Faculté des sciences de la motricité

What are the non-localized effects of the blood flow restriction training: a Scoping Review

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ABSTRACT

BACKGROUND: The BFR training has been stated as a safe strengthening technique used and a safe rehabilitation tool if it's properly applied but to the best of our knowledge, there are only some articles that reported the non-localized chronic adaptations of BFR training. The main objective of this scoping review is to assess the current literature on the non-localized effects of chronic use of the BFR technique. Secondly, this review will identify gaps in the existing research that could be addressed in future studies.

METHODS: The search equations were entered into three scientific databases: Embase, PubMed, and Scopus. The "Grey literature" was screened by searching on Google Scholar and through several websites. The studies had to meet the eligibility criteria to be included. The scoping review was drafted following the PRISMA guidelines.

RESULTS: A total of 56 articles were included in this exploratory review following the selection process. The results show a trend towards improvement in anaerobic and aerobic capacities, mainly for VO_2max and PPO. Adaptations were also observed for certain measures of body composition, such as percentage of fat mass and lean mass, as well as for certain blood homeostasis data: glucose levels, cholesterol (total and LDL-C), eGFR and triglycerides. Finally, neuromuscular effects were also observed in the EMG amplitude. Few and some conflicting results were found for BFR's cross-transfer effect, either in proximal cuff muscles or unrestricted limbs.

CONCLUSION: The use of BFR seems to lead to non-localized effects. However, further research is needed to confirm some of these effects. In the future, these non-localized effects could be advantageous in the management of pathological populations such as patients with chronic kidney disease, chronic heart failure or obesity.

1 Introduction

Mechanical and metabolic stresses are mandatory to produce muscle adaptations (1). Classical non-occluded resistance training is performed with the aim of increasing maximal strength, hypertrophy, power (2,3) and functional capacity (4). The requirement to carry heavy to moderate loads to trigger strength and hypertrophic muscular improvements may not be applicable in some patients. To this end, the BFR training has been tested in a large range of the healthy population at elite (5–7) and amateur-level.

Blood flow restriction (BFR) training is a strengthening technique that is also known as Kaatsu training (8). Originally, it was described in Japan during the 70s (9), the first scientific manuscript was published in 1987 (10). The principle of the BFR training is to place an inflated cuff or a tourniquet around the proximal part of the upper or lower limb in order to reduce arterial and venous blood flow (11,12). Most of the time, the applied pressure is set at 60% to 80% of the total arterial occlusion pressure for the lower limb and around 50% to 70% for the upper limb (13). During the BFR, different kinds of strategies could be applied, such as only the BFR or the BFR with resistance training as well as aerobic exercises (13). BFR muscle strengthening demonstrated similar muscle adaptation with small loads, i.e., around 20% to 30% of 1-RM (14,15), compared to a classical 70% to 85% of 1-RM strengthening program in novice and intermediate athletes (16).

The BFR training produces a reduction in the blood flow, resulting in the accumulation of metabolites distally, therefore increasing the metabolic stress (11). This accumulation of metabolites increases muscle cell swelling, intramuscular anabolic and anti-catabolic signaling, satellite cell activation and muscle fiber recruitment (17), which are factors that are considered to be beneficial for muscle adaptation (8,18). The accumulation of metabolites and mechanical stimuli during BFR training activate the exercise pressor-reflex (composed of the metaboreflex and the muscle mechanoreflex) that manages the body's response to exercise. This reflex is triggered by the stimulation of group III and group IV neural afferent fibers which finally induce an increase in heart rate, blood pressure and ventilation. In other words, BFR training stimulates the aerobic metabolism. The amplitude of these autonomic adaptations is greater with BFR training, compared to the same intensity exercise in free-flow training, and is relatively comparable to high intensity non-occluded training (19–21). Due to the restriction of the local oxygen supply, type-II muscle fibers are more activated and are activated more quickly to substitute for type-I muscular fibers, which are more sensitive to oxygen reduction. These type-II muscle fibers take their energy from the Cori cycle via the glycolytic pathway, which is an anaerobic pathway (22).

The BFR training has been stated as a safe strengthening technique used and a safe rehabilitation tool if it is properly applied (13,23–25). In addition, several studies have shown the benefits of this training for people with post-ACL reconstruction (26), people with knee osteoarthritis (27), people with myositis (28), older individuals (29) and patients with patellofemoral pain (30). While the effect of BFR could be explained by the increase in metabolic stresses below the cuff, several studies (31–33) reported non-localized effects could be defined as any effects that are not located on the limb where the blood flow is restricted. These effects are called: a) cross-education or cross-transfer effects, i.e., when unilateral resistance training increases the muscle capacities of the opposite non-occluded limb (34) or b) remote effects, i.e., most commonly used when a session of resistance training provokes an adaptation away from the occluded limb (32). The non-localized effects could be explained by a) the neural adaptation to unilateral training. More specifically, the reorganization of the central and peripheral motor pathways projecting to the opposite limb with the aim of a better coordination of both limbs (34). The b) increase in plasma anabolic hormones with higher concentration of growth hormone (GH), noradrenaline (NOR), lactate (La) after BFR training, compared to classical resistance training (32,35,36). The c) increase of muscle activation during the BFR exercise with higher electromyographic signal activation in non-restricted loco-regional muscles at the cuff (37). The d) widespread autonomic activation during and after BFR training.

1.1 Scoping review objectives

To the best of our knowledge, there are only a few articles that reported the non-localized chronic adaptations of BFR training. The objectives of this study were therefore to review the existing literature on the non-localized effects of chronic use of the BFR technique and to identify gaps for future research. The questions guiding this scoping review were: (1) what non-local effects are currently identified, and (2) for which types of patients these non-localized effects could be beneficial in future research.

2 Methods

This scoping review was drafted following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses - Extension for Scoping Reviews (PRISMA for Scoping Reviews) (38). The research question was formulated: *What are the non-localized effects of the blood flow restriction training?* To define the inclusion criteria, the PICOS strategy was chosen. (See Table 1 for more information).

2.1 Eligibility criteria

To be included in this review, the manuscript needed to: I) be written in English or in French, II) be available in full text, III) involve human subjects, IV) study the BFR as a strengthening technique for at least one week and V) measure a non-localized effect, i.e., an observable effect on a physiological system resulting from chronic adaptation after several sessions of BFR training and proximal to the occlusion cuff. There were no restrictions set on the publication dates of included studies or populations. Manuscripts with designs such as conference abstracts, protocols, or case studies were excluded from this scoping review.

2.2 Information sources

To identify the relevant papers for our review, a thorough research of the following scientific databases, i.e., Medline/Pubmed, Scopus and Embase was conducted. The "Grey literature" was screened by searching on Google Scholar and through several websites, including different national institutes for health, national sport associations, different national physiotherapy associations, different research registries and clinical trials registers (see Appendix 1 for a detailed list). Regarding the scientific databases (PubMed, Scopus, Embase), the search equations were built by the authors from the keywords (present in Table 1) using the boolean operators "OR" and "AND". The search equations have been adapted to each database according to their syntax. The Mesh (PubMed) or Emtree (Embase) terms used were "humans", "blood flow restriction therapy", "abdominal muscles", "back muscles" and "oxygen consumption". A filter was applied in the three scientific databases, so that the terms present in the equations are searched only based on the "Title" and "Abstract" of the articles. The different search equations are described in Appendix 1.

To adapt to Google Scholar's search functionality, keywords from the research question were combined to build simpler equations. Due to the high number of results on Google Scholar, the first ten pages were reviewed for each equation without applying any filters. To complete the "Grey literature" research, the authors checked different websites by typing the keywords: "blood flow restriction training", "BFR training" or "blood flow restriction" in the research toolbar of each of them.

The search results from the different sources were exported into Zotero software.

2.3 Selection of sources of evidence

The initial search was conducted in Mars 2024. The authors removed all the duplicates. The selection phase was then carried out by two reviewers (M. Latour and M. Lemans) with the help of the Rayyan website (https://www.rayyan.ai/). The first part of the selection phase was the sorting of the articles based on their titles and abstracts. If the title and abstract were not sufficient to determine if the article was eligible, a reading of the full article was performed. After this first part, any conflict was resolved by a third reviewer (F.D.).

2.4 Data extraction

The data extraction process was done by two authors (M. Latour, M. Lemans) and verified by a third author (F.D.). All data and variables resulting from a chronic adaptation of a physiological system after several sessions of BFR training and away from the restricted limb were extracted and synthesized in tables (See Appendix 2). Extraction data varied according to the type of scientific article. Extracted data for randomized controlled trials were the sample size, the age, the different groups, the training program, the BFR material, the cuff(s) location(s), and the occlusion pressure, the non-localized measurement. Extracted data for review articles were the main goals, number of articles included and conclusions.

Table 1: PICOS criteria

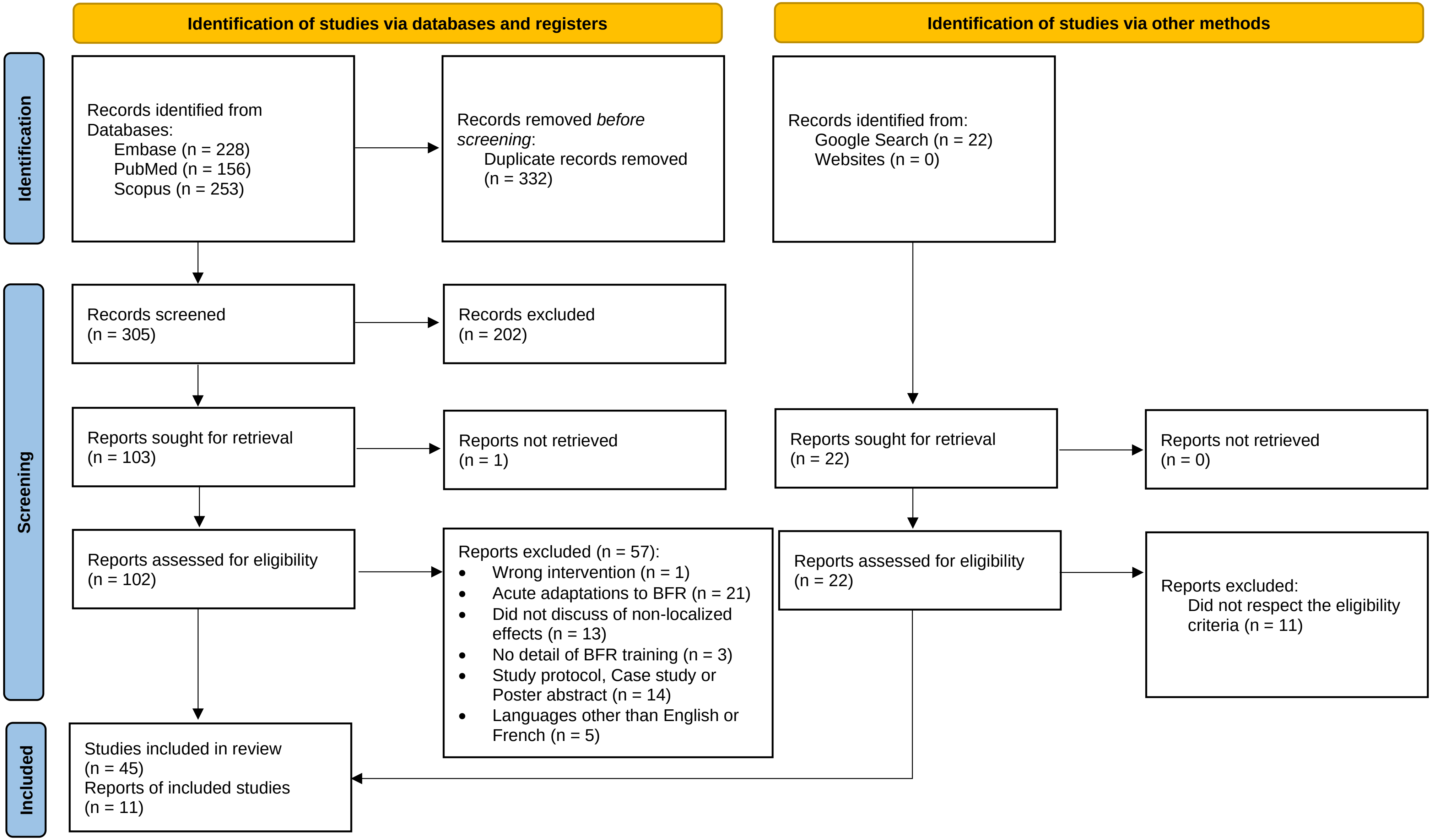
	English terms	Emtree terms	Synonyms	Associate terms
Patients	Humans	human	/	
Intervention	Blood flow restriction training	blood flow restriction	blood flow restriction exercise, kaatsu, katsu training, blood flow restriction therapy, occlusion training, vascular occlusion training	BFR
Comparison	/	/	/	/
Outcomes	Non-localized effects	/	remote, cross-transfer, cross transfer, untrained limb, mirror activation, non localize, non-localize, non localized, non-localized, unrestricted arm, unrestricted leg, unrestricted limb, untrained arm, untrained limb, cross over, contralateral,	
		abdominal wall musculature	abdomen muscle, abdominal muscle, abdominal muscles, abdominal musculature, musculus abdominis	
		back muscle	back muscles, intermediate back muscles, "muscle, back", spine musculature, superficial back muscles	
		maximal oxygen uptake	maximal oxygen uptake, maximal aerobic capacity, maximal consumption of oxygen, maximal oxygen consumption, maximal uptake of oxygen, maximum aerobic capacity, maximum oxygen consumption, maximum oxygen uptake, oxygen maximal uptake, vo2 max, vo2max	
		aerobic capacity	aerobic metabolism capacity, aerobic power	
		anaerobic capacity	anaerobic metabolism capacity,	
		oxygen consumption	O2 consumption, O2 uptake, oxygen demand, oxygen intake, oxygen requirement, oxygen uptake, oxygen utilization	
Study design	/	/	/	/

3 Results

3.1 Selection of sources and evidence

The selection flowchart is detailed in Figure 1. A total of 637 papers were screened through the different databases (PubMed, Embase and Scopus). Regarding the grey literature, the Google Scholar search yielded 22 papers, but no papers were screened via websites. At the end of the selection process, 56 articles met the eligibility criteria and were therefore included in this scoping review, among them one case series, 44 randomized controlled trials (RCTs), one narrative review, nine systematic reviews or meta-analyses, and one PhD thesis.

Figure 1: PRISMA flow diagram.



3.2 Study characteristics and results synthesis

3.2.1 Non-localized effects of the BFR on muscles either located upstream or close to the cuffs or on another limb that is not restricted

Participants and interventions

In total, six RCTs, one meta-analysis, one systematic review, and one narrative review reported non-localized effects upstream of the cuff (31,33,39–45) while seven RCTs and one PhD thesis reported non-localized effects on non-occluded limbs (32,46–52).

In the RCTs, a total of 469 subjects were included. Most of these studies included healthy participants (31–33,39,40,45,46,48–52) except for one study by Ampomah et al. (41), which included recurrent low-back pain patients. The duration of the intervention varied between 2 and 12 weeks with different frequencies, i.e., twice a day (31,33), twice a week (32,41,48,49), three times per week (46,52), four times per week (39,40,50) or five times per week (45,51). Most of the studies used free-weight resistance training with a percentage value of 1-RM such as 20% (51), 25% (41), 30% (31,32,46,48–50,52), 20 to 30% (39) and 50% (40). Two studies only did a walking aerobic training with the BFR (33,45).

Ten studies used a pneumatic cuff (39–41,45,46,48–52), while the other three used an elastic band (32,33,37). About the occlusion pressure, the protocols differed between the studies. Seven studies used a percentage of the AOP which was 40% (50), 50% (39,52), 60% (46,48,51) and 80% (49), four studies used a predetermined increased pressure-protocol (32,33,37,45), one study maintained a fixed pressure of 100 mmHg (40) and one study took the capillary refill time as a standard value : it had to be equal to 2 or 3 seconds downstream of the cuffs (41).

