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Blood Flow Restriction Training in Cardiovascular Disease Patients

Pavlos Angelopoulos, Konstantinos Mylonas, Grigorios Tsigkas, Elias Tsepis, Evdokia Billis and Konstantinos Fousekis

Abstract

Over the past two decades, blood flow restriction training (BFRT) has gained popularity not only in athletic performance training, but also with many researchers and physical therapists as an innovative rehabilitation tool. Blood flow restriction (BFR) exercise is a novel exercise modality in clinical settings, which induces muscle hypertrophy and increases strength with low to moderate training intensity through increased anabolic processes mediated by BFR (usually with cuff inflation). BFR limits arterial and venous blood flow and leads to blood pooling, which could increase the effects of exercise-induced training. Strength training at lower intensities (20–40% of maximum strength) in combination with BFR showed similar effects on muscle hypertrophy as training at 70% strength level without BFR. In this context, considering that periods of immobilization (or reduced functionality) due to pathology, injury, or surgery cause harmful effects on muscle mass and strength in both young and old people, muscular adaptations of occlusion exercise could be beneficial to the elderly and post-operative patients in rehabilitation regarding muscle regeneration. Furthermore, as this type of exercise does not require high loads, it might be a feasible method in cardiac rehabilitation. Therefore, this chapter aims to review all recent literature regarding the impact of low-load BFR resistance training in patients with cardiovascular pathologies on muscle strength and hypertrophy, vascular function, safety, cardiovascular responses, and inflammatory markers.

Keywords: blood flow restriction training, exercise, cardiovascular patients

1. Introduction

Even as we approach the third decade of the 21st century, cardiovascular disease continues to be the leading cause of death worldwide, accounting for one-third of deaths and being the leading cause of death in Europe [1–4]. More specifically, 4 million Europeans die of cardiovascular disease (CVD) each year (45% of all deaths) [5, 6].

CVDs are a group of disorders that include the heart, blood vessels (arteries, capillaries, and veins), or both [7]. The most common CVDs that are also important for public health are ischemic heart disease, coronary heart disease, and vascular strokes. This category also includes peripheral arterial disease, congenital heart disease, rheumatic heart disease, cardiomyopathy, and cardiac arrhythmias. Gender, age, race, and family history are among the non-modifiable factors of

CVDs, while clinical and behavioral factors are among the modifiable ones. Clinical factors include obesity, hypertension, dyslipidaemia, diabetes mellitus, and cholesterol. Behavioral factors include reduced physical activity, smoking, substance use, unhealthy eating habits and stressful lifestyle as well as the socio-economic level of individuals.

The treatment of these diseases is based mainly on medication of specialized drugs, specific medical invasive techniques, and specialized therapeutic exercises. Therapeutic exercise is one of the most documented approaches for functional rehabilitation of patients with CVD. There is ample research evidence that the recommended levels of exercise are sufficient to prevent ischemic heart disease, stroke, hypertension, and therapeutic exercise adjustments have been investigated to improve their effectiveness, quality of life, and function indicators as well as to reduce morbidity and mortality in patients with CVD [8–13].

Based on the findings of the above research, patients with CVD could benefit significantly if they joined rehabilitation programs using therapeutic exercise. These patients often have low levels of cardiovascular function, muscle mass, and strength [14]. Aerobic exercise as well as low-resistance exercise have been suggested in cardiovascular rehabilitation therapies with positive results in improving the above parameters [15, 16]. Given that high-intensity exercise can cause unwanted cardiovascular adjustments, such as high blood pressure or arrhythmias, it should be avoided in specific patient groups [17, 18]; and low-intensity exercise is identified at levels not exceeding the anaerobic threshold [19].

Low-intensity aerobic exercise has been reported to enhance peripheral circulation, reduce heart attacks and the need for hospitalization, and improve cardiovascular function and quality of life in people with CVD by enhancing their ability to perform daily activities without symptoms or limitations [20]. However, low-intensity aerobic exercise cannot provide adjustments to increase muscle strength and mass [21]; which is why low-resistance exercise is essential and can improve muscle strength, endurance and mass, as well as bone density [22–24].

In recent years, research has demonstrated a novel exercise model, low-load BFRT, which is a therapeutic approach that could lead to significant myodynamic adjustments without the need to apply high tensions and high loads, allowing the implementation of exercise programs even in high-risk groups of patients, such as CVD patients.

