upon together.

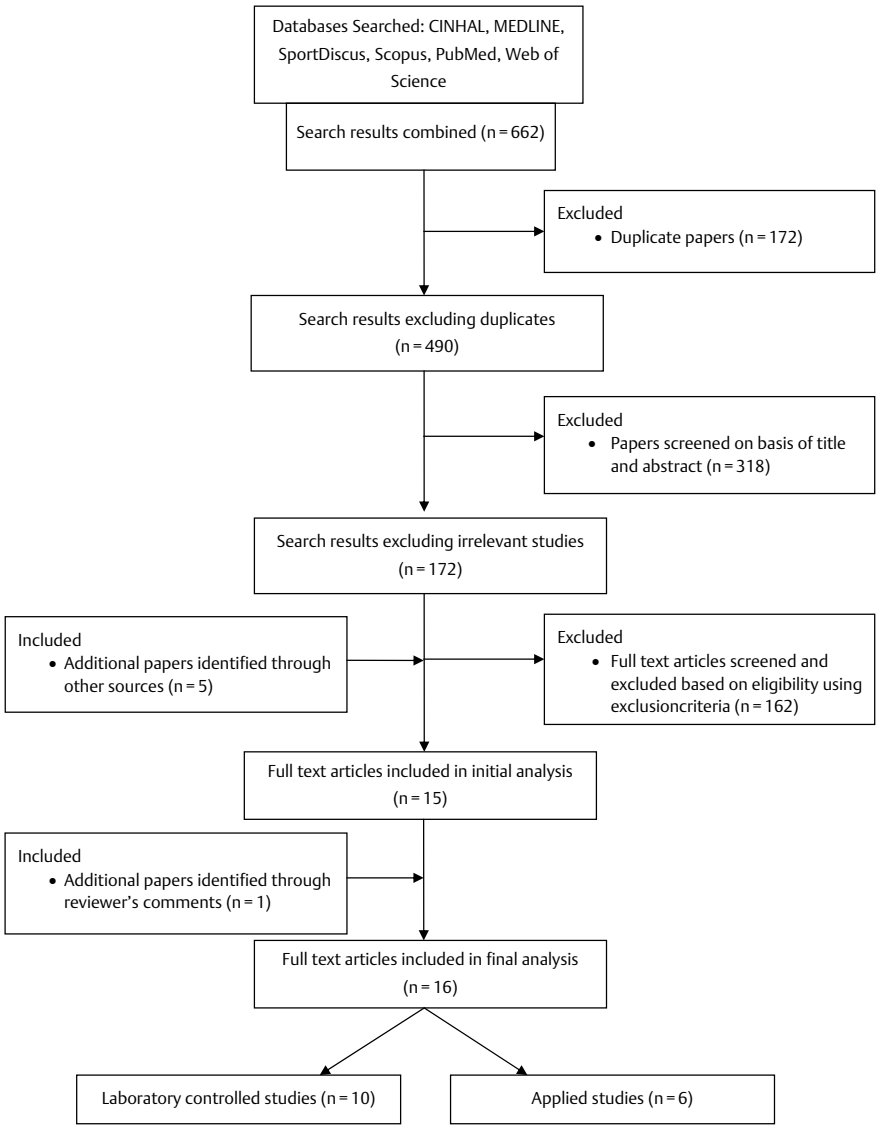
Cryotherapy was classified as exposing either the whole body or at least full lower body and torso to nitrogen gas of temperatures that were −110 °C at their warmest, with the common range being −110 °C to −150 °C. There was no restriction on the duration or frequency of exposure to the recovery treatment or its timing in relation to the exercise protocol. Studies were required to have included an outcome measure associated with muscle damage, including at least one of the following: inflammatory markers, subjective pain levels, muscle damage markers, and sport-specific athletic performance or muscle function indicators. Performance and/or muscle function indicators included for analysis consisted of maximal voluntary contractions (MVC) measured on dynamometers, force production during a squat jump, accuracy and skill-based activities, as well as aerobic endurance measured by oxygen consumption or time trial.

Participants included in the studies were required to be either from an athletic population or physically active, and otherwise healthy and void of any injury or illnesses at the time of the intervention. Articles must have included a form of physical exercise to induce muscle damage.

The Downs and Black quality analysis tool has been used to assess the rigor and quality of studies included in this analysis [10]. Studies were measured across 27 questions covering four main subscales (▶ **Table 1**). These include unbiased reporting, external validity, internal validity measuring bias and confounding, as well as a power value assessing the possibility of chance influencing the findings (▶ **Table 1**).

Results

A total of 16 articles were found that met the inclusion criteria, ten of which utilized a controlled damage protocol [7, 12–



▶ **Fig. 1** CONSORT diagram. Description of the CONSORT process used to identify and select the articles included in this review.