Results of studies on muscles located upstream or close to the cuffs

The various parameters were analyzed in either one or two separate studies. All these results are detailed in Appendix 2 - Table 2b. Some significant changes between pre- and post-intervention measurements were obtained ($p < 0.05$) in the BFR groups of three studies for different parameters, namely: pectoralis major muscle thickness (31), maximal dynamic strength (1-RM) at leg press (39) and finally for the score of the "Severity and impact on quality of life of urinary incontinence" questionnaire (ICIQ-SF) (40). In addition, the study by Due et al. showed a non-significant improvement post-intervention ($p = 0.054$) in the number of leakage episodes (40). Another study led by Sakamaki et al. showed a non-significant ($p = 0.07$) trend toward an increase in iliopsoas cross-sectional area (CSA) (33). There was no significant difference between pre- and post-intervention values ($p > 0.05$) in the exercise groups with BFR for the following parameters: para-spinal and gluteus maximus muscles CSA (33), trunk extensor mass (45), trunk extensor CSA or muscle strength or muscle endurance (41). Only one study found a significant difference ($p < 0.05$) between the different intervention groups in pectoralis major muscle thickness and 1-RM at the flat bench press in favor of the BFR groups (31). In the study that utilized 1-RM measurement during leg press (39), the control group did not exhibit any significant difference in maximal dynamic strength ($p > 0.05$) following the intervention, unlike the BFR group. On the contrary, in the study led by Ampomah, the control group demonstrated a significant time effect in trunk extensor muscle endurance ($p = 0.01$) and muscle strength ($p = 0.03$), unlike the BFR group (41). This study also revealed significantly greater trunk extensor strength in the control group compared to the BFR group ($p = 0.04$) (41). Finally, no significant difference between the different intervention groups for the other parameters was found (33,39–41,45).

Results of studies on muscles located on another limb that is not restricted

CSA

Three studies assessed the CSA of either the elbow flexor or soleus muscles (32,46,51). For the CSA of the elbow flexor muscles, in the two studies (32,46), the BFR group had cuffs on both lower limbs, and only one of the upper limbs was trained (the trained arm of the BFR or control groups). In the study by Madarame et al. (32), at the end of the intervention, there was no significant change for the untrained arm of the BFR group or for the control group (neither the trained nor the untrained arm) and, only the trained arm of the BFR group showed a significant time and group effect. The second study showed no significant time or group effects

(46). Regarding soleus CSA in the study by Mendonca et al. (51), no significant time effect and no difference between groups were found.

Strength

Three studies assessed the strength of either the elbow flexor or the handgrip (32,46,52). Regarding the 1-RM strength of the elbow flexor muscles, in the two studies that analyzed it (32,46), as cited above (see CSA), the BFR group had cuffs on both lower limbs, and only one of the upper limbs was trained. At the end of the intervention in the study led by Madarame et al., there was no significant change for the untrained arm of the BFR or control groups, but there was a significant change for the trained arm of the BFR and control groups (32). In the second study by May et al., they found a significant difference between pre- and post-intervention values for the BFR groups (the trained and the untrained arms) and for the trained arm of the control group (46). There was a significant group effect in favor of the trained arm of the BFR group ($p < 0.05$) (46). Finally, one study showed greater changes in handgrip strength in the untrained limb in the low-intensity BFR group than in the low-intensity or maximal-intensity non-BFR groups (BF10: 3.1 and BF10: 6.31, respectively) or than in the control group (BF10: 14.23) (52).

Neuromuscular adaptations

Two studies analyzed neuromuscular adaptations based on different criteria (50,51). Both found a significant improvement between the beginning and end of the intervention for the non-BFR limb in the BFR group in the EMG amplitude of the elbow flexors during eccentric and concentric movements (cuff placed on a single upper arm) (50) or the soleus during plantar flexion (cuff placed at the proximal part of a single lower limb) (51). No significant difference between groups for these different variables was demonstrated in either study (50,51), namely between the low-intensity group with BFR and the high-intensity group without BFR (51) or between the eccentric or concentric BFR groups and the control group without intervention (50).

Peak and Maximal torque

Two studies analyzed the elbow flexor muscles (32,50). No significant time effect was found for peak torque during concentric elbow flexion in both groups (50), nor for maximum isometric torque in the untrained arm of the BFR group or control group (32). In this last study, the trained arm of the BFR group showed a significant time effect (32). However, a significant time effect was shown for peak torque during eccentric elbow flexion (elbow extensor muscles) (50). Also, a study showed a greater peak torque during knee extension ($p = 0.04$) in favor of the BFR group (49).

Others results

Additional parameters were evaluated in only one of the included studies. All these results are detailed in Appendix 2 - Table 3b. No significant changes were observed between pre-intervention and post-intervention values for either the BFR or control groups regarding the plantar flexion maximal voluntary isometric contraction (MVIC) (51) and the thickness of the brachial biceps muscle (50). In a study led by Bowman et al. (49), they found a significant group effect in favor of the BFR group (cuff applied to a single lower limb) in terms of thigh circumference ($p = 0.01$) and the number of repetitions of the single-leg heel raise ($p=0.02$) of the unrestricted lower limb. Another study, also conducted by Bowman et al. (48), showed a significant difference in favor of the BFR group (cuff applied to a single upper arm) compared to the control group for grip strength of the unrestricted upper limb ($p < 0.01$). In the same study, there was no significant difference in a (fore-)arm circumference or in strength parameters (except grip strength) between groups (48). In addition, in another study led by Mendonca et al., there was a significant positive improvement in the post-intervention rate of torque development (RTD) ($p < 0.01$) and peak RTD ($p = 0.024$) for the unrestricted lower limb in the BFR group (cuff placed on the other lower limb) as well as in the control group (51).

3.2.2 Non-localized effects of the BFR on aerobic and anaerobic performance

Participants and interventions

A total of 33 studies investigated the long-term non-localized effects of the BFR training on aerobic and anaerobic performance. Twenty-six of these studies were RCTs (6,39,45,53–75), six were meta-analyses (19,42,76–79) and two were systematic reviews (80,81) and one was a case serie~~s~~ (64). Of all the RCTs, a total of 730 patients were included. Of these, 11 studies involved elite or well-trained subjects in different disciplines such as basketball (70), rowing (6), swimming (62), running (57,61), cycling (61,73,74), football (69) and the armed forces (58,64). Ten studies included healthy and physically active subjects, meaning that the participants were all involved in sports and recreational physical activities and had no known musculoskeletal or cardiorespiratory diseases (53–55,60,63,65,67,70,71,75), one of which included elderly people (45). Five studies targeted healthy but sedentary people (56,59,66,68), one of which included elderly people (39). Finally, one study included men with post-infarction heart failure (72).

The duration of the intervention varied from 1 week to 12 weeks for all studies except Tanaka et al. in 2018 (72) which ran for 6 months. The frequency of training sessions varied between 1 session per day (56,64), 2 sessions per day (70,75), 2 times per week (71,73,74), 3 times per week (6,53–55,57,60–63,65–69,72), 4 times per week (39,58) and 5 times per week (45,75). Only the study by Conceição et al. in 2019 (59) did not give a notion of training frequency. Nine studies carried out protocols involving either walking or running on a treadmill (39,45,55,57,65,68,70,71,75), 11 studies used a cycling protocol (53,56,59–61,63,66,67,72–74), 3 studies carried out resistance training (39,58,74), one study did a rowing protocol (6), one study did a swimming protocol (62) and one study used a modified Nustep recumbent cross trainer (64).

Nineteen studies used pressure belts (39,45,53,54,56–58,60–64,66,69,70,72–75) and seven studies used elastic belts (6,55,59,65,67,68,71). Pressures applied with tourniquets varied a lot between the different studies. Eight studies used a percentage of AOP with a range between 30% to 100% (39,59,61,62,65,69,73,75). Eight studies used a predetermined protocol of progressive pressure increase (45,53,55,60,63,67,68,70). Five studies used predetermined pressures ranging from 60 to 310 mmHg (54,56,64,66,74). One study used a perceived pressure scale to set the pressure (71). One study used a percentage of 75% elastic tightening to determine the occlusion pressure (6). Finally, two study took a percentage of the systolic blood pressure to set the pressure occlusion (57,72). The study by Cintineo et al. (58) did not report any precise information on occlusion pressure.

Results of studies on aerobic performance parameters

Relative VO2max

Regarding relative VO_2max, 16 studies compared pre-test and post-test relative VO_2max values. Among these studies, 13 showed that their intervention groups with BFR significantly improved ($p < 0.05$) their relative VO_2max measures from baseline to post-intervention assessment (6,53–56,59,60,68,70,71,73–75), and three studies found effect sizes ranging from small (ES = 0.2-0.5) (58,71) to large (ES > 0.8) (59). Only two studies reported no significant change in the relative values of VO_2max before and after the intervention (66,69). Four studies compared the BFR group with the control group and found no significant difference between groups after the intervention (56,59,69,71). However, out of the 13 studies that showed a significant increase in relative VO_2max in BFR groups, seven studies did not show any significant increase in some non-BFR groups (6,53,60,68,70,74,75). In the study by Thompson et al., no significant difference was found in relative VO_2max between the two BFR groups at either high or low training doses (35 walking sessions over four weeks versus 12 sessions over six weeks, respectively) (75). Finally, the study led by Amani-Shalamzari et al. showed a significant difference ($p = 0.01$) between a group with constant complete BFR pressure and another group with increased BFR pressure (both groups with increased exercise intensity) in favor of the first constant-pressure group (55).

Absolute VO2max

About absolute VO_2max, only two studies have analyzed it (73,75). Both showed a significant improvement ($p < 0.05$) in absolute VO_2max between pre- and post-intervention values for their BFR groups (73,75) and also for the high-intensity interval without BFR training group (73), while there was no change for the control groups in either study. In addition, one study found a significant difference in post-intervention measures in favor of the BFR group compared to the control group (73). In the second study by Thompson et al., as for relative VO_2max, there was no significant difference found in absolute VO_2max between the two BFR groups at either high or low training doses (75).

VO2peak

Regarding VO_2peak (relative and absolute), seven studies compared pre-test VO_2peak values with post-test values (39,45,61,63,64,67,72). Of these seven studies, four studies measured a significant ($p<0.05$) improvement in post-test relative VO_2peak values in the BFR groups (39,61,63,72) and four studies found no significant change in post-test relative (64,67) or absolute (45,61) VO_2peak values. Five studies investigated the differences in VO_2peak values between intervention groups (39,62,63,67,72). Three out of five studies showed no significant difference ($p > 0.05$) either with the control group or with the overall study groups (39,63,67). One study by Tanaka et al. found significantly greater VO_2peak values post-test in the group with BFR compared to control group (72). The last study by Held et al. in 2023 showed a favorable VO_2peak adaptations in the BFR group (SMD= 0.15) compared to non BFR group (SMD= -0.39)(62).

Maximal aerobic power

Regarding maximal aerobic power, 4 studies analyzed this parameter (61,69,74,75). A significant time effect was found in three out of four studies ($p<0.05$) (61,69,75). Two of the four studies have similar conclusions. Indeed, a significant increase was found for all groups in the studies after training (61,69). However, the study led by Thompson et al. demonstrated a significant time effect only for the BFR groups with a high-intensity program (75). The last study did not find a significant difference (74). Across all studies, no group or interaction effect (group x time) was observed (61,69,74,75).

Results of studies on anaerobic performance parameters

Peak power output

For anaerobic variables, peak power output was studied in 6 studies (55,60,69,70,73,74). Peak power output significantly increased for all groups in 2 out of the 6 studies (65,67), while in 2 other studies, this variable increased only in groups using BFR or performing high-intensity exercises ($p < 0.05$) (60,73). One study did not find a significant difference between groups (74). However, in the study conducted by Park et al., the BFR group showed a trend toward increasing their peak power output (3%) (70). Regarding the group effect, only Amani et al. found a significant difference between a group with constant complete BFR pressure and another group with increased BFR pressure in favor of the first constant pressure ($p < 0.05$) (55). Finally, two out of the 6 studies found a significant interaction (time x group) ($p < 0.01$) (60,73).

Mean power output

Subsequently, mean power output was analyzed in 3 different studies (66,69,74). Two studies out of the three found a significant increase in all groups after training ($p < 0.05$) (66,69), while the last one did not find a significant difference. Finally, two studies analyzed the interaction between group and time with opposite conclusions, one being significant (69) and the other non-significant (74).

3.2.3 Non-localized effects of the BFR on whole-body composition

Participants and interventions

Eleven RCTs investigated the effect of BFR training on the whole-body composition. A total of 589 patients were included in the 11 RCTs. Seven studies included healthy patients, with two of these studies specifically recruiting well-trained individuals (58,73). The other four studies included patients with pathologies including obesity (57,82) and chronic kidney disease (83,84). The duration of the intervention varied between 4 weeks and 6 months, with a frequency of 2 sessions per week (57,73,82), 3 sessions per week (55,60,68,83–86) and 4 sessions per week (58). For the interventions, four studies used resistance training (58) with either a load of 30% 1-RM (85) or a progressive increase in load during training from 30% to 50% 1-RM (83,84). Three studies used a cycling protocol (60,73,82). Walking or running protocols on treadmill were used in 4 studies (55,57,68,86).

Only one study used an elastic band (68) to apply the BFR, the rest, except one study that didn’t provide one (84), used a pneumatic cuff (55,57,58,60,73,82,83,85,86). For the pressure applied with a tourniquet, four studies used a predetermined protocol of progressive pressure increase (55,60,68,86), three studies applied distinct percentages of the AOP (30% (73), 40% (82), and 50% (85)), two studies used 50% of the resting systolic pressure to define the occlusion pressure (83,84), one study set the occlusion pressure at 200 mmHg (57) and one study did not mention occlusion pressure with precise values (58).

Results of studies on whole-body composition

Body fat percentage

Regarding body fat percentage, ten studies investigated this parameter (55,58,60,68,73,82,83,85–87). Among these, six reported a significant decrease in body fat percentage after training, either for all exercise groups (58,68,82), or specifically in BFR groups ($p < 0.05$) (86,87) or only in the exercises group without BFR (83). Furthermore, one of these studies also reported a significant increase in body fat percentage after training in the control group ($p < 0.01$) (68). With regard to group effects, only 2 studies did not investigate this (55,60), but among the 7 others, 5 studies demonstrated a significant effect. Indeed, the decrease in percentage of body fat favored the BFR groups compared to the groups without BFR (82,86,87) or favored all exercise groups compared to the control group ($p < 0.05$) (68), or only the exercise group without BFR (83). Additionally, among the nine studies, five analysed the interaction between group and time. Three out of five studies demonstrated a significant interaction (82,86,87), while two others didn't find any ($p < 0.05$) (58,73).

Fat mass

Secondly, six studies analyzed fat mass. After training, a significant decrease in fat mass was found in exercise groups with or without BFR in three out of the six studies (82,84,87). However, in three other studies, no change was observed in the BFR groups, but in the study led by Lan et al., a significant change was found in the moderate-intensity exercise group ($p < 0.05$) (68). In four out of the six studies, a group effect was observed (68,82,84,87). All these studies showed a significant difference between BFR groups and the control group ($p < 0.05$), except for the study conducted by Lan et al. where the moderate-intensity exercise group also exhibited a significant group effect compared to the control group ($p < 0.01$) (68). For the other two studies, no significant group effect was found (85,86). Finally, three out of the six studies found a significant interaction between groups and time ($p < 0.05$) (84,86,87).

Body mass index (BMI)

Next, five studies investigated the BMI (55,83,84,86,87). Among these five studies, two measured a significant difference between the beginning and end of training for the exercise group (86) or the BFR group (87) ($p < 0.05$). For the other studies, no significant time effect was found (55,83,84). Concerning the group effect, two studies identified a significant effect in favor of the BFR groups compared with the other experimental groups ($p < 0.05$) (83,86). The other studies did not find a significant group effect (55,84,87). Only the study by Kargaran et al. investigated the interaction between groups and time, which was significant in favor of the BFR group performing a dual task ($p < 0.01$) (86).

Fat-free mass

Regarding fat-free mass, four studies examined this parameter (58,83–85). Three out of four studies reported a significant increase in fat-free mass for exercise groups with or without BFR (58,84), or only for those without BFR ($p < 0.05$) (83). Among the four studies analyzed, two studies observed different group effects (83,84). Indeed, a significant group effect was reported in the study led by Corrêa et al., demonstrating an increase in fat-free mass in the exercise groups compared to the control group ($p < 0.01$) (84), while in the study by Deus et al., a group effect was identified between the non-BFR group and the control group ($p < 0.01$) (83). The study by Corrêa et al. also showed a significant interaction between groups and time ($p < 0.01$) (84), unlike the study conducted by Cintineo et al. (58).

