Effects of cryotherapy on inflammation, enhancing exercise recovery and improving performance

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EXPH 496: Senior Thesis Capstone Course

Spring 2018

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INTRODUCTION:

Athletes today are competing at a higher level than ever. This increase in competitive nature drives athletes to extreme efforts in performance and recovery methods. Such athletes, and non-athletes alike, have found cryotherapy to be a useful treatment in improving their level of fitness. Cryotherapy, in a broader sense, is defined as cold exposure below 10°C (22). More specifically, cryotherapy methods include ice cold compression, which is used by compressing an ice pack or other cooling device directly on a targeted area. Another method is in the form of cold water immersion. An example of this method is ice baths, in which an individual is partially submerged in ice water. Typically, an individual submerges in the ice bath for ten to twenty minutes at temperatures of 12-15°C (4). The last method described is nitrogenous cryotherapy, which involves the use of liquid nitrogen to create extreme cooling temperatures. This includes partial-body cryotherapy (PBC) and whole-body-cryotherapy (WBC).

PBC is a direct form of nitrogenous cryotherapy that is isolated to a specific part of the body, and ranges to temperatures of -60- -160°C for a duration of time (6). WBC is treated throughout the entire body at temperatures of -110- -140°C in a 1-4-minute session (1,6). WBC will be analyzed as it is the most invasive method, yet most under researched type of therapy. Additionally, WBC is becoming more widely used to enhance recovery performance and reduce inflammation (3,22). Thus, for the purpose of this review, the term "cryotherapy" shall be interpreted and discussed as WBC.

Methods of cold exposure have been practiced since ancient Greece for enhancing recovery and performance (3). Cryotherapy is widely used as a treatment for muscle relief and injury treatment. It was not until the 1970s, when the first WBC chamber was constructed in Japan (3). It later became widely used in the United States in the 1980s (3). Though cryotherapy

practices are becoming vastly more popular, its research has been lacking in the sports medicine field. Therefore, the effects of cryotherapy shall be analyzed to determine its effectiveness in recovery, rehabilitation, and performance modalities.

SIGNIFIGANCE OF THE PROBLEM:

Athletes often engage in one or more physically demanding workouts per day. In some sports, such as basketball or baseball, games can be held 3-4 times in one week. This gives minimal time for athletes' bodies to recover fully, which can impact their level of performance. Additionally, inadequate recovery can increase an athlete's risk of injury and infection. In non-athletes looking to increase their level of fitness, recovery methods are just as important in maintaining good health. Regardless of circumstances, an injury is bound to occur in one's life. Injuries disable a person to perform and can leave them sedentary for an extended period of time. In athletes, injuries can not only damage their career, but also take a toll on the number of years they can play the given sport. As such, it is critical for such athletes to be able to return to their level of play in a timely manner while preventing further risk of injury.

Cryotherapy has been used widely to enhance recovery, relieve muscle soreness, and treat injuries. However, over the past years cryotherapy has become more recognized as a therapeutic alternative world-wide. According to Grand View Research, the global cryotherapy market was reported to be $2.5 billion in 2015 with a projection of $5.5 billion by 2024. Athletes and other performers alike used these methods to improve recovery and increase endurance, however the market has much expanded. Cryotherapy has found interest in the clinical setting and is being used to treat several diseases such as arthritis, multiple sclerosis, fibromyalgia, dementia, and even cancer (3,26).

REVIEW OF LITERATURE:

Acute Effects Post-Exercise

During exercise, energy demands increase readily. Heart rate and blood pressure increase to pump blood throughout the body, providing ample amounts of oxygen to the muscle cells (30). As workload increases, the demand for oxygen increases (24,30). As a result, the body becomes depleted of most of its oxygen and energy capacity post-exercise. Muscle oxygenation is needed to increase after exercise to replenish energy loss and to repair the damaged muscle tissues (18,24,30). Glycolysis, the metabolic process of converting glucose to energy, is the primary source of ATP synthesis during short duration exercise bouts. Intense exercise rapidly depletes ATP reserves, and muscles begin to fatigue and become damaged post-exercise. As a result, the body must replenish and repair muscle fibers in order for them to properly heal and function (13,30).