BFRT is becoming very popular, and for some scientists it is considered ‘the state of art’. Restricting blood flow (not occluding) by itself, or in combination with exercise, results in beneficial adaptations to skeletal muscle and bones in various populations (old, young, trained, untrained). When BFRT is conducted, the blood flow to the exercising muscle is restricted by thin, computer-controlled, pressurized external constricting devices, such as pneumatic cuffs or inflated tourniquets, which are placed at the most proximal part of the arms or legs to reduce the amount of blood flowing back from the muscles in the extremities during a workout.

Historically, BFRT originated in Japan and involves the restriction of blood flow to exercising muscle. It was first described by Dr. Yoshiaki Sato, and the technique is based on blood flow moderation exercise (or vascular occlusion moderation training) involving compression of the vasculature proximal to the exercising muscles by specifically designed equipment. Dr. Sato evolved this technique called KAATSU, which is derived from the combination of the Japanese words for ‘additional’ (ka) and ‘pressure’ (atsu) [25]. KAATSU training is also known as vascular occlusion (VO) training. Dr. Sato evolved this technique during the period between 1973 and 1982 and developed various protocols that worked for people in different demographics (elderly, young, athletes, amateurs, etc.). The method was generalized for public use in the 1980s. Soon, the method was used by physicians, manipulative

therapists, acupuncture therapists, moxa therapists, athletic trainers, and physio therapists all over the world.

According to the American College of Sports Medicine (ACSM), a standard conventional training conducted at an intensity of at least 65% + of one-repetition maximum (1RM) is needed to achieve adaptations for muscle hypertrophy.² Nevertheless there are numerous studies that support low intensity exercise (20%–40% 1RM) combined with blood flow restriction could be beneficial for stimulating an increase of muscle strength, hypertrophy, and endurance [26–28]. At the same time, the suggested permissible levels of exercise intensity for cardiovascular patients is <30% 1RM, which makes it insufficient to make positive adjustments to increase muscle mass and strength [22, 29].

Approaching exercise with blood flow restriction could be a promising type of exercise for high-risk groups of patients, as research supports that with loads of 20–30% of 1RM, combined with blood flow restriction, it is feasible to yield hypertrophy responses comparable to that observed with heavy-load resistance training [30–32].

Especially in the case of cardiovascular patients where the American Heart Association recommendations currently suggest lower loads and intensity training, ‘occlusion exercising’ could be a valuable tool in the hands of therapists as it can accelerate patient rehabilitation by minimizing functional deficits in muscle mass and strength that arise during periods of reduced mobility and activity. Therefore, this chapter aims to review all recent literature regarding the impact of low-load BFR resistance training in patients with cardiovascular pathologies on muscle strength and hypertrophy, vascular function, safety, cardiovascular responses, and inflammatory markers.

1.1 Blood flow restriction mechanism of action

The definitive mechanism by which this kind of exercise provides stimulation for increased muscle strength and mass has not yet been elucidated; however, mechanisms of action of BFR have been reported. The potential physiological mechanisms underlying low-intensity exercise with BFR to improve muscle strength and mass include increased fiber type recruitment, decreased myostatin, stimulation of muscle protein synthesis, and cell swelling, an increase in metabolic stress, which theoretically activates systemic hormone production and fast-twitch muscle fibers, although it is likely that many of the aforementioned mechanisms work together [33]. Specifically, during BFRT, blood flow to the muscle being exercised is mechanically restricted by placing flexible compression cuffs or special straps proximally to the active extremity/extremities (at the upper extremities approximately peripherally at the point of deltoid insertion, at the lower extremities approximately at the top of the thighs peripherally of the gluteal line).

The restriction creates a kind of pressure that reduces blood flow to muscle fibers and, more specifically, to intracellular space. This alters the muscle’s biochemistry, increases lactate (lactic acid), and reduces pH, creating a low oxygen supply and intracellular swelling. All the above is thought to threaten the integrity of the cell membrane, which leads to the anabolic response and the increased release of growth hormones [34]. During BFRT, the external pressure applied is sufficient to maintain arterial inflow while occluding venous outflow of blood distal to the occlusion site. It has been suggested that cell swelling, induced by blood-pooling accumulation of metabolites and reactive hyperaemia, is detected by an intrinsic volume sensor, and may consequently lead to an activation of myogenic signaling pathways. This enhanced reperfusion and subsequent intracellular swelling are believed to threaten the structural integrity of the cell membrane, promoting an anabolic response [28].