Body mass

Finally, five studies studied the body mass (55,58,60,83,86). The study conducted by Kargaran et al. showed a significant decrease in values after training in exercise groups, which were significantly different from the control group ($p < 0.05$) (86). An interaction between the two was also found ($p < 0.01$) (86). Conversely, the study led by Cintineo et al. observed a significant increase in body mass after training in the exercise groups ($p < 0.01$) but did not find a significant interaction between groups and time (58). Finally, three studies did not observe any significant effect of time, group or interaction (55,60,83).

3.2.4 Non-localized effects of the BFR on blood homeostasis

Participants and interventions

Finally, seven articles investigated the long-term non-localized effects of the BFR training on blood parameters. One study involving 50 participants was carried out with well-trained subjects (73), while the other studies, totaling 367 participants, were carried out with patients with known pathologies such as chronic kidney disease (83,83,84), obesity (82,87), or post-infraction heart failure (72). The duration of treatment varied from 12 weeks to 6 months with a frequency of 2 (73,82,87) or 3 times per week (72,83,84,88). The interventions were resistance training in which the percentage of 1-RM increased progressively over the weeks of training, ranging from 30 to 50% (83,84) or 50 to 70% (88) depending on the protocol or a cycling protocol on a cycle-ergometer (72,73,82,87).

All the studies used a pressure cuff, however the study by Corrêa et al. didn't provide any information on the type of cuff (84). The occlusion pressure was set at 50% of the resting systolic pressure in 4 studies (72,83,84,88), maintained at 30% or 40% AOP (73,82), at around 40 to 80 mmHg above the systolic pressure (87) or maintained at 200 mmHg.

Results of studies on blood homeostasis

Regarding the results of studies on blood homeostasis effects, various parameters were investigated. All these results are detailed in Appendix 2-Table 6.

Blood glucose levels

Firstly, five studies analyzed blood glucose levels (72,73,82,83,87). Three studies showed a significant decrease post-training ($p < 0.05$) in blood glucose levels in exercise groups with the BFR and exercise groups without the BFR (82,83,87). Two of these three studies describe a group effect in favor of exercise groups with BFR (82,87). The study by Li et al. showed, in fact, a significantly higher rate of glucose decline in groups with BFR compared to a group performing high-intensity training and the control group ($p < 0.05$) (82). On the other hand, in the study by Deus et al., both exercise groups had significantly lower glucose levels compared to the control group ($p < 0.01$), but no difference was found between the exercise groups

(83). Finally, two other studies did not observe any significant difference either between the beginning and the end of training or between the different groups (72,73).

Cholesterol: total and different types

Moreover, regarding total cholesterol, two studies observed a significant difference in post-training values ($p < 0.05$) (82,87). In the two studies led by Li et al. (82) and Chen et al. (87), this variation was evident in the groups performing exercise programs with or without BFR, while the control group in the study by Li et al. (82), found no significant effect. Furthermore, a group effect was observed in three studies where a significant difference was found between the training groups and the control group ($p < 0.05$) (82,87). Finally, three studies did not find a significant difference, neither at the end of training nor compared to the control group (72,73,83). Regarding the different types of cholesterol, only one study observed a significant time effect in the different groups as well as a significant increase in high-density lipoprotein cholesterol (HDL-C) compared to the control group ($p<0.05$) (87). Other studies examining HDL-C did not observe any significant time or group effects (72,73,83). For low-density lipoprotein cholesterol (LDL-C), two studies showed a significant decrease compared to the control group (73,87), and the study led by Chen et al. also observed a significant difference between the beginning and end of training in the different groups ($p < 0.05$) (87). The two last studies did not report any significant change (72,83).

Estimated glomerular filtration rate (eGFR)

Three studies evaluating eGFR reached the same conclusion (83,84,88). They showed a significant decrease in eGFR at the end of training, as well as a group effect observed in the groups exercising with or without BFR compared with the control group ($p < 0.05$).

Triglycerides

Three studies reported a significant decrease in triglycerides between the beginning and end of training, either for all groups (87), only for the exercise groups (82) or for the exercise groups without BFR ($p < 0.05$) (83). Studies led by Li et al. and Chen et al. demonstrated a significant group effect in favor of BFR groups ($p < 0.05$) (82,87). On the other hand, a significant group effect in favor of the exercise group without BFR was found in the study by Deus et al. ($p < 0.01$) (83). The remaining studies did not show significant group effects or significant time effects concerning triglycerides (72,73).

Glycolated hemoglobin (Hba1c)

About the Hba1c assessed, two studies had opposite results (72,83). The first showed a time and group effect for the exercise groups ($p < 0.01$) (83), while the other study found no significant change (72).

3.3 Results of individual sources of evidence

Appendix 2-Tables 2a to 6 present all the relevant data charted for each included source. For ease of reading, papers are grouped according to the non-localized effect studied and according to the type of article.

- Appendix 2-Table 2a shows non-RCT scientific papers studying non-localized effects on muscles located upstream or close to the cuffs
- Appendix 2-Table 2b shows RCT studies that investigate non-localized effects on muscles localized upstream or close to the cuff.
- Appendix 2-Table 3a shows non-RCT scientific papers studying non-localized effects on muscles located on another limb that is not restricted.
- Appendix 2-Table 3b shows RCT's studying non-localized effects on muscles located on another limb that is not restricted.
- Appendix 2-Table 4a shows non-RCT scientific papers studying non-localized effects on aerobic and anaerobic performance.
- Appendix 2-Table 4b shows RCT's and case series studying non-localized effects on aerobic and anaerobic performance.
- Appendix 2-Table 5 shows RCT's studying non-localized effects on whole-body composition.
- Appendix 2-Table 6 shows RCT's studying non-localized effects on blood homeostasis.

4 Discussion

4.1 Summary of our study

The main objective of this scoping review was to synthesize the existing literature on the non-localized effects of chronic BFR technique use and identify gaps for future research. Indeed, the starting point of this study lies in understanding the various benefits that BFR training can offer. Traditional resistance training without occlusion can increase maximum strength, hypertrophy, power (2,3), and functional capacity (4). However, this type of training is not suitable for everyone since it requires lifting heavy loads to achieve these benefits. BFR training, therefore, presents a potential alternative. During BFR training, metabolic stress is created, leading to muscular adaptations like those obtained through heavy-load resistance training. While the effects of BFR could be explained by these metabolic changes under the cuff, several studies (31–33) have shown that BFR does not exclusively have localized effects. They have reported non-localized effects distant from the BFR site, which opens new perspectives on the potential benefits of using BFR in muscle strengthening.

4.2 Results discussion

4.2.1 Non-localized effects on muscles located upstream or close to the cuffs

The results from the RCTs included in this scoping review show a significant positive effect for several parameters, such as maximal dynamic strength at the flat bench press or at the leg press and pectoralis major thickness.

Firstly, concerning pectoralis major thickness, a significant difference was demonstrated after resistance training in favor of the BFR group (31). Moreover, a group effect was also observed in favor of the BFR group (31). However, the systematic review by Pavlou et al. (43), which included the Yasuda study (31), came to a slightly different conclusion from ours. The authors of this quantitative study reported, with low-certainty evidence, an absence of a significant difference in pectoralis major thickness between the low-load BFR group and the low-load training group. Additionally, meta-analysis by Floco et al. suggests similar results (42). Indeed, although a trend was observed in favor of the BFR groups, chest circumference did not change significantly. Given these discrepancies between studies and the small number of studies included in the systematic review, further similar studies are needed to refine the results.

Secondly, our results for bench press maximum dynamic strength indicate a significant improvement in favor of the group over the control group after training (31). These results coincide with those found in a systematic review led by Pavlou et al. (43). Indeed, data with low certainty show a significant increase in 1-RM bench press after training for the BFR group compared to the low-load-only training group. Conversely, in meta-analysis by Floco et al. (42), no significant improvement was observed, although there was a trend in favor of the BFR group.

Similar conclusions can be drawn for dynamic leg press strength. Our results indicate a significant group effect in favor of the BFR group, but in the meta-analysis by Floco et al. (42), the authors indicate a non-significant increase in favor of BFR.

With regard to the CSA of the gluteus maximus, trunk extensor and iliopsoas muscles, our scoping review did not reveal any significant benefit in favor of the BFR.

Nevertheless, it is important to point out that one or two studies in our scoping review investigated these parameters, which could explain the contradictions with the systematic reviews or meta-analyses. Further studies are therefore needed to complete the results.

4.2.2 Non-localized effects on muscles located on another limb that is not restricted

It is essential that further studies be conducted to clarify the results in this category. Our scoping review does not allow us to draw or advance any clear conclusions. Regarding CSA, it appears that BFR does not provide any added value, as the three studies investigating this parameter did not find any significant results (32,46,51).

About elbow or grip strength, there are contradictory results. Indeed, some studies showed a cross-effect of BFR (46,89), while others did not (32).

Only studies on neuromuscular adaptations found concordant results in EMG amplitude, indicating that untrained non-occluded limbs were improved in groups training with a BFR located on another limb (50,51).

These last two results are consistent with the findings of the thesis conducted by May (47), suggesting that an upper body distance effect following BFR training in the lower limbs can occur. Indeed, this was demonstrated by a significant increase in 1-RM for elbow flexion that was not trained with BFR. This adaptation occurs without any muscle hypertrophy, but the results suggest neurological adaptations.

4.2.3 Aerobic and anaerobic parameters of performance

The findings of this scoping review indicate that the application of BFR during aerobic exercise has a significant positive effect on a range of aerobic and anaerobic performance parameters, including relative and absolute VO_2max and peak power output (PPO).

First, about aerobic performance parameters, a significant increase in post-intervention VO_2max values (relative or absolute) was demonstrated at both high and low intensities and with different types of exercise such as cycling, walking, running, sprinting, rowing and, even resistance training. Despite the absence of a statistically significant difference between the two groups, a non-significant trend in favor of the BFR group relative to the non-BFR group was highlighted. The results obtained in the RCTs included in this scoping review are consistent with several systematic reviews and meta-analyses that have demonstrated a significant improvement in aerobic capacity in favor of groups with BFR compared to those without (42,77–81). The meta-analysis conducted by Castilla et al. also demonstrated a highly significant effect size in favor of training with BFR compared to no BFR for VO_2max increase in a population of athletes, both in low-intensity and high-intensity training (76).

Regarding maximal aerobic power, while some studies have identified a significant effect of time on post-intervention measures, no additional value of BFR application could be demonstrated in comparison with the overall study groups.

With regard to anaerobic performance parameters, the RCTs included in this review appear to indicate a significant improvement in PPO at the conclusion of the BFR intervention in healthy adults, some of whom are relatively active or trained in their discipline. However, the added benefit of BFR is less discernible, as some outcomes observed in groups with BFR are comparable to those of HIIT groups without BFR yet appear to surpass those of a low-intensity group without BFR. The systematic review conducted by Chua et al. yielded comparable outcomes (81), indicating that the incorporation of BFR into submaximal HIIT or mixed-intensity exercise interventions resulted in enhanced improvements in anaerobic components (PPO, mean power output (MPO)) compared to interventions without BFR.

Finally, about VO_2peak and MPO, the results of the RCTs are more heterogeneous, both in terms of the time effect and the group effect. Further research is required on these parameters.

In terms of exercise intensity, low-intensity aerobic exercise has been demonstrated to induce greater cardio-respiratory adaptations and, consequently, enhance aerobic capacity when BFR is applied, in comparison to when it is not. However, high-intensity aerobic exercise has been shown to elicit comparable positive adaptations, or even a slight advantage for the group without BFR, as evidenced by the meta-analysis conducted by Formiga et al. (19). The application of BFR would therefore seem to be of particular interest to subjects who are unable to train at high intensity. A recent meta-analysis by Floco et al. revealed that even among endurance-trained athletes (42), the increase in VO_2max was significantly higher in the BFR group during low-intensity exercise compared to high-intensity exercise without BFR.

4.2.4 Body composition

The majority of studies selected for this scoping review indicate that completion of a training program (with or without BFR) is significantly superior to the control group in terms of fat mass reduction, body fat percentage, and fat-free mass increase. However, given the discrepancies in the results of the studies selected for this review, further research is necessary to assess the true added value of BFR application in improving various body composition parameters. Nevertheless, this review has identified encouraging preliminary results concerning the use of BFR in obese young people and adults with chronic kidney disease.

In the first instance, three studies showed significantly better results for the exercise group with BFR compared to the exercise group without BFR and to the control group in terms of fat mass or body fat percentage both generally and localized (trunk, subcutaneous abdominal) (82,86,87), as well as for waist circumference (87). Two of these three studies included were conducted on obese young adults (82,87). Each of these studies involved two cycling sessions per week over a 12-week period, with one group performing high-intensity exercises (82) and the other performing low-intensity exercises (87). Moreover, in one of these studies led by Li et al. (82), the application of BFR during the rest phases between sprint repetitions was found to be significantly more effective in reducing abdominal visceral fat area than the application of BFR during sprints or to the other groups.

Furthermore, two RCTs included in this scoping review that selected participants with chronic kidney disease achieved similar results (83,84). Both studies performed a resistance training program of 3 sessions per week for 6 months for both exercise groups, and the BFR group (cuffs maintained at 50% of resting systolic pressure) exhibited a lower percentage of 1-RM than the non-BFR group (83,84). At the end of the intervention, significant improvements in body fat mass or body fat percentage, fat free mass and BMI were demonstrated in both resistance training groups (equal with or without BFR) and were significantly greater than the control group that did not engage in exercise (83,84).

4.2.5 Blood homeostasis

Most of the studies included showed that performing a training program with or without BFR is significantly superior to the control group in terms of reducing blood glucose, total cholesterol, LDL-C, eGRF and triglycerides. However, the BFR training program is even more interesting when it comes to an obese population (82,84,87) or adults with chronic kidney disease (83,88). In fact, all the studies with significant results were carried out on this type of patient. Conversely, the studies with no significant results concerning blood homeostasis measurements were carried out on trained patients (master road cyclists) (73) or patients with a previous cardiac history (72).

Firstly, three studies showed a decrease in post-training blood glucose levels for the group performing an exercise program with or without BFR compared with the control group (82,83,87). Of these three, two studies with either a low- or high-intensity aerobic exercise program found a significant group effect in favor of the BFR group (57,82). The third study found no group effect between the different exercise groups, with or without BFR (83). Nevertheless, the intensity of the program performed by the BFR group was lower for similar results than the non-BFR group. Thus, a low-intensity aerobic or resistance program with BFR would add value to the same training without BFR.

Then, three studies showed significantly better results for the group performing an aerobic (87), HITT (82), or resistance exercise program (83) with or without BFR compared to the control group regarding total cholesterol. However, the study by Chen et al. investigating two aerobic exercise program groups showed a significant group effect in favor of BFR (87), while the other two studies observed no difference between exercise groups (82,83). The study by Williams et al., cited in the study by Chen et al., may explain this difference. Indeed, the authors concluded that aerobic exercise was superior to resistance exercise in terms of improving blood lipid levels (90). Therefore, the protocols of the studies that found no group effect, resistance exercise, or HITT, may not have been the most appropriate to observe a group effect between those with a BFR or those without.

Regarding the different types of cholesterol, this scoping review indicates that LDL-C levels were significantly reduced after training in groups using the BFR (73,87). Unlike the other measures, this was also significant for master road cyclists (73). A similar hypothesis concerning the effect of LDL-C on a group effect in favor of BFR can be made. Indeed, the only study with no significant results used a resistance program (83), while the others carried out an aerobic program (73,87). Furthermore, this review shows no significant effect on HDL-C in this population.

Additionally, in three studies, the effect of an exercise program on obese people or those with chronic kidney disease was significantly positive in terms of triglyceride levels (57,82,83). For the two studies on obese patients, the hypothesis mentioned above can be applied. Aerobic programs with BFR could add value to triglycerides compared with other types of training. Indeed, the study by Chen et al. (57) showed a significant difference between exercise groups in favor of BFR, while the study led by Li et al. (82), using a high-intensity program, observed no difference.

On the other hand, in the study by Deus et al. (83), involving patients with chronic kidney disease, this hypothesis was not confirmed, as a significant time and group effect were only observed in the group performing a resistance program without BFR. However, the delta, i.e., the change between the start and end of training, was significant for both groups, i.e., resistance with and without BFR, compared with the control group.