Exertion of strenuous physical activity, whether in athletes or non-athletes, causes a buildup of lactic acid in muscle tissues (1,6,9,12,13,22,28). Lactic acid is generated through the anaerobic process of glycolysis and is a known inducer of delayed onset muscle soreness (30). Consequently, lactate levels rise with greater exercise intensities as the body's demand for energy increases (23,30). If an athlete has the perception of severe muscle soreness from strenuous training, they are likely not able to perform to optimum standards. Athletes, with their competitive edge, look for any possible tactic to improve their body's ability to perform. A study found that a single session of cryotherapy decreased lactate levels by 66.7% (11), whereas other studies have found decreased lactate levels but in lesser amounts (9,12). Krüger et al. found lactate to be 25% less than its control (22). Some studies have found lactate levels to be higher

with cryotherapy sessions, however levels of perceived muscle soreness were lower than in subjects where cryotherapy was not performed (9,13).

Additionally, intense physical training induces muscle damage. Adequate recovery time is required for such individuals, allowing the muscle tissues to heal and restore properly for the next bout of training. WBC has been integrated as a potential recovery method for reducing the recovery time post-exercise while also alleviating the symptoms of muscle soreness (1,2,3,22). According to Banfi et al., five WBC sessions decreases create kinase and lactate dehydrogenase, which are enzymes known to cause muscle damage (2). Additionally, decreases in lactate dehydrogenase also supports the decreased lactate levels (2).

Furthermore, strenuous exercise enhances oxygen consumption and absorption in muscle tissues. During the post-exercise recovery period, oxygen utilization increases for muscle tissue repair. Selfe et al. analyzed the effects of cryotherapy on fourteen elite rugby players who were competing mid-season (assuming some level of muscle damage) (27). The players showed significant reduction in tissue oxygenation followed by a significant increase five, ten, and/or fifteen minutes post-cryotherapy (27). Cold exposure causes rapid vasoconstriction of the arteries followed by rapid vasodilation (12,27,32). Though the process behind this physiological process remains relatively unknown, it can be suggested that rapid change in blood flow is attributed to the body's ability to diffuse oxygen (18).

Muscle damage can also be explained through the measure of blood parameters (12). The catabolic effect of muscle damage causes the release of an inflammatory pathway (11,12). The acute effects of exercise raise the stress response, causing a rise in cytokines, tumor necrosis factor-α (TNF- α), and interleukin's (28).

Cytokines. Cytokines are a crucial signaling protein that is required in the inflammatory response. Cytokines can include tumor necrosis factor- α (TNF-α), interleukins (IL-1β, IL-6, IL-12, IL-17), and various chemokines (23,28). Strenuous exercise induces the release of these pro-inflammatory cytokines and strongly correlates with exercise intensity (28). It also increases circulating cytokines, which also have a direct effect on the level of perceived soreness. Levels of interleukins can be elevated for several hours after long duration physical activity, whereas with shorter bouts of exercise they are elevated in lesser amounts. Moreover, the post-exercise inflammatory response leads to repression of lymphocyte and the activation of neutrophils and macrophages (28). Exercise stress increases levels of IL-6, which enhances the utilization of ATP and other energy substrates (23). These changes have significant impact on exercise endurance and recovery.

Cold exposure is a method to reduce immunity and decrease inflammation. WBC sessions have been linked to decreases in pro-inflammatory cytokine IL-2 and increases in anti-inflammatory cytokine IL-10 (7,23,27). Cryotherapy also has been found to decrease levels of IL-8 and prostaglandin E2 (PGE2), which play a strong role in the pro-inflammatory process (7,23). Crystal et al. found that TNF-α increased with sessions of WBC, despite its known anti-inflammatory effects (9).

Immunological Effects. Strenuous exercise suppresses immunity (7,9,28). Intense physical activity can blunt the immune system up to two hours post exercise (9,13). In long duration, vigorous activities, such as in marathons, the immune system can be compromised up to 24-hour post-event (30). A compromised immune system leaves an individual at an increased risk for infection (24,28). As such, endurance athletes have a much higher rate of upper respiratory tract infections than non-endurance athletes (30). The immune system is comprised of

various specialized cell types, including lymphocytes and NK cells. These cells are controlled by chemokines, and when elevated, activate immunosuppression (28). Cryotherapy has been found to decrease levels of IL-B and increase NK and lymphocyte count. In addition, white blood cell count increases with cryotherapy (12,23). White blood cells function as immune cells and play a role in fighting infectious disease.