In addition, during BFRT, there is a limited supply of oxygen to the muscles, which leads to the inactivation of the slow twitch muscle fibers (type I), which need oxygen as an energy source, while on the contrary it contributes to the activation of fast twitch fibers (type II) that have a higher hypertrophic potential than type I [28]. Type II muscle fibers have a relatively larger diameter and higher stimulation threshold. They receive energy mainly from the glycolytic pathway instead of oxidative metabolism, so they are preferentially recruited in a hypoxic environment. Tissue hypoxia from BFRT has been demonstrated to cause preferential recruitment of type II motor units, which typically are only recruited with high-load training [35]. Several studies have shown that the hypoxic intramuscular environment resulting from BFR leads to a high percentage of ATP hydrolysis, pH decrease, lactic acid increase, an increase of heat shock proteins (KSPAs) and protein S6, as well as in the inhibition of myostatin hormone, which inhibits the procedure of muscle mass hypertrophy. The above physiological responses significantly enhance the healing process and muscle hypertrophy [26, 32, 34, 35]. BFRT has also been shown to influence vasculature by promoting postexercise blood flow, oxygen delivery, and angiogenesis. Research indicates that it significantly increases vascular endothelial growth factor (VEGF) expression [36]; promotes vascular function [37]; enhances vascular conductance [52]; and partially alters hemodynamic parameters [38].

1.2 Cuff application

The main goal of the cuff used during BFRT is to provide sufficient pressure to restrict venous outflow while maintaining arterial inflow. Cuff width is a significant factor for determining safe BFRT pressures [39]. Furthermore, wider cuffs require significantly less pressure to achieve arterial occlusion pressure (AOP) [40]. Cuff pressures during BFRT were commonly greater than 200 mm Hg; but recent studies have found that similar positive outcomes could be achieved with pressures as low as 50 mm Hg, with less risk of adverse effects [35]. AOP is defined as the minimum pressure required to stop the flow of arterial blood into the limb. To calculate this, Doppler ultrasonography was placed on the radial or dorsalis pedis artery. The cuff is inflated until no pulse is detected, and then it is slowly released [41]. AOP can vary for each individual, even side-to-side, depending on limb circumference. Recent evidence reports two types of BFRT: personalized and practical. Personalized BFRT utilizes an advanced surgical tourniquet that allows the user to dial in a specific percentage of AOP and maintains this pressure throughout the training session. This has proven beneficial, especially in the research setting where it provides standardized results. On the other hand, practical BFRT includes a blood pressure cuff or elastic band to provide external pressure at a nonspecific value below AOP. Even though practical BFRT is not a standardized method as much as personalized BFRT, there is evidence that shows positive results when used for muscle hypertrophy [42, 43].

1.3 Safety

As far as safety is concerned, BFR training still requires further discussion, especially when performed with vulnerable people (patients, elderly). The idea of physically restricting blood flow to an extremity may raise red flags, especially regarding the cardiovascular system. It is well known that prolonged ischemia can cause necrosis of muscle tissue. Furthermore, a major concern with BFRT is the potential for thrombus formation [44]; because of the pooling of blood in the extremities. Of the evidence available, systematic reviews of BFR safety indicate it is not associated with additional cardiovascular stresses or morbidity [45–48].

Muscle damage through ischemic-reperfusion injury also occurs when there is blood flow restriction during exercise. Although ischemia reperfusion injury is most associated with long durations of severe ischemia [49]; the combination of short duration BFR with muscle contraction could elevate the possibility of muscle damage with this type of exercise. The risk of muscle damage while using BFRT has been analyzed by several investigations. Creatinine kinase, myoglobin, and interleukin 6 have not been shown to be elevated after BFRT more than traditional exercise [50]. There are case reports where rhabdomyolysis has developed after training; however, it is not known whether BFRT is the causing factor in thrombus formation. A previous survey out of Japan reported a rhabdomyolysis rate of 1 of 12,642 patients [51]. Overall, it appears that muscle damage is a minor risk with BFRT. To date, evidence shows that BFRT is not more risky than high-load resistance training, although careful selection of suitable patients and professional supervision is necessary to reduce the risk of side effects [48].