15, 17, 20, 26, 29, 32]. The remaining six articles assessed treatment amidst routine training cycles that cannot be considered a standardized stimulus for all participants [2, 21, 27, 30, 31, 33]. To account for this, we have chosen to separately summarize the results in two subgroups denoted as "Laboratory Controlled Studies" or "Applied Studies" (▶ **Table 2**). No studies were excluded based on the training status of participants recruited, as there were no studies retrieved that investigated the effect of WBC on untrained populations.

Evaluation of quality analyses of all studies included in the review, both applied and laboratory controlled, resulted in an average score of 19.1, and all studies scored above 18 on the Downs and Black quality analysis tool. Based on these results, we concluded that the studies selected for this review are of comparable quality (▶ **Table 3**).

Five articles measured subjective pain after damaging exercise, commonly using a visual analogue scale [7, 12, 14, 15, 32]. Functional or performance based measures including MVC, muscular power or endurance and sport-specific skills were measured in nine studies [7, 12–15, 17, 27, 29, 33]. Markers of inflammation (TNF-α, IL-2, IL-6, IL-8, IL-10, and CRP) were investigated in five studies [2, 20, 26, 32, 33]. Four studies measured the hormone cortisol as a marker of hypothalamic-pituitary-adrenal (HPA) axis activation [21, 30, 31, 33], and CK was measured in eight studies as a marker of muscle damage [2, 14, 15, 21, 30–33].

Highly trained athletes were recruited in ten studies [2, 15, 17, 20, 21, 26, 27, 30, 31, 33], with the remaining six articles comparing healthy, physically active participants [7, 11, 12, 14, 29, 32]. Of the 224 participants recruited across all studies included in this review, the mean age was 24.9 ± 3.5 years. Two studies included only female participants [21, 27], one recruited both genders [7], and the remaining 13 articles included men only [2, 12–15, 17, 20, 26, 29–33]. The largest study sample size was 26 participants, with an average of 13 participants in each study.

▶ **Table 1** Downs & Black Quality Analysis Tool[10].

Item no.	Reporting[$]	Score
1.	Is the hypothesis/aim/objective of the study clearly described?	0–1
2.	Are the main outcomes to be measured clearly described in the introduction or methods section?	0–1
3.	Are the characteristics of the patients included in the study clearly described?	0–1
4.	Are the interventions of interest clearly described?	0–1
5.	Are the distributions of principal confounders in each group of subjects to be compared clearly described?	0–1
6.	Are the main findings of the study clearly described?	0–1
7.	Does the study provide estimates of the random variability in the data for the main outcomes?	0–1
8.	Have all important adverse events that may be a consequence of the intervention been reported?	0–1
9.	Have the characteristics of patients lost to follow-up been described?	0–1
10.	Have actual probability values been reported (e. g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	0–1
External validity [*]		
11.	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	0–1
12.	Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	0–1
13.	Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?	0–1
Internal validity – bias[α]		
14.	Was an attempt made to blind study subjects to the intervention they have received?	0–1
15.	Was an attempt made to blind those measuring the main outcomes of the intervention?	0–1
16.	If any of the results of the study were based on “data dredging”, was this made clear?	0–1
17.	In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?	0–1
18.	Were the statistical tests used to assess the main outcomes appropriate?	0–1
19.	Was compliance with the intervention/s reliable?	0–1
20.	Were the main outcome measures used accurate (valid and reliable)?	0–1
Internal validity – confounding (selection bias)[β]		
21.	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?	0–1
22.	Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	0–1
23.	Were study subjects randomized to intervention groups?	0–1
24.	Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?	0–1
25.	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	0–1
26.	Were losses of patients to follow-up taken into account?	0–1
27.	Did the study have sufficient power to detect a clinically important effect where the probability for a difference being due to chance is less than 5 %	0–1

Description of the Downs and Black criteria items used to determine the quality of articles included.

Ten articles used a crossover design in which subjects experienced both cryotherapy and a control treatment [13–15, 17, 20, 21, 26, 27, 29, 30]. Control groups that received no recovery treatment were used in comparison with the WBC intervention group in four studies [7, 12, 31, 32]. Two research groups took baseline measures of variables from participants prior to commencement of the testing period with WBC, to compare results before and after treatment [2, 33].

In all studies, participants were exposed to the cryotherapy treatments for at least two minutes and for a maximum of three minutes, but with varying repeats of exposure of between one to thirty sessions over periods of one to ten days. Five articles report studies where participants had been exposed to the recovery treatment before exercise [20, 21, 30, 31, 33]. Krüger (2015) and Ferreira-Junior (2014) both conducted randomized crossover trials in which groups were administered WBC between two bouts of the same damaging exercise on one day, and on another occasion performed the two bouts of exercises in the absence of WBC [11, 17]. Eight studies exposed participants to the recovery modes WBC after exercise [7, 12 , 14, 15, 26, 27, 29, 32]. Finally, one study that used WBC daily during a standard five-day training cycle did not specify whether participants had been exposed before or after exercise [2].