Hormones. Hormones play an intriguing role in the immune system. The adrenal glands are a necessary component of metabolic function and are involved in the release of several types of hormones (21). The hormones can include estrogen, progesterone, and testosterone. An imbalance in these hormones can lead to immunosuppression and increase levels of stress hormones, such as cortisol (17,21). Intense, repetitive physical exercise can have a negative effect on these hormone levels. Grasso et al. found cryotherapy to cause significant reductions in cortisol levels in a group of elite rugby players (17). Furthermore, increases in testosterone and reductions in estradiol were measured (17). Having an imbalance between the levels of testosterone and estrogen, known as the T/E ratio, can cause immunosuppression and impair the exercise recovery process (21). A study found to increase the T/E ratio, suggesting an increase in anabolic stimulus and immune support (17,21). These changes in blood parameters are largely determined by the rapid physiological temperature change that occurs in the body from the immediate cold-exposure of cryotherapy.

Effects on Body Temperature

Multiple studies have shown that the drastic change in core body temperature from cryotherapy improves recovery and enhances endurance performance. In a study testing the impact of WBC in endurance athletes, it was found that the average individual's core body temperature dropped to an average of 17.8°C (30). Another study found that a -110°C (3 min)

cryotherapy session prior to high intensity endurance performance in a hot environment (27-34°C) displayed ~12% less muscle fatigue, lower VO2, lower HR, and lower RPE (22). Additionally, their core body temperature continuously declined one hour after the session, suggesting continuous improvements for longer duration endurance activities (22). Other studies have shown cryotherapy to improve VO2, SV, and cardiac output, all of which could improve performance (9).

Changes in core temperature are minimal due to the vasodilation effect to keep vital organs at a constant temperature (27). Moreover, changes in skin temperature occur more readily and can provide better readings for significance of cryotherapy sessions (7,8,27). It has been widely accepted that in order to reach the analgesic effects of cryotherapy, a skin temperature of 13°C must be reached (7). To reach the desired skin temperature, the temperature and time duration settings for cryotherapy sessions must be properly established. WBC temperatures can range from -110°C to -140°C. In addition, the duration of sessions can vary from one to three minutes (1,2). A longer time duration and cooler temperature causes more significant reductions in body temperature, and such can have more pronounced physiological effects (27).

Selfe et al. found that timing (1-3 minutes) had significant changes in hemoglobin levels and concluded that cryotherapy at -135°C for 3 minutes yielded the best recovery method in professional rugby players (27). At this temperature and duration, skin temperatures reached 15°C (27). In the same study at two and one-minute durations, skin temperatures reached 17°C and 22°C, respectively (27). Other studies have shown positive improvements in cryotherapy at a 3-minute duration (1,6,7,8,22).

Rehabilitation of Injury

The frequent intense bouts of training athletes endure can be very damaging to the body. It comes as no surprise that athletes are at much higher risk of musculoskeletal injuries. When an athlete undergoes an injury, it is crucial for that athlete to rehabilitate as quickly as possible so that the athlete can return to their level of play. Studies have shown that athletes have shown a decrease in muscle swelling following sessions of WBC (11,22,23,27,28). Such instances could have occurred through the known anti-inflammatory effects of cryotherapy (9). Additionally, the cold immersion results in decreased tissue temperature, which enhances blood flow through muscular tissues and reduces swelling (12).

Sessions of local cryotherapy caused a significant drop in lactate and histamine concentrations at the site of injury, leading to decreases in inflammation and improvements in muscle strength, flexibility, and functionality in patients with degenerative lumbar spines (16). These patients experienced long-term improvements in lumbar mobility as well as decreased levels of pain (16). The rapid drop in tissue temperature caused a release of beta-endorphins, which promote feelings of euphoria and calmness (5,16,26). A study of 102 participants showed that 57% of its participants concluded cryotherapy as a direct cause of their improvement from injury and reported feelings of mental clarity and decreased levels of pain (11).

In addition to recovering from training, athletes will participate in various methods which will prevent possible injury. Postural stability plays an important role in the dynamic movement of a functional athlete (14,15). Some studies have shown a decrease in ankle stability immediately following bouts of cryotherapy (25). However, other studies found that the short and long-term use of cryotherapy resulted in significant improvements in stability and functionality in individuals recovering from post-knee surgery (20). A group of elite athletes

found significant increases in both anterior post-lateral and posterior-medial flexibility in the ankles following cryotherapy (14). Such improvements lead to greater sagittal plane movements in the ankle, knee, and hip (14). Even in studies showing decreases in stability did not find any changes in performance or muscle functionality (25). To get a better understanding of how cryotherapy affects muscle functionality, the acute effects of range of motion shall be described.