2. BFRT in patients with cardiovascular comorbidities

Research examining the safety of BFR exercise and training has thus far concluded that BFR exercise is a safe and novel method not only for training athletes and healthy persons but also it could be a beneficial training method for athletes/patients (post-surgery or injury situations) and for vulnerable populations and individuals with varying comorbidities where exercise options are limited [34, 52].

Furthermore, Abe et al. [53]; and Conceição et al. [54]; reported positive effects of BFRT regarding muscle strength, mass, and cardiorespiratory capacity when it is combined with low intensity walking or cycling. Abe et al. examined the acute and chronic effects of walk training with and without KAATSU on MRI-measured muscle size and maximum dynamic (one repetition maximum) and isometric strength, along with blood hormonal parameters. Eighteen healthy men volunteered to participate in this study. Nine men performed BFR-walk training, and nine men performed walk training alone (control-walk). Training was conducted two times a day, 6 days/wk., for 3 wk. using five sets of 2-min bouts (treadmill speed at 50 m/min), with a 1-min rest between bouts. For the BFR-walk training group, a restriction pressure of 160–230 mmHg was selected for the occlusive stimulus, as this pressure has been suggested to restrict venous blood flow and cause pooling of blood in capacitance vessels distal to the restriction point, as well as restricting arterial blood flow [55]. They conclude that BFR with slow-walk training induces muscle hypertrophy and strength gain, despite the minimal level of exercise intensity. Moreover, Conceicao et al. assessed the effects of BFR endurance training compared with conventional endurance training and resistance training in functional, morphological, and molecular responses. They examined 30 healthy men who were randomly assigned to the endurance BFR group, to the endurance conventional training group, and to the resistance conventional training group. All the groups performed eight weeks of training protocol. The endurance BFR group underwent 30 minutes cycling at 40% of VO_{2max} , four days per week, while the conventional group performed 30 minutes cycling at 70% of VO_{2max} , four days per week. In the BFR endurance group, cuff pressure was set at 80% of the maximum tibial arterial pressure (approximately 95 mmHg). The resistance training group performed four sets of ten leg press reps at 70% of 1RM with 60 seconds rest, four days per week. They suggest that BFR endurance training could increase muscle strength and induce similar hypertrophy stimulation to resistance training, while cardiorespiratory capacity could be improved even with a significantly lower workload compared to conventional endurance training. Altogether, this suggests

that BFRT could be a potentially safe training method, particularly for older adults or clinical cohorts incapable of exercising at high training loads.

Moreover, Cezar et al. showed that eight weeks of wrist flexion exercise training with 30% of maximum dynamic force with vascular occlusion (70% of the resting SBP) was sufficient to reduce blood pressure in medicated hypertensive subjects [56]. Twenty-three women were randomly assigned to three groups: one was the control group and the other two underwent eight weeks of training performed twice a week, including three series of wrist flexion exercises with or without vascular occlusion. Blood pressure was assessed before each session and based on that measurement (blood pressure at rest), occlusion pressure was determined for use during exercise in the BFRT group. The cuff pressure was equivalent to 70% of the subject's resting systolic pressure (maintained from the beginning of the exercise period until the end of the last series). The exercised with occlusion group showed a pre- to post-test reduction in systolic and diastolic blood pressure, mean arterial pressure, and double product, whereas the other groups showed no significant hemodynamic changes.

Despite the positive adjustments of low-intensity aerobic exercise with BFR techniques, no research has been done to evaluate the effects of this type of exercise program on cardiovascular patients. Only one study has looked at short-term hemodynamic adjustments after low-intensity aerobic BFR in elderly hypertensive women, highlighting the potential benefits of this type of exercise in hypertensive patients [57]. Specifically, Barili et al. examined the acute responses of cardiorespiratory and oxidative stress parameters to low intensity aerobic exercise (LIAE) with blood flow restriction (BFR) in hypertensive elderly women. Each subject performed in random order three experimental protocols: (a) high intensity aerobic exercise (HIAE): 50% of the estimated maximum oxygen consumption; (b) low intensity aerobic exercise (LIAE): 30% of the estimated maximum oxygen consumption; and (c) low intensity aerobic exercise with blood flow restriction (LILIAE+BFR): 30% of the estimated maximum oxygen consumption and occlusion pressure equivalent to 130% of the measured systolic blood pressure at rest. Blood samples were collected at three different times: at rest, immediately after each exercise protocol, and after 30 min of recovery. The findings support the indication of low-intensity aerobic exercise with BFR, with potential benefits for the hypertensive elderly population.