▶ **Table 2** Summary of studies included.

Laboratory Controlled Studies							
		Recovery		**Outcome Measures**			
Study and design	**Damage protocol**	**Protocol**	**Intervention timing**	**Pain measure-ments**	**Functional or performance based measurements**	**Immune and inflammatory response**	**Systemic markers of muscle damage (creatine kinase)**
Hausswirth et al.[15] 2011 Randomized crossover trial, over 3 non adjoining weeks	n = 9 male runners ran a 48-min simulated trail run (31.8 ± 6.5yrs)	WBC: 3-min exposure to −110 °C CON: 30-min seated rest at room temperature.	3 sessions: immediately post, 24 h and 48 h **post** exercise	**Pain** ↓ (VAS) WBC + 39/100 CON + 59/100 (at 48 h)	**MVC** ↑ (isometric) WBC + ~15 % CON + ~5 % (of post exercise MVC at 24 h post)		←→ **CK**
Pournot et al.[26] 2011 Randomized crossover trial, 3 week washout period	n = 11 male runners ran a 48-min simulated trail run (31.8 ± 2yrs)	WBC: 3-min exposure to −110 °C CON: 30-min seated rest at room temperature.	4 sessions, immediately post, 24, 48, and 72 h **post** exercise			**CRP** ↓ WBC + 123 % (at 24 h) CON + 515 % (at 24 h) **TNF-α** ←→ **IL-6** ←→ **IL-10** ←→ **IL-1β** ↓ −65 % (at 1 h) **IL-1ra** ↑ +38 % (at 1 h)	
Costello et al.[7] 2012 Randomized control trial	n = 18 physically active undertook 100 maximal contractions of left knee extensors (14 male, 4 female, 21.2 ± 2.1yrs)	WBC (n = 9): 3-min exposure to −110 °C CON (n = 9): 3-min seated rest at 15 °C	1 session, 24 h **post** exercise	**Pain** ←→	**MVC** ←→		
Fonda et al.[14] 2013 Randomized crossover trial, 10 week washout	n = 11 physically active men undertook a bout of damaging exercise consisting of drop jumps and leg curls (26.9 ± 3.8yrs)	WBC: 3-min exposure to −140 °C to −195 °C CON: No specific treatment	6 sessions, 1, 24, 48, 72, 96, and 120 h **post** exercise	**Pain** ↓ (VAS) WBC + 0.8/10 CON + 1.9/10 (at 48 h, rest) WBC + 2.8/10 CON + 4.7/10 (at 48 h, during squat)	**Max jump power** ↑ WBC 97 % CON 94 % (at 48 h)		**CK** ←→
Mila-Kierzenkowska et al.[20] 2013 Randomized crossover trial, 2 week washout	n = 18 male volleyball players undertook 40 min of cycling (28.3 ± 4.0yrs)	WBC: 2-min exposure to −130 °C CON: No specific treatment	1 session, immediately **before** exercise			**IL-1β** ↓ WBC + 25 % CON + 158 % (post exercise) **IL-6** ↓ WBC - 11 % CON + 116 % (post exercise)	
Ferreira-Junior et al.[13] 2014 Randomized crossover trial, 1-week washout	n = 12 physically active men undertook two sessions of 120 maximal contractions of the knee extensors (23.9 ± 5.9yrs)	WBC: 3-min exposure to −110 °C CON: No specific treatment	1 session in **between** two exercise bouts on the same day		**MVC** (eccentric) ↑ WBC ~97 % CON ~86 % (at 40 min)		