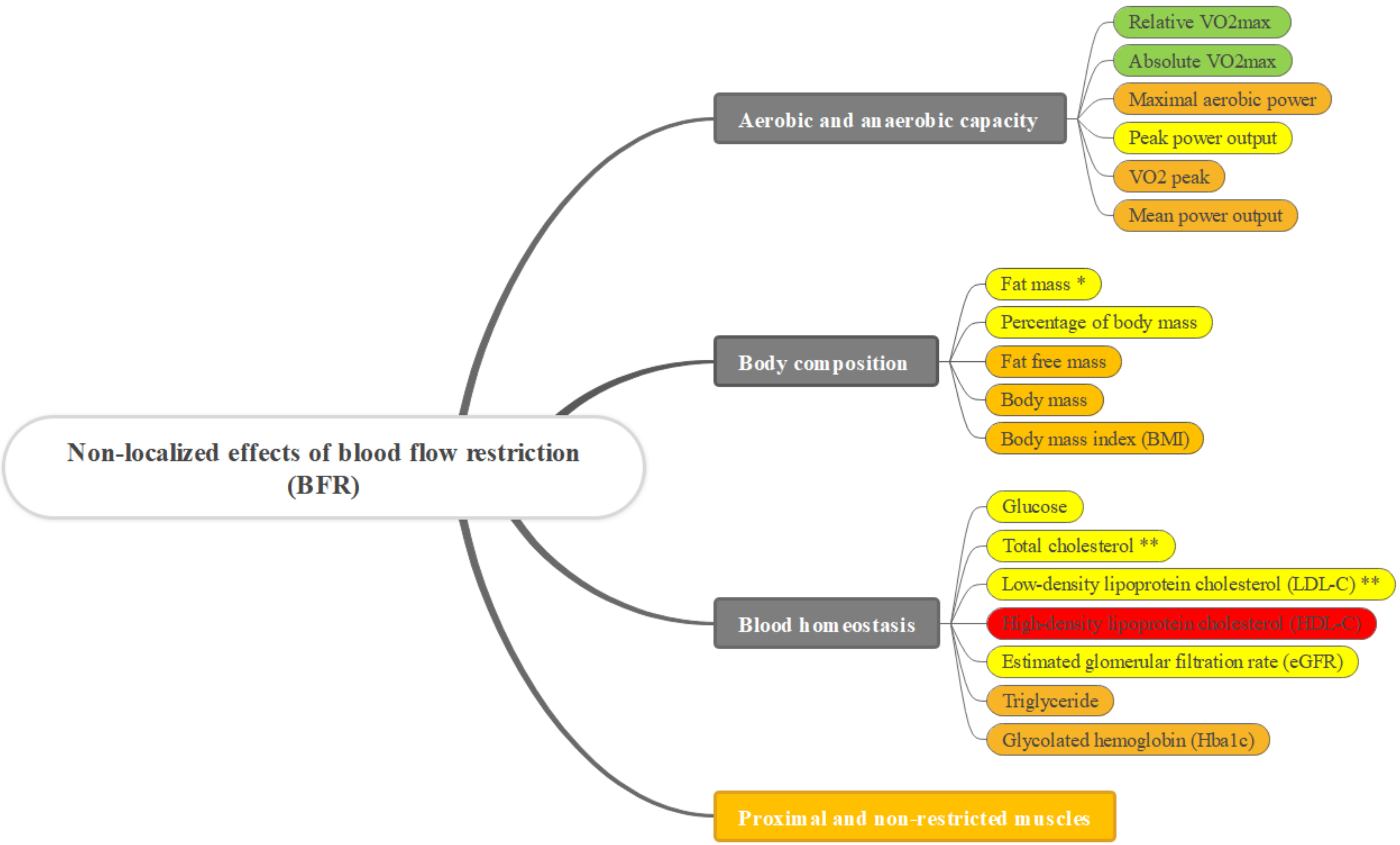
Finally, three RCTs involving participants with chronic kidney disease obtained similar results (83,84,88). All showed a significant decrease in eGRF in the exercise groups compared with the control group after resistance training. Although no significant difference could be demonstrated between the different exercise groups, with and without BFR, in two studies (83,84), the exercise program in the BFR group was carried out at a lower intensity. In both studies, patients in the different groups were required to perform the same number of repetitions and sets, but the percentage of 1-RM was lower in the groups using BFR.

However, given the discrepancies between the results of the studies selected for this review, further research is needed to assess the true added value of BFR application in improving the various parameters of blood homeostasis.

4.2.6 Summary of results and discussion in diagram form

The discussion of our results is synthesized in visual form in this diagram (see Figure 2). It is important to note that, given the limitations of this scoping review (see section 5), this diagram is only a draft and should be interpreted with a critical mindset. Nevertheless, it serves primarily to highlight issues to be clarified in future studies concerning the non-localized effects of BFR.

Figure 2: summary diagram of results and discussion



Legend:
- Proven positive effects of the BFR
- Slightly divergent results in favor of BFR
- Results too divergent
- No proven positive effects of the BFR

* For patient suffering from obesity or chronic kidney disease
** For aerobic programs

4.3 Future Research

4.3.1 Post-infarction heart failure Patients

Patients with chronic heart failure (CHF) frequently experience a reduction in exercise capacity, which also affects their quality of life (91,92). A key determinant of this reduction is muscle atrophy, since in these patients (but not healthy subjects), muscle mass significantly influences VO_2peak (93). The current international clinical guidelines recognize exercise-based cardiac rehabilitation as a Class 1 recommendation for all CHF patients to improve health-related quality of life and exercise capacity (92,94,95).

A study led by Tanaka et al. analyzed the non-localized effects of BFR (cuff applied proximally to both thighs) on VO_2peak values in adults with post-infarction heart failure (72). The group with BFR applied during cycling sessions (three 15-minute sessions a week for 6 months) significantly increased their post-intervention VO_2peak values compared to baseline (within group) and compared to the control group without BFR (between groups) (72). The limitations of this study include a relatively small sample size (n=30) and its all-male composition (72).

Further research is therefore warranted to assess the potential impact of BFR application during aerobic exercise on exercise capacity and quality of life in this population of patients. To enhance the clinical relevance of the study conducted by Tanaka et al., future investigations should include a greater number of participants, comprising both men and women.

4.3.2 Cancer and Sarcopenia

Chemotherapy is a common treatment for cancer. Although it improves the prognosis for survival, chemotherapy and the cancer itself generate a series of short- and long-term side effects, such as fatigue, reduced cardiorespiratory function, and sarcopenia (96–100), all of which have a significant impact on patient’s quality of life (101–103). It has been demonstrated that physical activity can be an effective non-pharmacological adjunctive treatment for mitigating the adverse effects of cancer and chemotherapy (104–111). In regard to the various physical activity modalities, it has been demonstrated that the higher the intensity, the more favorable the results (111,112). Furthermore, a combination of aerobic and resistance exercise has been shown to be more effective than an aerobic exercise program alone (113–116).

It has been demonstrated in previous studies that low-intensity BFR training produces more favorable adaptations than the same training without BFR, or produces similar results to high-intensity training without BFR in terms of muscle strength and hypertrophy of muscles downstream of the cuff (19,20). Furthermore, this scoping review highlighted a significant improvement in cardiorespiratory function (VO_2max, PPO).

It would then be beneficial to conduct studies in patients with cancer that examine the efficacy of BFR in conjunction with low-intensity (due to chronic fatigue) aerobic and resistance exercise, in comparison to the current standard of care involving non-BFR exercise. This would help assess its potential impact on adverse effects such as sarcopenia and reduced cardiorespiratory function.

4.3.3 Diabetes and metabolic syndrome

The treatment of type 2 diabetes involves an individualized, multimodal treatment plan to maintain optimal blood glucose and lipid levels. Regular physical activity has been shown to improve diabetes management by improving β-cell function (117), insulin sensitivity (118), gut microbiota (119–121) and vascular function (122,123). Additionally, an improvement in insulin sensitivity after physical activity lasts for several hours, depending on the intensity of the activity (124). Physical activity is therefore an integral part of the treatment of type 2 diabetes.

According to the recommendations of the American College of Sport Medicine, high-intensity aerobic exercise or a high-intensity resistance program are generally considered superior to low-intensity training, although they still have positive effects (117). Based on this observation and the results of our scoping review indicating a significant reduction in blood glucose and lipid levels in favor of BFR in obese populations or those with chronic kidney disease, future studies on diabetic patients would be interesting to see the effect of a low-intensity BFR program compared with the current treatment of diabetes.

Moreover, type 2 diabetes is often preceded by metabolic syndrome (125). In fact, metabolic syndrome increases the risk of developing type 2 diabetes by a factor of 5 (126,127). Metabolic syndrome includes several disorders such as insulin resistance, hypertension, and dyslipidemia, often associated with abdominal obesity (128). In view of our results on glucose levels and body composition indicating a positive trend towards BFR training, further studies with patients with metabolic syndrome could be conducted. This would demonstrate whether BFR training has an added value compared with physical activity, which is recommended for this type of patient (129).

5 Limitations

One of the main limitations of this scoping review limitation concerns the type of population. Only 8 out of 56 studies were carried out on pathological populations, which limits interpretations to clinical practice. Indeed, adaptations and damage may differ between this type of population and the general population. The pathologies studied in these papers were also not very diversified. Out of the 8 studies, three involved patients with chronic kidney disease (83,84,88), two others were carried out on obese people (82,87), and for the last three studies, they involved patients with urinary incontinence (40), recurrent back pain (41) or post-infarction heart failure (72). In addition, the sample size for half of these studies remained small, at around 30 patients. This low diversity of pathologies and small number of patients complicates the generalization of clinical conclusions and recommendations.

Another major limitation is the lack of homogeneity in the protocols used in all the studies included. Regarding training modalities, the number of repetitions, sets, and sessions per week differed from one study to another. In addition, the training duration ranged from one week to several months. There was also variability in pressure modalities. Studies used either elastic belts or pressure cuffs with different widths and occlusion pressures. Finally, population homogeneity was also lacking. Populations ranged from trained athletes to sedentary or pathological populations. In short, all these discrepancies within current BFR training protocols make it difficult to compare studies and draw clear conclusions.

Additionally, for each category of non-localized effects, many measures have only been studied in one or two studies, which makes it impossible to generalize conclusions. Further studies for these measures need to be carried out to clarify trends and reach clear conclusions.

Finally, only studies in English and French were included in this review. Relevant studies may have been excluded during our screening.

6 Conclusion

The objective of this scoping review was to examine the extant literature on the non-localized effects of chronic use of the BFR technique and to identify potential avenues for future research. Non-localized effects due to the use of BFR during exercise have been demonstrated on various aerobic and anaerobic performance parameters (mainly VO_2max and PPO), body composition (percentage of fat mass and lean mass), blood homeostasis (glucose levels, total cholesterol, LDL-C, eGRF and triglycerides), and neuromuscular adaptations (EMG amplitude). The use of BFR seems to be of particular interest for individuals who cannot exercise at high intensity, as demonstrated in this review for adults with chronic heart failure, chronic kidney disease and young obese patients. While some initial results are encouraging, they must be interpreted with caution due to the limitations previously mentioned. The most significant limitations are the heterogeneity of the protocols and the diverse types of sample populations, which included a relatively small number of participants with a pathology. Future research should therefore include a larger number of patients with a wider range of pathological conditions in order to generate more statistically and clinically significant results and enable comparisons between subpopulations.

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8 Appendixes

Appendix 1: search equations and websites

Search equation for PubMed:

((humans[MeSH Terms]) AND ((Blood Flow Restriction Therapy[MeSH Terms]) OR ("blood flow restriction "[Title/Abstract] OR "blood flow restriction exercise " [Title/Abstract] OR "kaatsu " [Title/Abstract] OR "kaatsu training " [Title/Abstract] OR "blood flow restriction therapy " [Title/Abstract] OR "occlusion training " [Title/Abstract] OR "vascular occlusion training "[Title/Abstract]))) AND ((((Abdominal Muscles[MeSH Terms]) OR (Back Muscles[MeSH Terms])) OR (oxygen consumption[MeSH Terms])) OR (("remote " [Title/Abstract] OR "cross-transfer " [Title/Abstract] OR "cross transfer " [Title/Abstract] OR "mirror activation " [Title/Abstract] OR "non localized " [Title/Abstract] OR "non-localized " [Title/Abstract] OR "unrestricted leg " [Title/Abstract] OR "untrained arm " [Title/Abstract] OR "untrained limb " [Title/Abstract] OR "cross over " [Title/Abstract] OR "contralateral "[Title/Abstract])) OR ("abdomen muscle " [Title/Abstract] OR "abdominal muscle " [Title/Abstract] OR "abdominal muscles " [Title/Abstract] OR "abdominal musculature " [Title/Abstract]) OR ("intermediate back muscles " [Title/Abstract] OR "muscle, back " [Title/Abstract] OR "spine musculature " [Title/Abstract] OR "superficial back muscles " [Title/Abstract] OR "maximal oxygen uptake " [Title/Abstract] OR "maximal aerobic capacity " [Title/Abstract] OR "maximal oxygen consumption " [Title/Abstract] OR "maximum aerobic capacity " [Title/Abstract] OR "maximum oxygen consumption " [Title/Abstract] OR "maximum oxygen uptake " [Title/Abstract] OR "vo2 max " [Title/Abstract] OR "vo2max " [Title/Abstract] OR "aerobic capacity " [Title/Abstract] OR "aerobic power " [Title/Abstract] OR "anaerobic capacity " [Title/Abstract]) OR ("O2 consumption " [Title/Abstract] OR "o2 uptake " [Title/Abstract] OR "oxygen demand " [Title/Abstract] OR "oxygen intake " [Title/Abstract] OR "oxygen requirement " [Title/Abstract] OR "oxygen uptake " [Title/Abstract] OR "oxygen utilization "[Title/Abstract]))

Search equation for Scopus:

(TITLE-ABS-KEY ("human") AND TITLE-ABS-KEY ("blood flow restriction " OR "blood flow restriction exercise " OR "kaatsu " OR "kaatsu training " OR "blood flow restriction therapy " OR "occlusion training " OR "vascular occlusion training ") AND TITLE-ABS-KEY ("remote " OR "cross-transfer " OR "cross transfer " OR "mirror activation " OR "non localized " OR "non-localized " OR "unrestricted leg " OR "unrestricted arm" OR "unrestricted limb" OR "untrained arm " OR "untrained limb " OR "cross over " OR "contralateral" OR "abdominal wall musculature " OR "abdomen muscle " OR "abdominal muscle " OR "abdominal muscles " OR "abdominal musculature " OR "back muscle " OR "intermediate back muscles " OR "muscle, back " OR "spine musculature " OR "superficial back muscles " OR "maximal oxygen uptake " OR "maximal aerobic capacity " OR "maximal oxygen consumption " OR "maximum aerobic capacity " OR "maximum oxygen consumption " OR "maximum oxygen uptake " OR "vo2 max " OR "vo2max " OR "aerobic capacity " OR "aerobic power " OR "anaerobic capacity " OR "oxygen consumption " OR "O2 consumption " OR "o2 uptake " OR "oxygen demand " OR "oxygen intake " OR "oxygen requirement " OR "oxygen uptake " OR "oxygen utilization"))