Improving Range of Motion

Range of Motion is a critical component in healing injury, preventing injury, and improving performance. Traditional cryotherapy methods, such as cold compression therapy, are known to cause muscle tightness (4,25). However, such indications differ with WBC (16). During sessions at -150°C, muscle tissue can fall more than 10°C from their baseline temperature (5). This rapid change in temperature during a two to three-minute session activates a variety of sympathetic nervous system activations, causing elongation of muscle fibers. Cryotherapy has been found to increase the sit and reach aptitude range of motion by two centimeters in both men and women (10). In one study, patients receiving therapeutic sessions through WBC experienced significant improvements in spinal mobility (16). Patients who received WBC five days per week showed significant improvements in the mobility of the erector spinae muscle, leading to improvements in overall muscle functionality. Similar studies have also shown improvements in elderly people (16).

Muscle functionality can also be measured by peak torque of muscle fibers. A stronger torque can be interpreted as a stronger, more functional muscle (15). Improvements in range of motion also improves muscle torque (11,13). Ferreira-Junior et al. found that athletes were able to maintain higher rates of peak eccentric muscle torque following repetitive bouts of intense exercise after sessions of WBC (13). No differences were found with concentric movements

(13). Muscle torque changes between exercise bouts can also measure the adaptive responses to recovery (6). The effects of cryotherapy also favor eccentric muscle forces 24 to 72 hours post-exercise, suggesting improvements in muscle recovery and adaptive responses to exercise (1,6,15).

Though cryotherapy seems to improve eccentric functionality, there are conflicting studies showing cryotherapy induces additional muscle stiffness. Point et al. found that the *gastrocnemius medialis* muscle became stiffer following bouts of cryotherapy (25). However, in this study, cold-compression therapy was used, as opposed to the WBC method from which other studies found decreases in muscle stiffness (25). Also, participants of the study rested for twenty minutes post cold compression prior to being tested (25). The study assumed this would give adequate time for the muscle to return to its basal temperature; however, studies show that muscle tissue temperatures remain decreased for up to 60 minutes post-therapy (7,8,18). Muscle tissues falling below 10°C undergo homeostatic regulation, involving tensing of the fibers to trap heat and lessen its surface area. As basal temperature increase, muscle fibers begin to relax and become more functional (11,14,23).

Acute Effects on Cardiovascular System

The sympathetic activation caused by cryotherapy raises questions as to how it affects the cardiovascular system. Under the presence of cryotherapy, the nervous system rises in sympathetic activation, causing an increase in cardiovascular function (32). Exercise endurance can be measured by one's cardiac output. The cardiovascular system is the framework from which an athlete performs.

Cryotherapy causes vasoconstriction of the skin vessels followed by rapid vasodilation, causing an increase in blood flow (12,31,32). This sudden change causes changes in blood

parameters. Red blood cell count (RBC), hemoglobin concentrations (HGB], hematocrit percentages (HCT %), white blood cell count (WBC), and platelet concentrations (PLT) are all increased after ten WBC sessions in both men and women (12).

Short and long-term use of cryotherapy has been shown to decrease levels of C-reactive proteins (CRP) in the blood (12,31,32). CRP is an acute inflammatory marker and is often used to measure the presence of inflammation. Studies have shown that elevated CRP levels induce an increased risk for diabetes, hypertension, and cardiovascular disease (3,19,31,32). Kang et al. found that in three weeks, CRP levels decreased from 3.5 mg/dl to 0.5 mg/dl in response to cryotherapy (19). In another study conducted by Kang described patients undergoing shoulder reconstruction. CRP levels decreased from 0.45 mg/dl to 0.37 mg/dl from just one session of cryotherapy (20).

Testing CRP levels in patients with cardiovascular disease is rather discouraged, as the sympathetic activation from cryotherapy could cause severe adverse effects (31,32). Moreover, studies have tested its safeness in patients with hypertension (31,32). Following a WBC session, the hypertensive group measured a slightly lower HR (66 bpm to 63.7 bpm), slightly lowered BP (138.5/87.9 to 133.2/85.2), improved stroke volume (107.4 ml to 110.4 ml), and cardiac output remained about the same (6.9 l/min to 6.8 l/min) (31).