▶ **Table 2** Continued

Laboratory Controlled Studies							
Study and design	**Damage protocol**	**Recovery**		**Outcome Measures**			
		Protocol	**Intervention timing**	**Pain measure-ments**	**Functional or performance based measurements**	**Immune and inflammatory response**	**Systemic markers of muscle damage (creatine kinase)**
Ziemann, et al.[32] 2014 Randomized control trial	n = 18 physically active men undertook 30-min of step up/down eccentric work (21.7 ± 0.9yrs)	WBC (n = 9): 3-min exposure to −110 °C CON (n = 9): No specific treatment	10 sessions, twice a day, 24 h, 48 h, 72 h, 96 h and 120 h **post** exercise	**Pain** ↓ (VAS) WBC + 2.9/10 CON + 4.2/10 (at 24 h post)		**IL-10** ↑ WBC + ~104 % CON + ~5 % (24 h after final exercise protocol) **IL-1β** ↓ WBC - ~10 % CON + ~112 % (24 h after final exercise protocol)	**CK** ↓ WBC - ~55 % CON - ~24 % (24 h after final exercise protocol)
Ferreira-Junior et al.[12] 2015 Randomized control trial	n = 26 physically active men undertook five sets of 20 drop jumps (20.2 ± 2.5yrs)	WBC (n = 13): 3-min exposure to −110 °C CON (n = 13): No specific treatment	1 session, immediately **post** exercise	**Pain** ↓ (VAS) WBC + ~45/100 (at 48 h) CON + ~55/100 (at 48 h)	**MVC** (isometric) ↑ WBC ~89 % CON ~76 % (at 72 h)		
Vieira et al.[29] 2015 Randomized crossover trial, 1-week washout	n = 12 physically active men undertook 120 maximal contractions of right knee extensors (23.9 ± 5.9yrs)	WBC: 3-min exposure to −110 °C CON: No specific treatment	1 session, immediately **post** exercise		**MVC** ←→ **Force** production during vertical jump ←→		
Krüger et al.[17] 2015 Randomized crossover trial, 1-week washout	n = 11 male endurance athletes undertook 5 × 5 min of high intensity running (25.9 ± 2.1yrs.)	WBC: 3-min exposure to −110 °C CON: No specific treatment	1 session, **between** two bouts of exercise on the same day		**RPE** ↓ WBC ~ 11.8/20 CON ~ 13.0/20 (during exercise) **Time to exhaustion** ↑ WBC ~ 96 % CON ~ 92 % (at 60 min)		
Applied Studies							
Study and design	**Damage protocol**	**Recovery**		**Outcome Measures**			
		Protocol	**Intervention timing**	**Pain measure-ments**	**Functional or performance based measurements**	**Immune and inflammatory response**	**Systemic markers of muscle damage (creatine kinase)**
Wozniak et al.[31] 2007 Within subject trial	n = 21 male kayakers undertook a 10-day training program (24.6 ± 4.3yrs)	WBC: 3-min exposure to −120 °C to −140 °C CON: No specific treatment	30 sessions, three times daily **before** each training session for 10 days			**Cortisol** ↓ WBC + 5 % CON + 22 % (after 10-day training)	**CK** ↓ WBC + ~61 % CON + ~146 % (after 10-day training)

▶ **Table 2** Continued

Applied Studies							
		Recovery		**Outcome Measures**			
Study and design	**Damage protocol**	**Protocol**	**Intervention timing**	**Pain measure-ments**	**Functional or performance based measurements**	**Immune and inflammatory response**	**Systemic markers of muscle damage (creatine kinase)**
Banfi et al. [2] 2009 Within subject trial	n = 10 male rugby players undertook a 5-day training program (26 ± 2.5yrs)	WBC: 2-min exposure to −110 °C for 2 min	5 sessions, once daily for 5 days			**CRP** ←→ **IL-2** ↓ -43 % **IL-8** ↓ -21 % **IL-10** ↑ -11 % (after 5-day training)	**CK** ↓ - 40 % (after 5-day training)
Mila-Kierzenkowska et al.[21] 2011 Randomized crossover trial, 4 month washout	n = 9 female kayakers undertook a 10-day training program (23.9 ± 3.2yrs)	WBC: 3-min exposure to −120 °C to −140 °C CON: No specific treatment	20 sessions, twice daily **before** training for 10 days			**Cortisol** ←→	**CK** ←→
Ziemann et al.[33] 2012 Randomized control trial	n = 12 male tennis players undertook a 5-day training program (23 ± 3yrs)	WBC (n = 6): 3-min exposure to −120 °C CON (n = 6): No specific treatment	10 sessions, twice daily **before** training for 5 days		**VO_2** at 6 min of tennis drill ↓ WBC - 10 % CON - 1 % **Sport specific accuracy** ↑ WBC + 7 % CON + 3 % (after 5-day training)	**TNF-α** ↓ WBC - 60 % CON - 35 % **IL-6** ↑ WBC + 23 % CON - 7 % **Cortisol** ↑ WBC + 13 % CON - 19 % (after 5-day training)	**CK** ↓ WBC - 21 % CON - 3 % (after 5-day training)
Wozniak et al.[30] 2013 Randomized crossover trial, unknown washout	n = 6 male rowers undertook a 6-day training program (26.7 ± 3.6yrs)	WBC: 3-min exposure to 125 °C to −150 °C CON: No specific treatment	12 sessions, twice daily **before** training for 6 days			**Cortisol** ↓ WBC + 11 % CON + 25 % (after 3-day treatment)	**CK** ↓ WBC + 73 % CON + 150 % (after 6-day treatment)
Schaal et al.[27] 2015 Randomized crossover design, 9-day washout	n = 10 female synchronized swimmers undertook 14-day training program (20.4 ± 0.4yrs)	WBC: 3-min exposure of whole body at −110 °C CON: No recovery treatment	14 sessions, immedi-ately **post** last training session for 14 days		**400 m TT swim** ↑ WBC −0.5 % CON −1.1 %		