Only five research attempts have examined the effect of low resistance BFRT in cardiovascular patients with positive results in terms of muscle strength, mass, and hypertrophy as well as the functionality of these patients [52, 58–61]. However, three of these studies are characterized by serious methodological problems as they are pilot studies and do not draw definitive conclusions [58–60]. In particular, they reported positive results in improving muscle strength and functionality without increasing the risk of adverse effects through hemostatic and inflammatory responses. Madarame et al. [60] investigated the haemostatic and inflammatory responses to BFR exercise in nine stable patients with ischaemic heart disease. The patients performed four sets of bilateral knee extension exercises with a load of 20% 1RM either with or without BFR. In each exercise session (total two separated at least by one week), one set of 30 repetitions was followed by three sets of 15 repetitions with 30 seconds of rest between each set. During the BFRT, the cuff was attached to the proximal portions of the thighs and compressed at a pressure of 200 mmHg. The cuff was kept throughout the session, including rest periods between sets, and was released immediately after the session. Blood samples were obtained before, immediately after, and 1 hour after the exercise. They suggest that low-intensity resistance exercise with BFR would be relatively safe for stable IHD patients, at least in terms of haemostatic and inflammatory responses.

Similar results were reported by Kambic et al. [58], who assessed the safety and efficacy of BFR resistance training in patients with coronary artery disease (CAD) compared to usual care. Twenty-four participants were included in this study: 12 (control group) performed conventional care (aerobic exercise training), while in the intervention group ($n = 12$), BFRT was added on usual care. Subjects in the BFR resistance training group trained for eight weeks, performing a total of 16 unilateral leg extension exercise sessions. During each week, two exercise sessions were performed with a 48-hour rest period in between. Each training session consisted of three sets of 8, 10, and 12 repetitions in the first, second, and third sets, respectively, with a 45-second inter-set rest interval. The load was set at 30% of 1RM. The cuff was inflated between 15 and 20 mmHg greater than resting brachial systolic pressure, and the pressure was maintained throughout the entire training session and was released at the end of the last set. Findings report that BFR resistance training is safe and associated with significant improvements in muscle strength and may therefore be provided as an additional exercise option to aerobic exercise to improve skeletal muscle functioning in patients with CAD.

Nakajima et al. [52]; also showed improvement in muscle strength and endurance in patients with cardiovascular disease after a low-resistance BFR program for three months with two workouts per week, while Fakuda et al. [61]; evaluated muscle activation in the biceps using low-resistance BFR compared to low-resistance exercise and showed that the BFR subgroup showed statistically significantly greater activation than the low-resistance exercise subgroup, suggesting that BFR could be a valuable tool for improving muscle hypertrophy in cardiovascular patients. However, it should be noted that the last two studies have been published in a newspaper dealing only with BFR (Int. J. KAATSU Training).

3. Conclusion

Prevention of muscle atrophy and enhancement of muscle strength and hypertrophy can facilitate and accelerate the rehabilitation process and prevent further re-injury. Blood flow restriction training has been shown to be an especially promising tool in the recovery of injured and postoperative patients. The loss of skeletal mass in vulnerable patients, such as elderly or cardiovascular disease patients, is accompanied by a decline in physical function and activities of daily living. Given the fact that these patients are often unable to tolerate high-load routines, BFRT may be used in these individuals to prevent muscle weakness and improve their daily living.

As far as cardiovascular patients are concerned, daily exercise is necessary to improve the quality of their lives. However, exercise in its classic form may be prohibitive in such groups (e.g., it is impossible to exercise high resistance to increase muscle strength). Hemostatic and inflammatory responses are the major concerns for patients with CVD when performing an exercise. However, recent literature [60]; proposed that BFRT with low load resistance will be safe as well as effective for this group of patients. In conclusion, we could assume that the innovative type of exercise with blood flow restriction could be a safe and effective tool in improving daily life in vulnerable groups, but further research is needed in order to determine the long-term adverse effects and the optimal training routines.

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