SUMMARY AND CONCLUSION

Both athletes and non-athletes alike look for ways to enhance recovery and improve performance. Cryotherapy has been used to relieve symptoms of muscle soreness, improve recovery between exercise bouts, and reduce inflammation from injury. Though this method has been widely used, the physiological effects of WBC have been unknown, and therefore its effectiveness as a therapeutic modality have remained largely unknown.

WBC has been found to reduce the amount of lactic acid buildup in muscle tissues by 66% (11). Since lactic acid is produced as a result from strenuous physical activity, it is also associated with muscle soreness (9,13,22). In addition to reductions in lactate, cryotherapy reduces the perception of muscle soreness in some individuals (4,23,24,27). Multiple sessions of WBC have found decreases in muscle damaging enzymes, such as lactate dehydrogenase and creatine kinases (2). These enzymes are involved in the inflammatory response, and these responses are supported by the anti-inflammatory effect of cryotherapy (2). Cryotherapy increases levels of anti-inflammatory cytokines, including IL-6 and IL-10, and decreases pro-inflammatory cytokines', IL-2, prostaglandin 2 (PGE2) and various chemokines (23).

The anti-inflammatory effect of cryotherapy is supported in the rehabilitation process. Studies have shown that the rapid drop in temperature causes the release of beta-endorphins, which provide feelings of pain relief (5,16,26). Though the physiologic effects of endorphin releases from cryotherapy are still unknown and rather unpredictable, it has been found to reduce symptoms of muscle soreness and pain associated with injury (26).

Cryotherapy has shown to improve flexibility in the ankle, knee, hip, and lumbar regions. Improvements have taken form in greater ankle stability, eccentric knee torque, and spine and hip mobility (5,10,14,16,20). These improvements can suggest that cryotherapy can be used in a rehabilitation setting to improve an individual's mobility.

The effects of cryotherapy on cardiovascular health seem to be beneficial, as it reduces CRP levels, from which chronic elevations can have damaging effects on the heart (19,20). Cryotherapy appears to be safe in individuals with hypertension; however, special precautions shall be accounted for and is not recommended in individuals with severe cardiovascular disease (31,32).

Cryotherapy appears to have a positive effect on the physiological systems of the body from the firing of the nervous system caused by rapid change in body temperature (7,8). This stimulation increases blood flow and activates the pro-inflammatory pathway system, changing the blood parameters to an anti-inflammatory state (12). Additionally, endorphins are released, providing feelings of comfort and happiness (5,12). The enhanced blood flow also improves oxygenation, which increases ATP synthesis and muscle rehabilitation (18). The increased circulation around muscle fibers allows them to rebuild and store energy at a faster rate. The movements around the joints also appears to improve, resulting in greater range of motion, stability, and functionality.

It was hypothesized that WBC would have positive anti-inflammatory effects, which would enhance recovery from performance and injury. It is to conclude that WBC has an anti-inflammatory effect and can be used to enhance recovery from intense exercise. Cryotherapy can also be used to improve range of motion and reduce feelings of pain in individuals suffering from an injury. It cannot be concluded that cryotherapy has a direct effect on exercise performance. However, cryotherapy does appear to reduce muscle soreness, inflammation, and muscle damage in between bouts of exercise. Through these pathways, it can be suggested that cryotherapy can have an impact on exercise performance.

FUTURE RESEARCH

There needs to be significantly more research on the uses of cryotherapy to conclude and further understand its effects. Though the anti-inflammatory effects of cryotherapy are concise and well recognized, the physiologic basis from which this occurs is relatively unknown. Much research alludes the anti-inflammation improves are related to the rapid change in body temperature, however, such studies have not provided an accurate mechanism behind its basis.

Additionally, more research on hormones shall be proceeded. The current studies show that hormone levels may be affected with cryotherapy, and some levels of hormones may actually decrease with cryotherapy. This research needs to be better understood as the implications of hormonal changes can become quite enhancing or catastrophic in some individuals.

Out of all the studies analyzed, the average participant population has been quite low; averaging about 12-30 participants in each study. The only large-participant study was done by Derewuecki et al, in which 102 participants were used (11). A larger population size for future studies could provide more accurate results and the data could be better interpreted. Larger studies could also lead to a stronger consensus of certain outcomes. Furthermore, a larger group of participants would better promote to overall message of cryotherapy and its significance could be more well-known across researchers and health professionals alike.