Search equation for Embase

('human'/exp) AND ('blood flow restriction'/exp OR 'blood flow restriction' OR 'blood flow restriction exercise':ti,ab,kw OR 'kaatsu':ti,ab,kw OR 'kaatsu training':ti,ab,kw OR 'blood flow restriction therapy':ti,ab,kw OR 'occlusion training':ti,ab,kw OR 'vascular occlusion training':ti,ab,kw) AND ('remote':ti,ab,kw OR 'cross-transfer':ti,ab,kw OR 'cross transfer':ti,ab,kw OR 'mirror activation':ti,ab,kw OR 'non localize':ti,ab,kw OR 'non-localize':ti,ab,kw OR 'non localized':ti,ab,kw OR 'non-localized':ti,ab,kw OR 'unrestricted arm':ti,ab,kw OR 'unrestricted leg':ti,ab,kw OR 'unrestricted limb':ti,ab,kw OR 'untrained arm':ti,ab,kw OR 'untrained limb':ti,ab,kw OR 'cross over':ti,ab,kw OR 'contralateral':ti,ab,kw OR 'abdominal wall musculature'/exp OR 'abdomen muscle':ti,ab,kw OR 'abdominal muscle':ti,ab,kw OR 'abdominal muscles':ti,ab,kw OR 'abdominal musculature':ti,ab,kw OR 'musculus abdominis':ti,ab,kw OR 'back muscle'/exp OR 'back muscles':ti,ab,kw OR 'intermediate back muscles':ti,ab,kw OR 'muscle, back':ti,ab,kw OR 'spine musculature':ti,ab,kw OR 'superficial back muscles':ti,ab,kw OR 'maximal oxygen uptake'/exp OR 'maximal aerobic capacity':ti,ab,kw OR 'maximal consumption of oxygen':ti,ab,kw OR 'maximal oxygen consumption':ti,ab,kw OR 'maximal uptake of oxygen':ti,ab,kw OR 'maximum aerobic capacity':ti,ab,kw OR 'maximum oxygen consumption':ti,ab,kw OR 'maximum oxygen uptake':ti,ab,kw OR 'oxygen maximal uptake':ti,ab,kw OR 'vo2 max':ti,ab,kw OR 'vo2max':ti,ab,kw OR 'aerobic capacity'/exp OR 'aerobic metabolism capacity':ti,ab,kw OR 'aerobic power':ti,ab,kw OR 'anaerobic capacity'/exp OR 'anaerobic metabolism capacity':ti,ab,kw OR 'oxygen consumption'/exp OR 'O2 consumption':ti,ab,kw OR 'o2 uptake':ti,ab,kw OR 'oxygen demand':ti,ab,kw OR 'oxygen intake':ti,ab,kw OR 'oxygen requirement':ti,ab,kw OR 'oxygen uptake':ti,ab,kw OR 'oxygen utilization':ti,ab,kw)

Search equations for Google Scholar

human and blood flow restriction training and remote effects
human and blood flow restriction training and trunk muscles
human and blood flow restriction training and aerobic capacities

Websites for the "Grey litterature"

https://www.who.int/
https://www.sportaus.gov.au
https://www.apta.org/
https://australian.physio/
https://www.ais.gov.au/
https://www.cihi.ca/en
https://www.sanfordhealth.org/
https://kce.fgov.be/fr
https://world.physio
https://reporter.nih.gov/
https://www.nlm.nih.gov/hsrph.html
https://www.crd.york.ac.uk/prospero/
https://clinicaltrials.gov/
https://trialsearch.who.int/Default.aspx
https://www.isrctn.com/

Appendix 2: tables of results

Table 2a: scientific papers studying non-localized effects on muscles located upstream or close to the cuffs

Author	Review goal	Number of articles in the review	Conclusions – key points
Floco, 2023 (42) – Systematic Review and Meta-Analysis	To compare the effect of low load with BFR training and high load training without BFR in a population of healthy athletes.	14 (Systematic Review) 7 (Meta-Analysis)	For chest girth, the results of the meta-analysis do not show any significant differences between the two groups (p=89) but the results suggest a difference in favor of the experimental group (MD = 0.22, 95%, Confidence Interval = - 2.83, 3.27) For the bench press and squat, the meta-analysis showed non-significant results in favor of the BFR group. (p=0.1, p=0.06 respectively).
Pavlou, 2023 (43) – Systematic Review with Meta-Analysis	To assess the impact of low-load training with the BFR on tissue adaptations in the different muscle groups proximally to the cuff.	9 (Systematic Review) 6 (Meta-Analysis)	In terms of strength, there was a significant increase in bench press (SMD = 0.87) and shoulder flexion strength (SMD = 1.64) in the LL-BFRT group compared to the non-BFR group. In contrast, between the LL-BFR and HL-RT groups, there was no significant difference (SMD = -0.17) between them for the bench press. Conflicting evidence was found for abduction, scapation, internal and external rotation movements. No differences were found for back and shoulder muscles between the different groups. About muscle size, a significant increase in shoulder lean mass (kg) was observed in favor of the LL-BFRT group (MD = 0.18) compared with the LL-RT group. No significant differences were found in pectoralis major thickness or chest circumference. On the other hand, between the LL-BFRT and HL-RT groups, a significant increase was found in favor of the BFR group only for pectoralis major thickness, while the other muscles did not observe significant increase.
Dankel, 2016 (44) – Narrative Review	To analyse the impact of BFR training and the training variables used on the size and strength of the upper body muscles.	19	Increased muscle size and strength in groups close to the cuff.

Table 2b: RCT's studying non-localized effects on muscles located upstream or close to the cuffs.

Author – article type	Sample, age, and groups	Training program	BFR material, cuff site(s) and occlusion pressure	Measures	Results for non-localized effects
Abe, 2010b (45) – R.C.T.	19 men and women Age: between 60 to 78 yrs Groups: **INT**: BFR-walk. **CON**: no exercise.	30 sessions, 5x/wks for 6wks INT: walking on a treadmill at 67 m/min for 20 min. CON: daily physical activity.	Pressure belts (Kaatsu-Master, Sato Sports Plaza, Tokyo, Japan) On both legs Initial pressure at 160 mmHg increased by 10 mmHg each wk. Final pressure: 210 mmHg	Trunk skeletal mass	No significant change (p>0.05) in trunk skeletal mass for INT and CON groups for pre-to-post intervention values.
Ampomah, 2019 (41) – R.C.T.	32 subjects with recurrent low back pain Age: between 18 and 50 yrs Groups: **BFR**: exercises with BFR **CON**: exercises without BFR	20 sessions, 2x/wk for 10 wks BFR: 3 sets of leg extension, plantar flexion, elbow flexion with BFR on upper limb for exercises with upper limb and on lower limb for exercises with lower limb (30–60 sec rest between sets), then 3 sets of trunk extension for 15 reps (30–60 sec rest between sets) with BFR on upper limb. All exercises done at 25% of 1-RM. BFR applied continuously even during rest periods. CON: 3 sets of leg extension, plantar flexion, elbow flexion without BFR (30–60 sec rest between sets), then 3 sets of	Pneumatic cuff Proximal portion of the leg and proximal portion of the arm Capillary refill time of the leg just above the knee (for the leg pressure cuff) or the palms of the hands (for the arm pressure cuff) is between 2 and 3 sec.	CSA Trunk extensor Trunk extensor muscle strength	No significant change in trunk extensor CSA within or between groups at primary endpoint (BFR: p=0.2; CON: p=0.5; group difference: p=0.5) and at the secondary endpoint (BFR: p=0.8; CON: p=0.5; group difference, p=0.8). No significant change in trunk extensor strength within and between group at the first endpoint (BFR: p=0.6; CON: p =0.3); group difference (p=0.7). At the secondary endpoint, significant improvement in trunk extensor strength for CON (p=0.03), not for BFR (p=0.9). Significant difference between groups (p=0.04).

		trunk extension for 15 reps (30–60 sec rest between sets). All exercises done at 25% of 1-RM.		Trunk extensor muscle endurance	No significant change for trunk extensor muscle in endurance at the first endpoint (BFR: p=0.2; CON: p=0.2), No difference between groups (p=0.8). At the secondary endpoint, significant change for the CON (p=0.01), but not the BFR (p=0.5). No difference between groups (p=0.09).
Due, 2019 (40) – R.C.T.	31 women with stress urinary incontinence <u>Age:</u> 45 (35-72) yrs <u>Groups:</u> **INT**: PFMT with BFR **CON**: PFMT without BFR	48 sessions, 4x/wks for 12 wks <u>Both groups:</u> 3 sets of 12 pelvic floor muscle contractions at 50-60% of 1-RM. <u>INT group:</u> BFR performed directly after PFMT. Two sets of 15 sitting knee extensions at 50% of 1-RM and giving at least 13/20 on a modified Borg scale.	Pressure cuff (VBM Medizintechnik GmbH) Placed proximally around the thigh Pressure set at 100 mmHg	Severity and impact on quality of life of urinary incontinence (ICIQ-SF) Number of leakage episodes	Significant improvement for INT (p=0.011) and CON (p=0.002) groups from pre- to post-intervention in ICIQ-SF scores. No significant difference between group (p=0.47). Number of leakages decreased for pre- to post-intervention for INT with a trend of significance (p=0.054) and CON (p=0.020) groups. No significant difference between group post intervention (p=0.15).
Libardi, 2015 (39) – R.C.T.	25 older individuals <u>Age:</u> **CT**: 65 ± 3.7 yrs **BFR-CT**: 64 ± 4 yrs **CTRL**: 65 ± 4 yrs <u>Groups:</u> **CT**: endurance training and HI-RT without BFR **BFR-CT**: endurance + RT with BFR **CTRL**: endurance and RT	48 sessions, 4x/wk for 12 wks <u>For all:</u> walking and running at 60 to 85% VO_2max for 40 min for the first 6 wks and then increased to 50 min for the next 6 wks. <u>HI-RT without BFR:</u> 4×10 reps 70% 1-RM in the leg press exercise for the first 6 wks then increased to 80% 1RM for the next 6 wks. <u>RT with BFR:</u> 30/15/15/15 reps, 1-min rest between set at 20% 1-RM for the first 6 wks and then	Pneumatic cuff Placed in the inguinal fold Pressure set at 50% of the AOP	1RM 45° leg-press test	CT and BFR-CT groups increased the leg press 1-RM values for pre- to post-test (p<0.001 and, p=0.001). No significant difference between these two groups at post-test. No significant difference for pre- to post-test values for the control group.

		increased at 30% of 1-RM for the next 6 wks. BFR applied all time.			
Sakamaki, 2011 (33) – R.C.T.	17 healthy men Age: 21.2 ± 1.9 yrs Groups: **BFR-walk**: walk training with BFR **CON-walk**: walk training without BFR	36 sessions, 2x/day, 6 days/wk for 3 wks For both: Supervised walk training on a treadmill at 50m/min. 5 2-min bouts. 1 min rest period BFR-walk: BFR is maintained even during rest periods.	Elastic cuffs Proximal portion of each leg 160 mmHg. The pressure was increased by 10 mmHg each day until a final belt pressure of 230 mmHg	CSA for para-spinal muscles (L4-L5), iliopsoas, gluteus maximus	No significant changes in CSA for gluteus maximus and para-spinal muscles for BFR-walk and CON-walk for pre-to-post values and between groups after the intervention ($p>0.05$). CSA of iliopsoas tended to increase for the BFR-walk group for pre-to-post values ($p=0.07$).
Yasuda, 2010 (31) – R.C.T.	10 healthy men Age: **BFR-T**: 25.8 ± 6.3 yrs **CON-T**: 25.6 ± 3.2 yrs Groups: **BFR-T**: flat bench press exercise with BFR **CON-T**: flat bench press exercise without BFR	24 sessions, 2x/day, 6 days/wk for 2 wks For both: free weight flat bench press exercise at 30 % of 1-RM. 30-15-15-15 reps. 30 sec rest between set BFR-T: BFR is maintained even during rest periods.	Elastic cuffs Proximal region of both arms during training 100 mmHg increased by 10 mmHg until 160 mmHg	Muscle thickness with ultrasound: pectoralis major (MTH) Maximal dynamic strength (1-RM)	Significant increase of MTH for pectoralis major for BFR-T ($P<0.05$) with an increase of 16 % for pre-to-post intervention. Significant difference between BFR-T and CON-T after the intervention ($p<0.05$). No significant change in MTH for pectoralis major for CON-T ($p>0.05$) for pre-to-post values. Significant difference between CON-T and BFR-T for the bench press 1-RM test ($p<0.05$). BFR-T (6%), CON-T (-2%) at the end of the intervention.

Legend: 1-RM=1-Repetition Maximum, BFR=blood flow restriction, min=minute, HI=high-intensity, PFMT=pelvic floor muscle training, R.C.T.=randomized controlled trial, reps=repetitions, RT=resistance training, sec=second, wk=week, wks=weeks, yrs=year, CSA= Cross sectional area

Table 3a: scientific papers studying non-localized effects on muscles located on another limb that is not restricted.

Author	Goal	Conclusions – key points
May, 2018 (47) – PhD Thesis	Contributing to a greater understanding of the local and remote mechanisms that regulate skeletal muscle adaptations to blood flow restriction training.	Upper body remote effect following blood flow restriction training at lower limb can occur. This was demonstrated by a significant increase in 1-RM for elbow flexion that was not trained with the BFR. (See table 3b – May, 2018). This remote adaptation occurs without any muscle hypertrophy. This adaptation suggests a neurological adaptation. However, these remote adaptations should be investigated. Presently, results suggest neurological adaptations like neuroplasticity. The blood flow restriction training could increase stimulation of the lower limb in the motor cortex which may have also increased drive to the control site for arms. This change in excitability could be measured by transcranial magnetic stimulation by measuring the amplitude of motor evoked potentials.

Table 3b: RCT's studying non-localized effects on muscles located on another limb that is not restricted.

Author – article type	Sample, age and groups	Training program	BFR material, cuff site(s) and occlusion pressure	Measures	Results for non-localized effects
Bowman, 2019 (49)– R.C.T.	27 healthy patients <u>Age:</u> 20 to 40 yrs <u>Groups:</u> **BFR:** Exercises with BFR **CON:** Exercises without BFR	12 training sessions, 2 x/wk for 6 wks <u>BFR:</u> straight-leg raise hip flexion, side-lying hip abduction, long-arc quadriceps extension, and standing hamstring curl at 30% 1-RM, 30 – 15 – 15 – 15 reps, 30 sec rest between sets. Performed on both sides. One limb with BFR and one limb without BFR. BFR applied during all the exercises, even during rest periods. <u>CON:</u> straight-leg raise hip flexion, side-lying hip abduction, long-arc quadriceps extension, and standing hamstring curl. Performed on both sides. Both limbs without BFR.	Pneumatic cuff (Delfi Personalized Tourniquet System 4-inch wide) Proximal portion of the chosen lower limb 80% of the AOP to the extremity – recalibrated weekly	Knee extension and flexion, hip abduction and extension, plantar flexion, thigh and leg circumference, single leg-heel raise of the unrestricted lower limb	Significant increase between BFR and CON in thigh circumference (p=0.01), greater peak torque during knee extension (p=0.04) and higher number of single leg-heel raise (p=0.02).

Bowman, 2020 (48) – R.C.T.	24 healthy subjects <u>Age:</u> 26.2 ± 3.4 yrs <u>Groups:</u> **BFR**: exercises with BFR **CON**: exercises without BFR	12 training sessions, 2x/wk for 6 wks <u>For both:</u> external rotation in the side-lying position, internal rotation standing with a pulley, biceps curl while standing with the palm up, triceps extension while supine with 90° of shoulder flexion, and prone horizontal shoulder abduction off the side of the table with the palm down. performed on both sides at 30% 1-RM, 30 – 15 – 15 – 15 reps, 30 sec rest between sets. <u>BFR:</u> BFR on one limb for the entire session and without BFR on the other limb. BFR applied during all the exercises, even during rest periods.	Pneumatic cuff (Delfi Personalized Tourniquet System 4-inch wide) Applied to the upper arm of the subject's preferred limb 60% of AOP in the extremity	shoulder internal and external rotations, shoulder scaption, shoulder flexion, shoulder abduction, elbow flexion, elbow extension, grip strength, arm circumference, forearm circumference	Significant difference between BFR and CON after the intervention for the grip strength for the upper limbs without occlusion ($p<0.01$). No significant difference between groups post-intervention in circumference and strength parameters (except grip strength) for the unrestricted limb ($p>0.05$).
Hill, 2020 (50) – R.C.T.	36 healthy women <u>Age:</u> 22 ± 2 yrs <u>Groups:</u> **ECC**: Eccentric with BFR. **CON**: Concentric with BFR. **Control**: no intervention.	12 sessions, 3x/wk for 4 wks <u>For both:</u> untrained arm performed a warm-up (10-15 submaximal contractions) and maximal strength testing on the baseline. <u>ECC:</u> elbow extension (eccentric) in one upper limb randomly chosen. At 30% 1-RM. 30 – 15 – 15 – 15 reps, 30 sec rest between sets. BFR is applied continuously even during the rest period. <u>CON:</u> elbow flexion (concentric) in one upper limb randomly chosen. At 30% 1-RM. 30 – 15 – 15 – 15 reps, 30 sec rest between sets. BFR is applied continuously even during the rest period.	Pneumatic cuff. (30-mm wide cuff) (KAATSU Master, Sato Sports Plaza, Tokyo, Japan) Applied to the most proximal portion of the upper arm. Pressure was set at 40% of AOP	Eccentric and concentric peak torque Neuromuscular adaptation of the untrained limb Thickness of the biceps brachii in an untrained limb	Significant increase in peak torque in the ECC group for pre- to post-intervention values at wk 2 and wk 4 ($p<0.05$). No significant difference between wk 2 and wk 4 ($p>0.05$). No significant difference in CON group and control group ($p>0.05$). EMG amplitude increased in the ECC and CON groups for pre- to post-values from 0 to 2 wks and 4 wks and increased from 2 wks to 4 wks ($p<0.05$). No significant difference ($p>0.05$) between groups or interactions (time x group). No significant difference in all groups for muscle thickness ($p>0.05$).