WBC, whole body cryotherapy; MVC, maximal voluntary contraction; CK, creatine kinase; TNF, tumor necrosis factor; IL, interleukin; CRP, C-reactive protein; ↑, increase with WBC compared to control; ↓, decrease with WBC compared to control; ↔ no significant difference between recovery treatment groups; ~ measurement estimate taken from graphs

Discussion

Studies will be discussed according to four key outcome measures of DOMS, including pain, muscle function and performance, immune and inflammatory responses, and CK as a marker of muscle damage (▶ **Fig. 2**). The studies have also been separated into laboratory controlled studies, which investigate WBC following one bout of exercise, and applied studies, which investigate the effect of several WBC sessions in the context of several days of training.

Laboratory controlled studies

Ten studies examined one bout of standardized exercise, using either single or multiple exposures to WBC. Notably, all (four) studies using multiple WBC exposures found a significant decrease in muscle pain, in conjunction with improvements in muscle function.

Five articles reported that WBC positively influenced muscle function or performance capacities that are otherwise detrimentally affected by exercise [13–15, 17, 33]. Two further studies with controlled exercise protocols found no influence of WBC on MVC or other marker of athletic capacity after damaging exercise [7, 29]. One of these, Costello (2012), provided treatment 24 h after the exercise protocol. Recovery of MVC after damaging exercise with WBC may not be effective when WBC is administered only once, 24 h after the exercise protocol [7]. Vieira (2015) found no influence of WBC on vertical jump recovery 30 minutes after treatment. However, it was suggested that because the functional testing in this study was performed so soon after WBC, there may have been a confounding effect of limited muscle functionality due to reduced muscle temperature [29]. The influence of timing of treatment exposure after exercise should be examined directly in future trials.

Of the studies that found positive influences on performance with WBC, one observed a reduced rate of perceived exertion (RPE), and another a faster return to MVC baseline after damaging exercise with WBC compared to without [13, 17]. Hausswirth (2011), Fonda (2013) and Ferreira (2015) also found both a faster recovery of MVC or performance markers with WBC treatment alongside a reduction in pain [12, 14, 15]. These findings may suggest a connection between WBC reducing pain and promoting a faster return to peak functional capacity, both important factors in sport-specific recovery.

Pain has been widely used throughout literature as a marker of exercise-induced muscle damage [5, 18]. Reduced joint ranges of motion and altered recruitment patterns are often observed in athletes suffering from severe muscle soreness. This is part of a compensatory mechanism to avoid exerting more pain on damaged tissue in the major muscle groups affected by EIMD [5, 22]. After damaging exercise, there is a reduction in overall force production, due to the recruitment of smaller groups of muscles to compensate for damaged tissue. This reduced force-producing capacity, along with the onset of pain, has been identified as a factor that increases the risk of injury for the affected muscle groups [5]. Across all five laboratory-controlled studies that reported pain measurement, a visual analogue scale was used [7, 12, 14, 15, 32]. Four studies found that WBC reduced pain levels at rest by at least 18 % when compared to a control at 48 h post treatment [12, 14, 15, 32]. Unlike these four studies, Costello (2012) reported that there was no significant change in pain measurements during recovery with WBC [7]. Treatment in this trial though, was provided 24 h post exercise where in the four aforementioned studies WBC was administered immediately following the damaging exercise. One study also reported that WBC reduced pain measurements significantly not only at rest but also during a body weight squat when compared to the control, suggesting that this recovery treatment may also reduce pain during subsequent muscle contractions [14].

Out of the ten studies that employed standardized damage protocols, three reported on biomarkers of muscle damage through the measurement of circulating CK [14, 15, 32]. In the study conducted by Ziemann [32], participants exhibited a pronounced decline (approximately 30 %) of circulating blood CK after multiple exposures to WBC over a five-day period when compared to a control group. These participants were exposed to cryotherapy twice a day for five consecutive days after exercise, totaling 10 exposures. Both Hausswirth (2011) and Fonda (2013) found no significant changes in CK with protocols using either three or six exposures to WBC respectively [14, 15]. The results from these three studies suggest that there may be a dose response to WBC when assessing CK concentration, where a reduction in circulating CK is in proportion to the number of exposures to WBC during the recovery process.