These studies around cryotherapy have only involved the acute effects of its uses and have not taken into account the chronic implications of regular cryotherapy use. Cryotherapy has shown improvements in individuals endurance capacities from improved VO2, cardiac output, and oxygen diffusion (9,18). In these studies, however, the chronic implications of cryotherapy and endurance has yet to be analyzed. Though the acute effects do need to be better understood, its chronic effects could show more significant physiologic changes. It is hypothesized that the body will adapt to the repetitive, chronic nature of cold exposure and develop a significantly higher level of anti-inflammatory cytokines with stably low levels of pro-inflammatory compounds. The significance of these findings could be drastic, as almost every chronic disease is caused by chronic high levels of inflammation.

Cryotherapy is being introduced in the clinical setting to treat diseases such as arthritis, dementia, and cancer (3,25). There is research showing benefits of cryotherapy in individuals

with arthritis, and various clinics are having success in treating such patients using cryotherapy methods (3). The treatment of arthritis through cryotherapy is likely due to anti-inflammatory effects (3). Studies also show cryotherapy also reduces inflammatory collagenase enzymes, which break down collagen fibers, and are highly present in individuals with arthritis (3). Though the cause of dementia is not fully understood, the disease is prevalent with high amounts of inflammatory compounds in the brain, leading to permanent degeneration (3,25). Cryotherapy has been introduced to treat such individuals with early onset Alzheimer's and dementia, and some success has been shown (25). However, for these implications to be used as a viable treatment option, further research is needed.

Perhaps the most researched methodology of cryotherapy in a clinical setting is in the treatment of cancer. Several clinics currently offer cryotherapy treatments to eliminate benign tumors (3). The extremely cold temperatures of cryotherapy have been found to freeze the mass growths, kill the cancer cells, and prevent them from replicating. Cryosurgery, a surgical method crafted through the science of cryotherapy, has been used to treat the early progressions of prostate cancer (3). Cryosurgery has been used as a noninvasive treatment method and is also being used in other types of cancer. With further research and enhancement of its procedures, cryotherapy could be used as a method of treatment for several chronic diseases.

REFERENCES

1. Abaida AE, et al. Recovery from exercise-induced muscle damage: cold water immersion versus whole-body cryotherapy. *International Journal of Sports Physiology and Performance.* 2013;12(3).
2. Banfi G, Lombardi G, Colombini A, Melegati G. Whole-body cryotherapy in athletes. *Sports Med.* 2010;40(6):509-17.

3. Bouzignon R, Grappe F, Ravier G, Dugue B. Whole-and partial body cryostimulation/cryotherapy: current technologies and practical applications. *Journal of Thermal Biology.* 2016;61:67-81.
4. Chan YY, Yim YM, Bercades D, Cheng TT, Ngo KL, Lo KK. Comparison of different cryotherapy recovery methods in elite junior cyclists. *Asia-Pacific Jour Sport Med.* 2016;5:17-23.
5. Ciosek Z, et al. The influence of kinesiology taping method in conjunction with local cryotherapy on the range of motion and low-back pain in patients with degenerative disease of the lumbar spine. *Fizjoterapia Polska.* 2017;17(2):36-46.
6. Costello JT, Algar LA, Donnelly AE. Effects of whole-body cryotherapy (− 110°C) on proprioception and indices of muscle damage. *Scand J Med Sci Sports.* 2011;22(2):190-8.
7. Costello JT, Culligan K, Selfe J, Donnelly AE. Muscle, skin and core temperature after -110 °C cold air and 8°C water treatment. *PLoS One.* 2012;7(11):e48190.
8. Costello JT, Donnelly AE, Karki A, Selfe J. Effects of whole-body cryotherapy and cold water immersion on knee skin temperature. *Intern J Sport Med.* 2013;35(1).
9. Crystal NJ, Townson DH, Cook S, Laroche DP. Effect of cryotherapy on muscle recovery and inflammation following a bout of damaging exercise. *Arbeitsphysiologie.* 2013;113(10).
10. De Nardi M, La Torre A, Benis R, Sarabon N, Fonda B. Acute effects of whole-body cryotherapy on sit-and-reach amplitude in women and men. *Cryobiology.* 2015;71(3):1-3.
11. Derewiecki T, Mroczek, Duda M, Majcher P. The importance of cryotherapy in rehabilitation. *Zdrowie publiczne / Polskie Towarzystwo Higjeniczne.* 2013;123(2):161-171.