Madarame, 2008 (32) - R.C.T.	15 healthy men Age: **OCC**: 21.6 ± 2.4 yrs **NOR**: 21.9 ± 4.2 yrs Groups: **OCC**: training with BFR. Trained arm named OCC-T and untrained arm named OCC-C. **NOR**: training without BFR. Trained arm named NOR-T and untrained arm named NOR-C.	20 sessions, 2x/wk for 10 wks Both groups: dumbbell curl, 3x10 reps at 50% 1-RM without BFR for one of the two upper limbs randomly chosen. The other upper limb was the control one. OCC: knee extension, knee flexion, 30 - 15 - 15 reps. 30 sec rest period between sets. 30% 1-RM with BFR maintained even during rest periods. NOR: knee extension, knee flexion, 30 - 15 - 15 reps. Rest period of 30 sec between sets and training load of 30% 1-RM without BFR.	Elastic belt: width 4cm, length 175cm Proximal portions of both sides of their thighs 160 mmHg during the first 2 wks, increased by 20 mmHg every 2 wks	Maximal isometric torque: elbow flexor CSA: right and left upper arms 1-RM strength of the elbow flexor muscles	Maximal isometric elbow flexor torques increased significantly for OCC-T ($p<0.05$) for pre- and post-intervention values. No significant changes for OCC-C, NOR-T and NOR-C ($p>0.05$). CSA of the elbow flexor muscles increased significantly for OCC-T ($p<0.05$) for pre- to post-intervention values and between all other groups at the end of the intervention ($p<0.05$). No significant changes for OCC-C, NOR-T and NOR-C. 1-RM strength of the elbow flexor muscles increased OCC-T and NOR-T ($p<0.05$) for pre- to post-intervention values. No significant change for OCC-C and NOR-C ($p>0.05$).
May, 2018 (46) – R.C.T	24 recreationally active young men Age: **EXP**: 22.6 ± 3.3 yrs **CON**: 22.1 ± 2.5 yrs Groups: **BFR:** exercises with BFR. Trained arm named OCC-T and untrained arm named OCC-C. **CON:** exercises without BFR on lower limb. Trained arm named NOR-T and untrained arm named NOR-C.	24 sessions ,3x/wk for 8 wks Both groups: dominant arm biceps curl (50% 1-RM), 3x10 reps, 3 min rest, without BFR, then: BFR: knee flexion, leg extension at 30% 1-RM, 30 – 15 – 15 – 15 reps, 30 sec rest between sets, with BFR maintained even during rest periods. CON: knee flexion, leg extension (30% 1-RM), 30 – 15 – 15 – 15 reps, 30 sec rest between sets.	Pneumatic cuff (Automatic tourniquet system 86-cm length, 10.5-cm width, and 8-cm bladder width) Most proximal portion of both leg during leg exercises Pressure set at 60% of AOP	1-RM elbow flexion Muscle size, CSA for the arms	Significant difference in baseline values for 1-RM elbow flexion in CON group between CON-U and CON-T ($p<0.001$). 1-RM elbow flexion significantly increased ($p<0.05$) for OCC-T, OCC-C and NOR-T for pre- to post-intervention. 1-RM elbow flexion increased significantly at 4 wks and 8 wks ($p<0.05$). Moreover, the increase of 1-RM elbow flexion was significantly greater for OCC-T compared with OCC-C and NOR-C ($p<0.05$). No significant difference in muscle CSA within and between BFR and CON ($p>0.05$). However, muscle CSA of the trained arms was larger than untrained arms ($p<0.001$).

Mendonca, 2021 (51) – R.C.T.	30 healthy adults Age: **HI**: 21.9 ± 3.3 yrs **LIBFR**: 22.3 ± 2.9 yrs Groups: **HI**: high-intensity unilateral resistance training **LIBFR**: low-intensity unilateral resistance training with BFR	20 sessions, 5x/wk for 4 wks For both: unilateral plantar flexion with their dominant leg HI: 4 sets of 10 repetitions at 75% 1-RM (2 sec concentric - 2 sec eccentric), with 60 sec of passive recovery between sets LIBFR: 4 sets of 30 + 15+ 15+ 15 repetitions at 20% 1-RM (1 sec concentric - 1 sec eccentric), with 30 sec of passive recovery between sets. BFR applied continuously even during rest periods.	Pneumatic cuff (SC12L Tourniquet Cuffs, D. E. Hokanson, Inc. Bellevue, WA) At the most proximal portion of the thigh of the dominant leg Pressure was set at 60% of AOP.	Plantar flexion MVIC in the untrained limb Rate of torque development (RTD) (N m s−1) Neuromuscular adaptation of the untrained limb CSA of soleus in untrained limb	No significant increase in MVIC from pre- to post-training in both groups ($p>0.05$). An overall significant increase in RTD of the untrained limb from pre- to post-training values in both intervention groups ($p<0.01$). A significant time main effect was also obtained for peak RTD ($p=0.024$; ES=0.13). Significant increase in LIBFR and HI groups from pre- to post-training in soleus normalized EMG within the first milliseconds (0 to 50 ms) of the rising torque-time curve ($p=0.038$; ES=0.15). No significant changes ($p>0.05$) in V-wave amplitude and level of co-activation of the tibialis anterior muscle during MVIC between groups and from pre- to post-training values. No significant increase in soleus CSA from pre- to post-training in both groups ($p>0.05$). No difference between groups.

Wong, 2024 (52) – R.C.T.	179 subjects Age: 21.5 ± 3.5 yrs Groups: **LI:** low intensity **LI-BFR**: low intensity with the BFR **MAX**: maximal effort **CON**: no exercise	18 sessions, 3x/wk for 6 wks For all: Isometric handgrip training for the dominant hand LI: 4 sets of 2 min at 30% of their maximum handgrip strength. 1 min rest between sets. LI-BFR: same training as the LI group with a BFR for the entire training period. MAX: 4 sets of 5 sec at maximum grip strength. 1 min rest between sets	Nylon pneumatic cuff, 12 cm wide (E20 Rapid Cuff Inflator, Hokanson, Bellevue, WA) At the proximal portion of the dominant arm Inflated to 50% individual's resting AOP	Strength in the untrained arm Muscle thickness in the untrained arm (MTH-ulna and MTH-radius)	Greater changes in strength, with moderate evidence, in the untrained limb in the LI-BFR group than in the others (LI: BF10 = 3.1, MAX: BF10 = 6.31 and CON: BF10 = 14.23). No evidence of difference between groups for MTH-ulna and MTH-radius (BF10 = 0.077, 0.056 respectively)

Legend: 1-RM=1-Repetition Maximum, BFR=blood flow restriction, CSA= cross-sectional area, MVIC=maximal voluntary isometric contraction, reps=repetitions, sec=second, wk=week, wks=weeks, yrs=years, AOP=arterial occlusion pressure

Table 4a: scientific papers studying non-localized effects on aerobic and anaerobic performance.

Author	Review goal	Number of articles in the review	Conclusions – key points
Bennett and Slattery, 2019 (80) – Systematic Review	Identify all relevant studies that assess the effect of BFR training on aerobic fitness or aerobic performance.	14	Exercising with BFR led to an improvement in the VO_2max for 11 articles. BFR exercise has been suggested to reduce arterial blood flow and increase venous pooling within the limb. Thus, increase heart rate and increase mechanical stress on it and driving to cardiovascular adaptations. BFR exercise at light intensities could improve aerobic fitness (VO_2max and VO_2peak) and aerobic performance (time to exhaustion) for young adults with high occlusion pressure (130 mmHg or higher).
Castilla-López, 2022 (76) – Systematic review and Meta-Analysis	Describe the effects of aerobic and/or anaerobic training programs combined with BFR on the aerobic capacity and related sport performance of trained athletes.	10 (Systematic review) 6 (Meta-Analysis)	No statistical differences ($p>0.05$) were found in aerobic capacity or sport performance between training with BFR or without BFR at either low-to-moderate or high intensity in trained athletes. However, there is a suggestion that training sessions with BFR may yield slightly better results. The meta-analysis for VO_2max increase demonstrated an extremely large effect sizes (d=1.02) in favor to athletes who trained with BFR compared to without BFR, both in low-intensity (d=1.79) and high-intensity training (d=0.73).
Chua, 2022 (81) – Systematic Review	Evaluate the chronic effects of BFR combined with HIIT based on performance (aerobic, anaerobic) adaptations	13	BFR combined with HIIT (sprint-based protocols) lad to significantly greater improvements in VO_2max compared to the control group ($p<0.05$). BFR added into mixed intensities or submaximal aerobic protocols also led to superior (non-significant) improvements in VO_2max compared to the control group and may also likely enhance improvements in exercise economy and time to fatigue. Anaerobic components (PPO, MPO, sprint speed) showed greater improvements when BFR was added to submaximal HIIT or mixed intensity exercise interventions compared to interventions without BFR. The addition of BFR to all-out maximal efforts (sprint-based protocols) did not result in additional benefits compared to the control group.

Formiga, 2019 (19) – Meta-Analysis	Examining effect of aerobic exercises performed with and without BFR training.	7	Low-intensity aerobic exercise (30% VO_2max) induces more cardio-respiratory adaptations when BFR is applied versus the same aerobic exercise without BFR. SE=0.57, in favor to BFR. High-intensity aerobic exercise (>60% VO_2max) produces the same cardio-respiratory adaptations when BFR is applied or not. SE=-0.01, in favor to no BFR. Minimal clinically important difference (MCID) for aerobic capacity changes correspond to a small effect size (SE=0.20).
Li, 2024 (77) – Systematic review and Meta-Analysis	Consolidate and extend the existing research of the effects of BFR training on physical and technical performance in athletes.	18	VO_2max significantly increased in BFR training (p=0.003), with a large effect size in favor to BFR training compared to Non-BFR training (SMD=1.65). Vertical jump height significantly improved in the BFR training group compared to the Non-BFR training group, with a large effect size (SMD=1.39, p=0.01). No significant changes in sprint time after BFR training (p=0.115), with a trivial effect in favor to Non-BFR training (SMD= -0.18).
Yang, 2022 (79) – Meta-Analysis	Examining the effects of BFR training compared with training without BFR on aerobic capacity.	13	Aerobic capacity, as assessed by VO_2max, showed a significantly greater increase with BFR training at a low intensity compared to without BFR (SMD=0.40, p<0.01). Effect size results from subgroup analysis suggested that a frequency of 12 training sessions/week (d=1.480, p=0.015) was better for improving aerobic capacity than a frequency of 2-4 training sessions/week (d=0.439, p=0.005). The effect size of the intervention on enhancing aerobic capacity was more pronounced in interventions lasting 2–4 weeks (d=0.565, p=0.014) compared to interventions lasting 4–8 weeks (d=0.439, p=0.011). Low intensity BFR training combined with treadmill groups effect size was greater (d=0.567, p=0.015) compared with low intensity BFR training combined with the cycling group (d=0.484, p=0.014).

Xiong, 2023 (78) – Systematic Review and Meta-Analysis	To explore the impact of training with BFR on muscular endurance and aerobic capacity in different populations (patients, healthy subjects, athletes, and the elderly).	19	Meta-analysis: In healthy subjects, non-significant improvement in muscular endurance in the LBFR-RT group compared with the LL-RT group (p>0.05). Non-significant improvement in aerobic capacity for the group with BFR compared to the group without BFR (p>0.05). In athletes, significant improvement in muscular endurance for the LBFR-RT group compared to the LL-RT group (SMD = 1.15, p<0.01). No difference in improvement in muscular endurance for the AE-BFR and AE groups (p>0.05). Significant effect on aerobic capacity (p<0.01) in group AE-BFR compared with group AE. No significant difference in aerobic capacity between groups HITT-BFR and HITT. The quantitative analysis of this review did not find any clear conclusion on the improvement of aerobic capacity and muscular endurance concerning elderly people and patients. The conclusions of the various studies differ from one another.
Floco, 2023 (42) – Systematic Review and Meta-Analysis	To compare the effects of low with load BFR training and high load training without BFR in a population of healthy athletes.	14 (Systematic Review) 7 (Meta-Analysis)	The results of the meta-analysis show that there is a significant increase in VO_2 max in favor of the LI+BFR group in endurance-trained athletes (p<0.0002)

Legend: BFR=blood flow restriction, HIIT= high-intensity interval training; VO_2max= maximal oxygen consumption, VO_2peak= highest value of oxygen attained upon an incremental or other high-intensity exercise test

Table 4b: RCT's and case series studying non-localized effects on aerobic and anaerobic performance.

Author – article type	Sample, age and groups	Training program	BFR material, cuff site(s) and occlusion pressure	Measures	Results for non-localized effects
Abe, 2010 (53) – R.C.T.	19 healthy young men Age: 20-26 yrs Groups: **BFR:** cycling with BFR **Non-BFR:** cycling without BFR	24 training sessions, 3x/wk for 8 wks BFR: 15 min of cycling on a cycle-ergometer at 40% VO_2max. non-BFR: 45 min of cycling on a cycle-ergometer at 40% VO_2max.	Pressure belts (Kaatsu-Master, Sato Sports Plaza, Tokyo, Japan) On both legs Initial pressure at 160 mmHg increased by 10 mmHg each wk. Final pressure: 210 mmHg	VO_2max ($mL.kg^{-1}.min^{-1}$) Exercise time to exhaustion (min)	VO_2max increased in the BFR-training group ($p<0.05$) for pre- to post-intervention values. No significant change in the non-BFR-training group. Increase in exercise time until exhaustion was observed in the BFR ($p<0.01$) but not in the non-BFR for pre- to post-intervention values.
Abe, 2010b (45) – R.C.T.	19 men and women Age: between 60 to 78 yrs Groups: **INT**: walking with BFR **CON**: no exercise.	30 training sessions, 5x/wks for 6wks INT: walking on a treadmill at 67 m/min for 20 min. CON: daily physical activity.	Pressure belts (Kaatsu-Master, Sato Sports Plaza, Tokyo, Japan) On both legs Initial pressure at 160 mmHg increased by 10 mmHg each wk. Final pressure: 210 mmHg	VO_2peak ($L.min^{-1}$) Functional tests: timed up and go test and chair stand test	No change in VO_2peak for INT and CON group for pre-to-post intervention values ($p>0.05$). INT significantly improved in both functional fitness tests: timed up and go ($p<0.001$), chair stand ($p<0.05$). CON did not change pre- to post-intervention values.