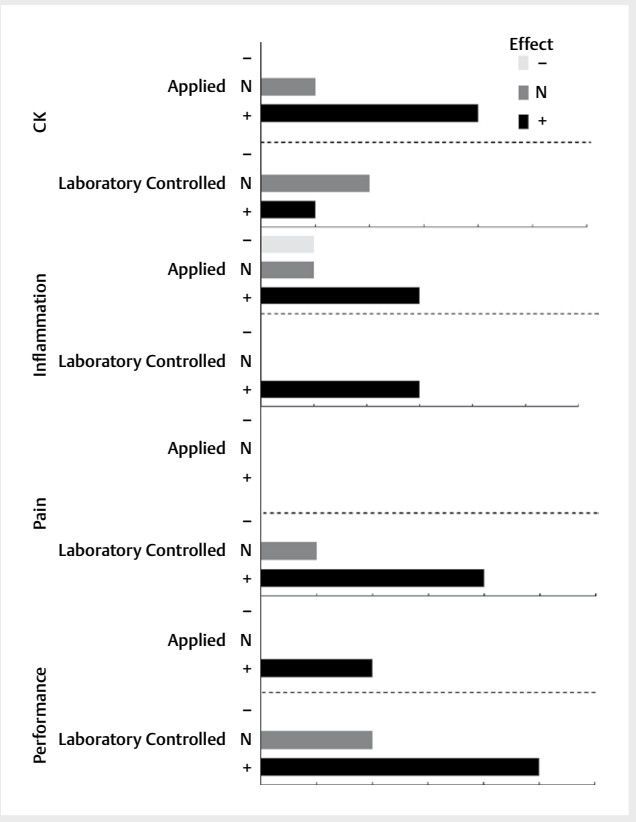
Pournot [26] conducted one of the three studies that measured the inflammatory response with standardized damage protocol. The authors investigated the inflammatory response in well-trained runners following a 48-minute simulated trail run and found no significant differences in the time course changes of circulating IL-6, IL-10 and TNF- α concentrations between either the WBC or control treatments. However, concentrations of the acute inflammatory phase response protein, CRP, were increased by 515 % from baseline in the control group at 24 h post exercise compared to an increase of 123 % in the WBC condition [26]. The increase of inflammatory IL-1β that naturally occurs after damaging exercise was limited when participants were exposed to WBC compared to the control. There was also a larger increase in cytokine inhibitor IL-1ra concentrations at one-hour post WBC exposure compared to the control. It was proposed that the cold stress from WBC treatment may have stimulated β-adrenoreceptors that synthesize IL-1ra, which in turn balances and moderates the synthesis of IL-1β. This potentially affects the magnitude of CRP circulating due to a dampened inflammatory response and faster repair of damaged muscle cells [26].

Similarly, Mila-Kierzenkowska [20] found an anti-inflammatory effect of WBC. When subjects were exposed to one WBC treatment before exercise, there was a stunted increase in IL-1β compared to the control condition. In the control trial, the concentration of this pro-inflammatory interleukin increased more than six times than when treated with WBC. It was also found within this study that while concentrations of IL-6 increased from baseline in the control condition after exercise, a drop of 11 % in IL-6 concentration was observed within the WBC condition, indicating that treatment blunted the inflammatory response and possibly reduced muscle damage. It should be considered that this study, as with the Pournot [26] trial, was executed as a randomized crossover trial with a two- and three-week washout periods respectively. In these cases, the repeated bout effect may confound results as it has been evidenced that after an initial bout of damaging exercise, a subsequent bout within six weeks will not produce as much tissue damage [19] and results in a smaller inflammatory response.

▶ **Table 3** Articles retrieved as assessed on the Downs & Black quality analysis tool.