12. Dybek T, Szygula R, Kilmek A, Tubek S. Impact of 10 sessions of whole body cryostimulation on aerobic and anaerobic capacity and on selected blood count parameters. *Biol Sport.* 2012;29:39-43.
13. Ferreira-Junior J, et al. Effects of partial-body cryotherapy (− 110°C) on muscle recovery between high-intensity exercise bouts. *Inter Jour Sport Med.* 2014;35(14):1155-1160.
14. Fullam K, Caulfield B, Coughlan GF, Delahunt E. The effect of cryotherapy application to the ankle joint on dynamic postural stability in an elite athletic population. *British J Sport Med.* 2014;48(7):596.
15. Furmanek MP, Slomka K, Juras G. The effects of cryotherapy on proprioception system. *BioMed Research International.* 2014;2014(2014): 1-14.
16. Giemza C, Matczak-Giemza M, De Nardi M, Ostrowska B, Czech P. Effect of frequent WBC treatments on the back pain therapy in elderly men. *The Aging Male.* 2014;18(3).
17. Grasso D, et al. Salivary hormone response to whole-body cryotherapy in elite rugby players. *International journal of immunopathology and pharmacology.* 2014;28(2):291-300.
18. Jurecka A, et al. Whole-body cryostimulation in kayaker women: a study of the effect of cryogenic temperatures on oxidative stress after the exercise. *J Sports Med Phys Fitness.* 2009;49(2):201-7.
19. Kang JI, Jeong DK, Choi H. Effects of microcurrent and cryotherapy on C-reactive protein levels and muscle tone of patients with rotator cuff reconstruction. *J Phys Ther Sci.* 2018;30:37-41.
20. Kang JI, Kim YN, Choi H. Effects of low-intensity pulsed ultrasound and cryotherapy on recovery of joint function and c-reactive protein levels in patients after total knee replacement surgery. *J Phys Ther Sci.* 2014;26:1033-1036.

21. Korzonek-Szlacheta I, Wielkoszynski T, Stanek A, Swietochowska E, Karpe J, Sieron A. Effect of whole-body cryotherapy on the levels of some hormones in professional soccer players. *Endokrynologia Polska.* 2007;58(1):27-32.
22. Krüger M, de Mareés M, Dittmar KH, Sperlich B, Mester J. Whole-body cryotherapy's enhancement of acute recovery of running performance in well-trained athletes. *Inter Jour Sports Phys and Performance.* 2015;10:605-612.
23. Moses MO, Sarpong PA, Segede JK, Appiah EJ, Osei F, Akwa LG. Perception of track and field athletes on the use of cryotherapy in injury management in Ashanti region of Ghana. *American Scientific Research Journal for Engineering, Technology, and Sciences.* 2017;28(1):215-224.
24. Ortiz da Silva LP, Mendes de Oliveira MF, Caputo F. Post-exercise recovery methods. *Revista da Educação Física/UEM.* 2013;24(3):489-508.
25. Point M, Guilhem G, Hug F, Nordez A, Frey A, Lacourpaille L. Cryotherapy induces an increase in muscle stiffness. *Scandinavian Jour Med Sci in Sports.* 2017;28(1).
26. Rymaszewska J, Pawik M. Does whole body cryotherapy become a form of therapy?. *Family Medicine and Primary Care Review.* 2013;15(2):247-250.
27. Selfe JT, et al. The effect of three different (-135°C) whole-body cryotherapy exposure durations on elite rugby league players. *PLoS One.* 2014;9(1):e86420.
28. Suzuki K. Cytokine response to exercise and its modulation. *Antioxidants.* 2018;7(1):17.
29. Urbanska K, Stanczykiewcz B, Szczesniak D, Trypka E, Zablocka A, Rymaszewska J. Mild cognitive impairments and whole-body cryotherapy— placebo control study. *Euro Psych.* 2017;415:5645-5709.

30. Wilson L, et al. Recovery following a marathon: a comparison of cold water immersion, whole-body cryotherapy and a placebo control. *Euro J Appl Physiol.* 2018;118(1):153-163.
31. Wujek-Krajewska E, et al. The influence of systemic cryotherapy on selected hemodynamic parameters and the assessment of the safety of its use in patients with successfully treated hypertension. *Cryobiology.* 2017;78:22-26.
32. Zalewski P, et al. Cardiovascular and autonomic responses to whole-body cryostimulation in essential hypertension. *Cryobiology.* 2014;69(2).