Alexander, 2018 (54) – R.C.T.	24 young men Age: **BFR-HIIT:** 23.4 ± 3.3 yrs **HITT:** 22.6 ± 2.9 yrs Groups: **BFR-HIIT:** high intensity interval training with the BFR **HITT:** high-intensity interval	3x/wk for 4wks For both: 4 sets of deep body weight squats with 40, 25, 20 and 15 reps followed by HIIT training: 3x 4 min intervals with 1-min rest on a cycle-ergometer (Kardiomedbike) between 80 to 90 rpm. The intensity corresponded to the second ventilatory threshold, plus 5%. BFR-HITT: BFR applied during squat deep only	KAATSU-cuffs (5cm width) On the proximal part of the legs Inflated to the optimal individual pressure. The mean optimal individual pressure in this study was 273±33 mmHg	VO_2max ($mL.kg^{-1}.min^{-1}$)	No significant change in VO_2max in both groups between the start and end of training ($p<0.05$). No significant change in VO_2 max at ventilatory threshold 1 and 2 ($p<0.05$).
Amani-Shalamzari, 2019 (55) – R.C.T.	32 physically active women Age: 22.8 ± 2.9 yrs Groups: **IP-CE:** increase BFR pressure with constant exercise intensity. **CPP-IE:** constant partial BFR pressure with increase exercise intensity. **CPC-IE:** constant complete BFR pressure with increase exercise Intensity.	12 sessions, 3x/wk for 4 wks For all: bouts of 2-min running on a treadmill with the BFR interspersed by 1 min of recovery without BFR IP-CE, CPP-IE, CPC-IE: 10 sets of training in each session, IP-IE: completed 10, 8, 6, and 5 bouts in wks 1, 2, 3, and 4.	Pneumatic cuff (5x120cm - Ghamat Pooyan, Tehran, Iran) On the proximal portions of the thighs Pressure in groups across wks (mmHg): IP-CE: 160, 190, 210, 240 CPP-IE: 160 CPC-IE: 240 IP-IE: 160, 190, 210, 240	VO_2max ($mL.kg^{-1}.min^{-1}$) Time to fatigue on treadmill (TTF) (sec) Speed at VO_2max (vVO_2max) ($km.h^{-1}$)	VO_2max increased significantly in all groups for pre- to post-intervention values with a very large size effect ($p<0.05$, $d >0.95$). Significant difference between CPC-IE with IP-IE group ($p = 0.01$) in favor of CPC-IE. TTF increased significantly in all groups. Significant difference between CPC-IE and CPP-IE group ($p = 0.04$) The vVO_2max increased significantly in all groups. No significant difference between groups ($p = 0.21$)

	IP-IE: increase BFR pressure with increase exercise intensity.	Intensity across wks (%vVO_2max): IP-CE: 60% IP-IE, CPP-IE and CPC-IE: 60%, 70%, 80%, 85%		RE (L.min^{-1}.km.h^{-1}) Anaerobic capacity on a cycle-ergometer for peak power (PP), average power (AP) and minimum power (MP) (W.kg^{-1})	RE decreased significantly from pre-to-post intervention for IP-CE ($p=0.024$). Significant difference between IP-CE, IP-IE and CPC-IE ($p=0.04$). The PP increased significantly in all groups (IP-CE: $p=0.001$, CPP-IE: $p=0.012$, CPC-IE: $p=0.001$and IP-IE: $p=0.02$; Cohen's d : 0.83, 0.87, 2.05, 0.82 respectively). Significant difference between CPC-IE with IP-IE group ($p = 0.021$). Significant increase in AP for all groups from pre-training to post-training (IP-CE: $p=0.012$, CPP-IE: $p=0.012$, CPC-IE: $p=0.001$ and IP-IE: $p=0.01$; Cohen's d : 0.6, 0.52, 1.54, 0.96 respectively). Significant difference between CPC-IE group with CPP-IE and IP-IE ($p<0.05$). MP increased significantly in all groups (IP-CE: $p=0.009$, CPP-IE: $p=0.01$, CPC-IE: 0.001 and IP-IE: $p=0.003$; Cohen's d : 0.15, 0.22, 0.9, 0.24 respectively) The results of CPC-IE group were significantly different from all other groups ($p<0.05$).
Amano, 2015 (56) – R.C.T.	18 sedentary young males Age: **CON**: 21 ± 0.5 yrs **INT**: 20.8 ± 0.6 yrs Groups: **CON**: cycling without BFR	7 sessions, 1x/day for 7 days For both: cycling at 50% VO_2max for 60min/day, consisting of two sets of 30-min exercise, each followed by a 10-min rest. CON: no BFR applied.	Pressure cuffs (SC12L; Hokanson, Bellevue, Washington, USA) On proximal part of both thighs Pressure set at 60 mmHg	VO_2max (mL.kg^{-1}.min^{-1})	Significant improvements for VO_2max in both groups for pre- to post-intervention values ($p< 0.05$). No significant difference between groups for post intervention values ($p> 0.05$).

	INT: cycling with BFR	<u>INT:</u> BFR on both thighs. BFR deflated during rest intervals.			
Chen, 2022 (57) – R.C.T.	20 endurance-trained male runners <u>Age</u>: **RIT:** 21.6 ± 2.1 **RIT-BFR**: 21.5 ± 2.2 <u>Groups</u>: **RIT:** running interval training without BFR **RIT-BFR**: running interval training with BFR	24 sessions, 3x/wk for 8 wks <u>For both</u>: 5 sets of 3 min of running at 50% heart rate reserve on a treadmill with a 1-min rest interval <u>RIT-BFR</u>: the cuffs were applied continuously throughout the running session, including during the rest periods between sets	Inflatable cuffs (14.2 cm×67.5 cm, CK-113; Spirit, Taipei, Taiwan) At the most proximal portion of each thigh (inguinal fold region) Pressure was set at 1.3 times systolic blood pressure at rest	Maximal running performance (RPmax) ($km.h^{-1}$)	Significant increase in RPmax for pre- to post-intervention values in the RIT-BFR ($p<0.05$). The normalized RPmax (% of pre-training) post-intervention was significantly higher ($p<0.05$, $\eta2=0.30$) in the RIT-BFR group compared with the RIT group.
Cintineo, 2024 (58) – R.C.T	54 reserve officers' training corps <u>Age:</u> 20.5 ± 2.6 yrs <u>Groups:</u> **MIN+BFR:** minimal-equipment resistance training with BFR. **MIN:** minimal-equipment resistance training **TRAD:** traditional-equipment resistance training	24 sessions, 4x/wk for 6 wks <u>For all:</u> full-body routine with an alternance between 2 different workouts <u>MIN+BFR</u>: rest periods lasted 1-3 min. BFR applied only during working sets <u>MIN:</u> rest periods lasted 1-3 min <u>TRAD</u>: rest periods lasted 2-3 min	Pneumatic cuffs (BStrong, Park City, UT) At the proximal portion of both arms and legs Cuffs were inflated to appropriate pressures relying on the manufacturer and existing guidelines Cuffs were adjusted throughout the 6-wk intervention based on subjective ratings as Borg's CR10	VO_2max ($mL.kg^{-1}.min^{-1}$) Anaerobic peak power assessed by countermovement vertical jump (CMJ) (cm)	A small to moderate improvement of VO_2max for pre- to post-intervention values was measured in MIN and MIN+BFR groups (MIN+BFR: d=0.21; MIN: d=0.31). TRAD group showed negligible improvement (d=0.05). The biggest size effects were obtained in the MIN group followed by MIN+BFR group. CMJ height for pre- to post-intervention values improved with a small to moderate effect in MIN+BFR and TRAD groups ($p<0.001$, MIN+BFR: d=0.18 ; TRAD: d=0.38). TRAD group obtained the largest size effect and MIN+BFR group in second place. MIN group showed negligible improvement (d=0.09)

Conceicao, 2019 (59) – R.C.T.	30 young sedentary males Age: no information Groups: **RT:** resistance training. **ET:** endurance training. **ET-BFR:** low intensity endurance training with BFR.	8 wks No information about the frequency RT: 4 sets of leg press. Max bilateral repetitions per set at 70% of 1-RM interspersed by 1-min rest. ET: 30 min of continuous cycling at a power output that elicited 70% of VO_2 reserve. ET-BFR: 30 min continuous cycling with a cuff strapped over the thigh at a power output that elicited 40% of VO_2 reserve.	Pressure cuff (18-cm wide) Placed on the proximal portion of the thigh. Pressure maintained at 80% of AOP	VO_2max ($mL.kg^{-1}.min^{-1}$)	VO_2max increased significantly for pre-to-post intervention values for ET and ET-BFR groups (ET: $p<0.001$, ES=0.96 ; ET-BFR: $p=0.012$, ES=0.84). No significant change in VO_2max for pre-to-post intervention values for RT group. No significant difference between groups post-intervention ($P>0.05$).

de Oliveira, 2016 (60) – R.C.T.	37 young adults Age: 23.8 ± 4 yrs Groups: **HIIT**: high intensity interval training. **BFR**: low intensity interval training with BFR. **LOW**: low intensity interval training without BFR. **HIT+BFR**: combined HIT and BFR.	12 sessions, 3x/wk for 4 wks For all: cycling protocol, 2 sets of 5 reps for the first 3 sessions. Then one rep per set was added each wk. Each rep lasted 2 min and was interspersed by 1-min passive rest. Rest interval 5-min between set. HIIT: each repetition began at 110% Pmax with a progressively 5% decrease in the intensity every 30 sec. BFR: applied intermittently: inflated during the 2-min rep and deflated during the 1-min rest period. LOW and BFR: training power output at 30% of Pmax.	Pressure cuff Proximal part of both thighs Belts inflated at 140 mmHg and then pressure increased by 20 mmHg every 3 sessions. Final pressure: 200 mmHg.	VO_2max ($mL.kg^{-1}.min^{-1}$) Lactate threshold ($W.kg^{-1}$) Maximal power output (Pmax) ($W.kg^{-1}$)	VO_2max increased from pre- to post-training periods for BFR (p=0.006, ES=0.33), HIT (p=0.002, ES=0.9), and HIT + BFR (p=0.03, ES=0.33), but was unchanged in LOW (p=0.75). The lactate threshold increased from pre- to post-training periods for all groups (BFR: ES = 0.43; HIT: ES=1.8; HIT+ BFR: ES=0.7) Pmax increased from pre- to post-training periods for BFR (p<0.001, ES = 0.44), HIT (p< 0.001, ES = 1.5), and HIT+BFR (p< 0.001, ES = 0.39), but was unchanged in LOW (p=0.34). Significant interaction (group × time, F = 9.61, P < 0.001)

Giovanna, 2022 (61) – R.C.T.	39 men trained in endurance <u>Age:</u> 25.6 ± 5.7 yr <u>Groups:</u> **HG**: training exercises in hypoxia **BFRrG:** training exercises with the BFR during recovery **BFRG:** training exercises with the BFR **CG**: training exercises	6 sessions, 3x/wk for 2 wks <u>For both</u>: 4 series of 5x10 seconds maximal cycling sprints separated by an active recovery of 20 seconds at 75W. Between series 1 and 2, 3 and 4, 5 min of active recovery and between series 2 and 3 10 min of active recovery. <u>HG</u>: stimulated altitude of 4000m <u>BFRrG</u>: cuffs inflated during active rest between sprints. <u>BFRG</u>: cuffs inflated during sprints and deflated during active recovery	Automated cuff (11x85cm) (SC10D Rapid Version Cuff, D.E Hokanson, inc. Bellevue, WA, USA) On the proximal part of thighs Inflated to 45% of femoral artery occlusion pressured measured at rest	Peak aerobic power (W) VO_2 peak ($mL.kg^{-1}.min^{-1}$) Maximal accumulated oxygen deficit ($mL.kg^{-1}$) Accumulated O_2 uptake ($mL.kg^{-1}$) Peak minute ventilation (VE peak) ($L.min^{-1}$) Fatigue index	Significant increase for HG, BFRrG, BFRG, CG. (d=0.5, 0.2, 0.2, 0.2, respectively) after training for peak aerobic power. Non-significant interaction or groups effect was found. Significant increase in relative VO_2max in the BFRrG group (p=0.03, d=0.7) after training. Significant increase after training for maximum accumulated oxygen deficit (p=0.002). No interaction or group effect was found at the end of the training. Significant increase for the accumulated O_2 uptake between pre- and post-training. VE peak was significant higher in HG compared to BGFrG (p=0.019; d=1.4). Significant increase after training for VE peak (p=0.028). Significantly greater fatigue index between the first and subsequent sessions (p=0.011 compared with the second session and p<0.01 for sessions 3-4-5 and 6). No significant interaction (groups x time) was found.

Held, 2020 (6) – R.C.T.	31 elite athletes Age: **INT:** 21.9 ± 3.2 yrs **CON:** 21.7 ± 3.7 yrs Groups: **INT**: rowing with the BFR. **CON**: Rowing without BFR.	15 sessions, 3x/wk for 5 wks For both: rowing (low, moderate and high intensity), cross (running and cycling) and strength training. INT: BFR during low intensity. BFR continuously applied even when rest time.	Elastic wraps (200x13 cm, Best Body Nutrition, Auerbach, Germany) At the proximal part of the upper thighs Wraps pulled to 75% of their maximum length	VO_2max ($mL.kg^{-1}.min^{-1}$) Power at VO_2max threshold (PVO_2max) (W)	VO_2max increases for INT for pre-to-post intervention ($p<0.001$; ES=1.335), CON did not show significant change ($p>0.05$; ES=0.354) in VO_2max for pre-to post-intervention PVO_2max increases significantly ($p<0.001$; ES=1.412) for pre- to post-intervention values. CON did not show significant ($p>0.05$; ES=0.298) individual PVO_2MAX increases for pre- to post-intervention values.
Held, 2023 (62) – R.C.T.	18 trained males swimmers Age: **BFR:** 22.6 ± 3.7 **noBFR:** 22.8 ± 1.8 Groups: **BFR:** low-intensity swimming with BFR **noBFR:** low-intensity swimming without BFR	3x/wk for 5 wks For both: 2x10 min swimming (continuously or intermittent) at a low intensity with a 10 min break in-between BFR: the occlusion was only maintained during swimming periods and not during the 10-min break	Pneumatic bands (Occlusion Cuff Elite, The Occlusion Cuff, Belfast, United Kingdom; 8 cm cuff width) At the proximal part of both upper limbs Pressure maintained at 75% of arterial occlusion pressure	VO_2peak ($L.min^{-1}$) Swimming speed at first (LT1) and second (LT2) lactate threshold ($m.s^{-1}$)	Favorable VO_2peak adaptations in the BFR group compared to noBFR group (BFR SMD=0.15 ; noBFR: SMD =-0.39). Swimming speed at LT1 and LT2 were not affected neither for BFR or noBFR after the 5 wks intervention (BFR SMD: LT1=-0.03, LT2=0.01 ; noBFR SMD: LT1=0.09, LT2=0.05).

Hori, 2022 (63) – R.C.T.	18 healthy adults Age: **BFR**: 22 ± 2 yrs **CON**: 21 ± 1 yrs Groups: **BFR**: aerobic cycle training with BFR **CON**: aerobic cycle training without BFR	3x/wk for 8 wks For both: 30 min at a moderate-intensity constant-load exercise on a cycle ergometer. BFR: The BFR pressure was applied for 5 min every 10 min of exercise. Each session included 15 min with pressure and 15 min without.	6-cm wide cuff (SC5, D.E. Hokanson, WA, USA) At the upper thighs approximately 1-2 cm distal to the inguinal folds Pressure was set at 160 mmHg in the first wk then increased by 10 mmHg each wk until a final pressure of 230 mmHg	VO_2peak ($mL.kg^{-1}.min^{-1}$) Time constant (τ) of oxygen uptake increasing mono-exponentially before reaching a steady-phase (sec)	VO_2peak and peak load significatively increased ($p<0.05$) in both groups for pre- to post- values. VO2peak values at mid- and post-training were not significantly different between groups ($p>0.05$, $\eta p_2=0.03$). The peak load at mid-training was significantly higher ($p<0.05$) in the BFR group than in the CON group but no longer at post-training. A significant decrease from pre-training in the τ at Mid in the BFR group but not in the CON group ($p<0.05$). there was a significant difference in the τ values at Mid between groups ($p<0.01$). The τ values were significantly lower at Post than those measured at Pre in the CON and BFR groups ($p<0.05$) but there was no significant difference at Post between groups ($p=0.39$).
Jensen, 2016 (64) – Case series	18 military warfighters Age: 36.8 ± 2.2 yrs Groups: **BFR:** BFR + military warfighter daily training.	20 training sessions for 20 days BFR: 20 min of exercise on a modified NuStep recumbent cross trainer with continuous application of the BFR.	Pressure cuffs Attached to the proximal part of each arm and on each thigh, 10 cm proximally from the patella Pressure maintained between 60 and 80 mmHg	VO_2peak ($mL.kg^{-1}.min^{-1}$)	No significant difference in VO_2peak ($p>0.05$) for pre- to post-intervention values.