Type of Study	Author	Year	Reporting[$]										External Validity[*]			Internal Validity														Power	Score
																Bias[α]							Confounding[ß]								
		Items	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	27
Lab Control Studies	Hausswirth et al.[15]	2011	1	1	1	1	1	1	1	1	1	0	0	0	X	X	0	1	1	1	1	1	1	0[#]	1	0[#]	0[#]	1	1	18
	Poumot et al.[26]	2011	1	1	1	1	1	1	1	1	1	0	0	0	X	X	0	1	1	1	1	1	1	0[#]	1	0[#]	0[#]	1	1	18
	Costello et al.[7]	2012	1	1	1	1	0	1	1	1	1	1	1	1	X	X	0	1	1	1	1	1	1	0[#]	1	1	0[#]	1	1	21
	Fonda et al.[14]	2013	1	1	1	1	0	1	1	0	1	1	0	0	X	X	0	1	1	1	1	1	1	0[#]	1	0[#]	0[#]	1	1	17
	Mila-Kierzenkwoska et al.[20]	2013	1	1	1	1	1	1	1	1	1	0	0	0	X	X	0	1	1	1	1	1	1	1	1	0[#]	0[#]	1	1	19
	Ferreira-Junior et al.[13]	2014	1	1	1	1	1	1	1	1	1	1	0	0	X	X	0	1	1	1	1	1	1	0[#]	1	0[#]	0[#]	1	1	19
	Ziem ann et al.[32]	2014	1	1	1	1	1	1	1	1	1	1	0	0	X	X	0	1	1	1	1	1	1	0[#]	1	0[#]	0[#]	1	1	19
	Ferreira-Junior et al.[12]	2015	1	1	1	1	1	1	1	1	1	1	0	0	X	X	0	1	1	1	1	1	1	0[#]	1	0[#]	0[#]	1	1	19
	Viera et al.[29]	2015	1	1	1	1	1	1	1	1	1	1	0	0	X	X	0	1	1	1	1	1	1	0[#]	1	0[#]	0[#]	1	1	19
	Krüger et al.[17]	2015	1	1	1	1	1	1	1	1	1	1	0	0	X	X	0	1	1	1	1	1	1	0[#]	1	0[#]	0[#]	1	1	19
Applied Studies	Wozniak et al.[31]	2007	1	1	1	1	1	1	1	1	1	0	0	0	X	X	0	1	1	1	1	1	1	1	1	0[#]	0[#]	1	1	19
	Banfi et al.[2]	2009	1	1	1	1	0	1	1	0	1	0	1	1	X	X	0	1	1	1	1	1	1	1	1	1	0[#]	1	1	20
	Mila-Kierzenkwoska et al.[21]	2011	1	1	1	1	1	1	1	1	1	0	0	0	X	X	0	1	1	1	1	1	1	1	1	1	0[#]	1	1	20
	Ziem ann et al.[33]	2012	1	1	1	1	1	1	1	1	1	1	0	0	X	X	0	1	1	1	1	1	1	1	1	0[#]	0[#]	1	1	20
	Wozniak et al.[30]	2013	1	1	1	1	1	1	1	1	1	0	0	0	X	X	0	1	1	1	1	1	1	1	1	0[#]	0[#]	1	1	19
	Schaal et al.[27]	2013	1	1	1	1	1	1	1	1	1	0	0	0	X	X	0	1	1	1	1	1	1	1	1	0[#]	0[#]	1	1	19

See ▶ **Table 2** for corresponding item descriptions. 1, criteria met; 0, criteria not met; [#], unable to determine if criteria met and scored 0; X, not applicable; [$], Reporting category includes items such as study aims, reported outcomes, patient characteristics, confounders, adverse events and loss to follow-up; [*], external validity includes items regarding study population; [α], bias internal validity includes items such as blinding, follow-up and compliance; [β], confounding internal validity includes items such as study selection, randomization and study power.



▶ **Fig. 2** CK, creatine kinase; **lab**, studies with laboratory controlled exercise or training stimulus; applied, studies with non-laboratory controlled exercise or training stimulus; -, negative effect; +, positive effect; N no significant effect.

Ziemann [32] found WBC increased the concentration of the anti-inflammatory cytokine IL-10 to twice that of baseline where no change was seen in the control group. In conjunction with this, IL-1β concentrations dropped by 80 % in the WBC group where control subjects only presented a drop of 50 % [32]. These consistent results suggest that WBC may influence the pathways of inflammatory modulation, which may indicate a propensity for this treatment to prevent detrimental overexpression of inflammatory proteins.

Applied studies

All of the included studies that used an applied exercise protocol applied more than one WBC treatment, with 15 exposures on average across the six studies. The four studies that treated participants to WBC less than the average of 15, all reported enhanced recovery in inflammatory and muscle damage markers, as well as for athletic performance. WBC was administered more than 15 times in two studies, one of which found no significant results and another that found positive results in inflammatory and damage markers. Interestingly, for applied training studies, none measured pain and only two investigated performance markers, both of which improved with the inclusion of WBC.

Only two of the applied studies investigated functional or athletic skill recovery after exercise, and both studies found an improvement in performance with WBC. Ziemann [33] studied a group of tennis players over a five-day training program, exposing players to WBC every day. When exposed to WBC, players reached fatigue significantly later during a progressively more difficult tennis drill. They also found the WBC group experienced a 7.3 % increase in stroke effectiveness during a tennis skill game that became progressively more difficult where the control group only increased by 2.6 % [33]. Synchronized swimmers were exposed to WBC each day during a period of intensified training and found that a 400 m time trial swim speed was only 0.5 % slower after WBC compared to a 1.1 % time reduction without treatment. A smaller amount of damage after exercise with WBC may explain the improved performance in these treatment conditions, as was seen with a reduced CK concentration in tennis players within Ziemann et al.'s study [27].

Five of the six applied studies measured CK as a marker of muscle damage, four of which found that WBC significantly lowered circulating CK levels amongst athletes during a regular training period [2, 30, 31, 33]. Wozniak [31] reported that CK concentrations were 34 % lower with the inclusion of WBC treatment six days into a training protocol compared to the concentration of CK without treatment. A subsequent study conducted by Wozniak [30] observed a group of rowers exposed to WBC twice daily over a six-day training period. Significant changes from baseline CK concentrations were found across both control and treatment conditions, yet without WBC treatment these athletes expressed a 31 % larger increase in CK than with WBC [30]. These results were supported by an additional study reporting that daily exposure to WBC over a five-day training program with elite rugby players reduced CK by 40 % [2]. Another group found WBC treatment significantly reduced CK in tennis players where concentrations of this muscle enzyme in the control group remained virtually the same after five days of training [33]. Only one of the studies that measured CK found no significant difference in concentrations after ten days of training with three exposures each day [21].

Ziemann [33], one of four studies that tracked cortisol, was the only study that found the cryotherapy group showed an increase in cortisol levels. This is in contrast to two other studies that found a reduced concentration of the hormone in participants exposed to WBC [30, 31]. Mila-Kierzenkowska [21] found no significant effect of WBC treatment on salivary cortisol concentration. The cumulative effect of cortisol as part of the stress response to exercise is difficult to compare across studies due to its sensitivity to time of day, caffeine and exercise. As such, studies investigating this variable often measured it at the same time of day, with fasting and no exercise, except for that prescribed within the study [33]. Even slight methodological variations in the timing of taking samples can produce vastly different concentrations. Care must be taken in comparing these results and also to replicate protocols for sampling this variable in future studies.

Two of the six applied studies reported significant effects in concentrations of circulating cytokines with WBC. Banfi [2] found that during seven days of typical training combined with exposure to WBC on each of these days, there was a significant increase of 11 % in the anti-inflammatory cytokine IL-10. Ziemann [33] found that a five-day training protocol combined with WBC induced a decrease in TNF-α of 60 %, yet also induced a 23 % increase in IL-6 concentration. The intensity and duration of the exercise prescribed in the

study may account for the increase in the cytokine IL-6 concentration. The concomitant decrease in inflammatory marker TNF-α could either be a natural return to homeostasis after the exercise bout, or a result of IL-6 stimulating an anti-inflammatory response, thus limiting TNF-α production [33]. The sensitivity of cytokine profile changes in participants across these studies seems specific to both the baseline status of these variables and also to the type and amount of control over the exercise stimulus. To ensure reproducible and comparable results in future trials regarding cytokine activity, it will be necessary to ensure that exercise and health status prior to the beginning of the study are controlled and screened for.

Limitations and future research

The lack of ability to blind for recovery treatment in this research makes it impossible to eliminate the potential placebo effect, as highlighted from the application of the Downs and Black quality analysis tool in ▶ **Table 3**. Study designs within the articles retrieved were vastly different, making inferences across studies difficult. There was inconsistency in the exercise damage protocols used which results in differences between studies in the magnitude and nature of damage to skeletal muscle tissue. Furthermore, analysis of muscle function parameters were inconsistent, making assumptions of the effect of WBC on muscle function difficult to confirm. This is a result of studies choosing either to investigate sport-specific parameters, such as vertical jump height [29], VO2 aerobic capacity, or other performance markers such as shot accuracy during a tennis drill [33], or more controlled markers of performance such as maximal voluntary contractions [15]. This is combined with a lack of standardized treatment protocols with regard to temperature ranges, timing and frequency of exposure to WBC, which is likely to elicit different responses of recovery to the therapy.

The effectiveness of WBC as a recovery method should be explored to validate its use when an athlete's pain levels and magnitude of cellular muscle damage impede exercise. A greater understanding of the role and time course changes of pain and immune function in the recovery from micro-trauma in muscle cells may be required to fully understand the responses to exercise and this treatment. Further investigation into the effects of multiple WBC exposures during extended periods of athletic training is warranted to determine potential effects on recovery, performance and processes of muscle adaptation. Future studies will require larger sample sizes to determine the significance of immunological changes and stringent methodological control to identify the exact influence of WBC on these pathways.

Conclusion

Overall, studies indicate that within both laboratory-controlled and applied settings, WBC may be successful in enhancing MVC and returning athletes to pre-exercise strength at a faster rate than control conditions. With WBC treatment conditions recording pain scores on average 31 % lower than control, evidence tends to favor WBC as an analgesic treatment after damaging exercise. Nevertheless, further investigation of pain in a practical athletic setting is needed. Data from inflammatory markers, as well as CK, and cortisol concentrations indicate with reasonable consistency that WBC may dampen the inflammatory cytokine response, which may suggest less secondary tissue damage in the regeneration process, thus accelerating recovery.

Practical applications based on the evidence presented suggest a positive dose-response relationship between WBC exposures after exercise with the recovery of some muscle damage indicators. Multiple exposures of three or more sessions of three minutes conducted immediately after and in the two to three days post exercise have presented the most consistent results with little to no difference seen in temperatures colder than the average of − 140 °C. Further controlled studies, including a more strategic approach to study design, are essential to conclusively determine the impact of time course effects from WBC on muscle recovery after mechanical overload in athletic populations.

Conflict of Interest

The authors have no conflict of interest to declare.

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