Karabulut, 2021 (65) – R.C.T.	39 young active males <u>Age</u>: between 18 and 50 yrs <u>Groups</u>: **HI**: high intensity **LI**: low intensity **LI-BFR**: low intensity with BFR **C**: control	3x/wk for 6 wks <u>For all</u>: a 5-min warm-up followed by 30 min aerobic exercise on a treadmill and 5 min cool-down. <u>HI</u>: 60-70% of VO_2 reserve <u>LI</u>: 30-40% of VO_2 reserve <u>LI-BFR</u>: 30-40% of VO_2 reserve and cuffs applied during training sessions	Elastic cuffs (KAATSU-Master System, Sato Sports Plaza, Tokyo Japan, width 5cm) On the uppermost portion of the thighs Pressure depending on thigh circumference (120-210 mmHg). Pressure estimated around 60% of AOP and was increased by 20 mmHg for the next session if RPE<14.	VO_2max ($mL.kg^{-1}.min^{-1}$) Percent changes of VO_2max (%)	Significant difference in VO_2max between LI-BFR and control groups ($p<0.05$) after the 6-wks intervention. LI-BFR achieved the highest percentage improvement in VO_2max followed by HI, then LI, and finally C.
Keramidas, 2012 (66)– R.C.T.	20 young subjects <u>Age:</u> **CUFF**: 23.3 ± 3.9 yrs **CON:** 22.7 ± 4.7 yrs <u>Groups:</u> **CUFF**: cycling with BFR **CON:** cycling without BFR	3x/wk for 6 wks <u>For both</u>: cycling on a Monak cyclo ergometer at a cadence of 70 rpm at the same relative intensity. 2 min-work at 90% of VO_2 max or VO_2 press max, 2 min of active recovery at 50% of VO_2 max <u>CON</u>: without cuff <u>CUFF</u>: with cuff during work and deflated cuff during active recovery.	Cuff on the thighs Pressure maintained at 90 mmHg	VO_2 max ($mL.kg^{-1}.min^{-1}$) PPO (W) Anaerobic threshold (AT) (%VO_2max)	No significant change of VO_2max in both groups ($p>0.05$) PPO was significantly higher after training program in both groups ($p<0.001$) No significant change of AT after training in both groups ($p>0.05$).

Kim, 2016 (67) – R.C.T.	31 college-aged males Age: 22.4 ± 3 yrs Groups: **VI:** high-intensity cycling. **LI-BFR:** low-intensity cycling. **Control:** no exercise.	18 sessions, 3x/wk for 6 wks VI: 20 min of cycling at 60% HRR for the initial 3 wks followed by cycling at 70% HRR for remaining 3 training wks. LI-BFR: 20 minutes of cycling at 30% HRR for 6 wks.	Elastic belts (5-cm width) At the proximal ends of both thighs Initial pressure at 160 mmHg increased by 20 mmHg after the initial 3 wks. Final pressure: 180 mmHg	VO_2peak (mL.kg^{-1}.min^{-1})	No significant difference for pre- to post-intervention values and between groups ($p>0.05$).
Lan, 2022 (68) – R.C.T	56 students Age: between 18 to 25 yrs Groups: **LICT-BFR**: low-intensity continuous training with the BFR **MICT**: moderate intensity continuous training **HITT**: high-intensity interval training **CON**: to maintain the same lifestyle	3x/wk for 8 wks For all: a standardized 5 min warm-up. A 10 min resting phase followed. All sessions were performed on the treadmill. LICT-BFR: 15 min at 57-63% HRmax MICT: 45 min at 64-76% HRmax with the cuff HITT: 4x4min at 85-95%HR max followed by 3min active resting to 64-76% between the interval training	Elastic cuffs (B Strong, USA, width 5-8cm) At the proximal ends of the thighs Pressure set at 200 mmHg and increased by 20 mmHg for each wk (200 to 360 mmHg)	Relative VO_2max (mL.kg^{-1}.min^{-1})	VO_2max significantly increased between baseline and the last wk for all exercise groups from wk 4 for MICT and wk 8 for LICT-BFR and HIIT ($p<0.01$). After 8 wks, VO_2max decreased significantly for the CON ($p<0.05$). A group effect was found in HITT and LICT-BFR groups compared to CON from wk 4 ($p<0.05$) and at wk 8 ($p<0.01$). In contrast, the significant group effect for MICT in comparison to CON was only observed at wk 8 ($p<0.05$).

Libardi, 2015 (39) – R.C.T.	25 older individuals Age: over 60 yrs CT: 65 ± 3.7 BFR-CT: 64 ± 4 Control: 65 ± 4 Groups: **CT:** endurance training and HI-RT without BFR. **BFR-CT:** endurance + RT with BFR. **Control:** endurance and RT.	48 sessions, 4x/wk for 12 wks Endurance training: walking and running at 60 to 85% VO_2max for 40 min for the first 6 wks and then increased at 50 min for the next 6 wks. HI-RT without BFR: 4×10 repetitions 70% 1-RM in the leg press exercise for the first 6 wks then increased at 80% 1-RM for the next 6 wks. RT with BFR: 30 – 15 – 15 – 15 reps 1 min rest between sets at 20% 1-RM for the first 6 wks and then increased at 30% of 1-RM for the next 6 wks. BFR applied continuously even during rest period.	Pneumatic cuff Placed in the inguinal fold 50% of the AOP	VO_2peak ($mL.kg^{-1}.min^{-1}$)	Increase in VO_2peak for CT and BFR-CT groups (p=0.04 and p=0.02) in pre- to post-intervention values. No significant difference between groups for post-test values.

McKee, 2024 (69) – R.C.T.	26 adult male team-sport players Age: **BFR:** 21 ± 5 yrs **Non-BFR:** 20 ± 4 yrs Group: **BFR:** sprints with BFR **Non-BFR:** sprints without BFR	9 sessions, 3x/wk for 3 wks For both: a 5-min warm-up, 3 sets of 5 sec sprints, 25 sec recovery between repetitions, 3-min rest between sets. An additional sprint was added after every third session. All sessions were performed on a cycle ergometer BFR: cuffs applied continuously throughout session even between-set rest periods	10-cm wide cuffs (Sport Rehah Tourniquet) At the proximal portion of both legs Pressure maintained at 45% of AOP	VO_2max ($mL.kg^{-1}.min^{-1}$) Peak aerobic power ($W.kg^{-1}$) PPO assessed by Repeated-sprint ability (RSA) test and anaerobic capacity assessment ($W.kg^{-1}$) MPO($W.kg^{-1}$)	No significant change in VO_2max for pre- to post- intervention values for both groups. No significant difference between groups post-intervention (p>0.05). Peak aerobic power significatively improved for both groups from pre- to post-intervention values (p=0.013 ; g=0.25). Regarding the RSA test and the anaerobic capacity assessment, there was a significant main effect of time in PPO (p=0.01 and p=0.045, respectively), with small improvements (g=0.25 and g=0.32, respectively) from pre- to post-testing in both groups. A significant main effect was observed in MPO for time only (p= 0.003), with small improvements (g = 0.47) from pre- to post-testing in both groups. Significant interaction (group x time) was found (p<0.046)
Park, 2010 (70) – R.C.T.	12 college male athletes Age: OCC: 20.1 ± 1.2 NOR: 20.8 ± 1.3 Groups: **OCC**: walking with BFR. **NOR**: walking without BFR.	24 sessions, 2x/day, 6x/wk for 2 wks. For both: 5 sets of 3-min walking and 1-min rest between, with a slope of 5% to reach approximately 40% of the VO_2max. BFR: Speed at 4km/h, BFR applied continuously even during rest period. NOR: Speed at 6km/h.	Pneumatic cuff (110-mm wide belt) Applied on the most proximal portion of each leg 160 mmHg and increased by 10 mmHg every day. Final pressure at 220 mmHg on day 7	VO_2max ($mL.min^{-1}.kg^{-1}$) Maximal minute ventilation (VE) ($L.min^{-1}$) Anaerobic power capacity with a Wingate anaerobic test: peak power (W) and relative peak power ($W.kg^{-1}$)	Significant increase in VO_2max (p<0.005) and VE (p<0.003) for OCC group for pre- to post-intervention values. No change for NOR group. OCC group significant increased anaerobic capacity (p=0.022) for pre- to post-intervention values. No change for NOR group.

Paton, 2017 (71) – R.C.T.	16 healthy subjects Age: 25 ± 7 yrs Groups: **BFR:** treadmill running with BFR. **CON:** treadmill running without BFR.	8 training sessions, 2x/wk for 4 wks For both: treadmill speed at 80% of the peak running velocity. Bouts of 30-sec interspersed with 30-sec of rest. Initial: 2 sets of 5 reps. After, increased by 2 min/session. Rest between set: 150 sec. BFR: applied during the running and released 60 sec during the rest period.	Elastic wraps (Get Strength Heavy Duty 75 mm, Waiuku, New Zealand) Placed proximally on the subjects' thighs Wrap pressure was increased by the experimenter until subjects reported a perceived pressure of 7 out of 10 (moderate but pain-free pressure)	VO_2max ($mL.kg^{-1}.min^{-1}$) Running economy (RE) ($mL.kg^{-1}km.h^{-1}$) High intensity time to exhaustion (TTE) run (sec) Peak running velocity (PRV) ($km.h^{-1}$) Incremental run time (sec)	No significant change ($p>0.05$) between groups for post intervention values (VO_2max, RE and TTE). No significant change in RE within and between groups ($p>0.05$). Small effect size (ES 0.2–0.5) for BFR group in VO_2max, VE, PRV and incremental run time, and a large (ES=0.85) increase in TTE for pre- to post-test values. Small and moderate increases in VO_2max and TTE (ES=0.37 and 0.62, respectively) for CON for pre- to post-intervention.
Tanaka, 2018 (72) – R.C.T.	30 men with post-infarction heart failure Age: 60.7 ± 11.1 Groups: **CG**: control. **IG**: exercises with BFR.	6 months, 3x/wk For both: 15 min of cycling on a cycle ergometer at 40-70% of the VO_2peak. IG: BFR applied during the training session.	Pneumatic cuff (width: 90 mm; length: 700 mm) On the proximal ends of the thighs 40–80 mmHg over the systolic blood pressure that is required for vascular occlusion	VO_2peak ($mL.kg^{-1}.min^{-1}$)	Increase in VO_2peak in the IG group after 6 months of training. Significant difference between IG and CG group after 6 months ($p= 0.002$).

Tangchaisuriya, 2022 (73) - R.C.T	50 males masters road cyclists Age: **BFRIT**: 39.6 ± 3.8 yrs **CON**: 41.5 ± 4.5 yrs **HIIT**: 41.7 ± 3.8 yrs Groups: **BFRIT**: high intensity interval training with the BFR **CON:** continuous training **HIIT:** high intensity interval training	2x/wk for 12 wks For all: a standardized 6-min warm-up. A 10-min cool-down after the session. All sessions were performed on a cycle ergometer BFRIT: 2x4 min at 80% PPO and 2x4 min at 60% alternated with 2 min at 30% PPO. BFR during all training session after the war-up. CON: 75 min 65-70% PPO HIIT: 4x4 min at 80% PPO alternated with 2 min at 30% PPO	Pneumatic cuff (SC10 segmental pressure cuff; Hokanson, Bellevue, WA) At the proximal portion of both tights Pressure maintained at 30% of AOP	Absolute VO_2max ($L.min^{-1}$) Relative VO_2max ($mL.kg^{-1}.min^{-1}$) Ventilatory threshold PPO (W)	Absolute VO_2max for pre- to post-intervention values significatively increased for both BFRIT and HIIT groups ($p<0.001$). The BFRIT group achieve a significatively higher VO_2max than the CON group ($p=0.025$). Relative VO_2max significatively increased in all three groups (CON: $p=0.047$; HIIT: $p<0.001$; BFRIT: $p<0.001$) for pre-to post-intervention values. Ventilatory threshold significatively increased ($p<0.05$) for pre- to post-intervention values in all three groups. PPO significatively increased for both BFRIT and HIIT groups from pre- to post-intervention values ($p<0.001$) and in comparison with the CON group ($p<0.05$). Significant interaction (time x group) was found ($p<0.001$).
Taylor, 2016 (74) – R.C.T.	20 healthy trained men Groups: **CON:** sprint interval training without BFR. **BFR:** sprint interval training with post-exercises with BFR.	8 sessions, 2x/wk for 4 wks For both: 4, 5, 6 and 7 maximal 30 sec cycling bouts in wks 1, 2, 3 and 4, respectively, with each bout separated by a 4.5 min recovery period on a cycle ergometer. BFR: BFR after each sprint.	Pneumatic cuff On the proximal portion of each thigh On average 130 mmHg	VO_2max ($mL.kg^{-1}.min^{-1}$) Maximal aerobic power (MAP) (W) PPO (W) MPO (W)	Increase in VO_2max for pre- to post-test ($p=0.01$) values for BFR group. No change for CON group. No change in any group in pre- to post-test values for MAP, PPO and MPO

Thompson, 2024 (75) – R.C.T.	28 young subjects <u>Age</u>: 26 ± 11 yrs <u>Groups</u>: **BFR-HV**: very high-dose treadmill walking with BFR **BFR-LV**: low-dose treadmill walking with BFR **CON**: treadmill walking without BFR	**CON** and **BFR-HV:** 35 sessions, 2x/day and 5x/wk for 4wks **BFR-LV**: 12 sessions, twice a wk for 6 wks <u>For both</u>: 5 intervals of 3 minutes with 1-minute rest on a treadmill (5° grade and at 5km/h) <u>BFR-HV and BFR-LV</u>: continuously applied except during the rest periods	Cuff on the proximal part of thigh. Inflated to 100% of the lowest individualised occlusion pressure (LOP) measured at rest and at the beginning of each wk	VO_2 max ($mL.min^{-1}$) Peak power aerobic (W)	Absolute and relative VO_2max increased respectively after 2 wks and 4 wks of training for the BFR-HV and BFR-LV groups (p<0.01). No change observed for the CON group. No difference in increase of VO_2max between BFR programs. A effect time significative was found for only BFR-HV on peak power aerobic (p<0.0067).

Legend: 1-RM=1-Repetition Maximum, AOP= arterial occlusive pressure, BFR=blood flow restriction, ES=effect size, HRR=heart rate reserve, min=minute, rep(s)=repetition(s), RPE=rate of perceived exertion, sec=second, VO_2max= maximal oxygen consumption, VO_2peak= highest value of oxygen attained upon an incremental or other high-intensity exercise test, vVO_2max=speed at VO_2max, wk=week, wks=weeks, yrs=years, PPO=peak power output, MPO=mean power output, SMD=standardized mean difference

Table 5: RCT's studies studying non-localized effects on whole body composition.

Author – article type	Sample, age and groups	Training program	BFR material, cuff site(s) and occlusion pressure	Measures	Results for non-localized effects
Amani-Shalamzari, 2019 (55) – R.C.T.	32 physically active women Age: 22.8 ± 2.9 yrs Groups: **IP-CE:** increase BFR pressure with constant exercise intensity **CPP-IE:** constant partial BFR pressure with increase exercise intensity. **CPC-IE:** constant complete BFR pressure with increase exercise intensity. **IP-IE:** increase BFR pressure with increase exercise intensity.	12 sessions, 3x/wk for 4 wks For both: bouts of 2-min running on a treadmill with the BFR interspersed by 1 min of recovery without BFR IP-CE, CPP-IE, CPC-IE: 10 sets of training in each session, IP-IE: completed 10, 8, 6, and 5 bouts in wks 1, 2, 3, and 4. Intensity across wks (%vVO_2max): CE: 60% IP-IE, CPP-IE and CPC-IE: 60%, 70%, 80%, 85%	Pneumatic cuff (5x120cm - Ghamat Pooyan, Tehran, Iran) On the proximal portions of the thighs Pressure in groups across wks (mmHg): IP-CE: 160, 190, 210, 240 CPP-IE: 160 CPC-IE: 240 IP-IE: 160, 190, 210, 240	Body mass (kg), BMI (kg.m^{-2}), BF (%)	No significant change in pre-to-post intervention in all groups for body mass, BMI and body fat. No significant difference between groups.
Chen, 2022 (87) – R.C.T.	37 obese male students (>25% body fat or >28kg/m2 BMI Age: EG: 20.3 ± 1.07 yrs CG: 20.1 ± 1.08 yrs Groups: **EG**: training at low intensity with BFR **CG:** training at low intensity without BFR	24 sessions, 2x/wk for 12 wks For both: 3 sets of 15 min cycling on a cyclo-ergometer at 40% of vo2 max, 1-min rest between sets. EG: BFR applied for the entire training period	Air pressure belts (Kaatsu-Master, Sato Sports Plaza, Tokyo) On the proximal thighs Pressure maintained at 200 mmHg	Waist circumference (WC) (cm), weight (kg) Abdominal skinfold thickness (AST)(mm), FFM (kg), Fat mass (FM)(kg), %BF, BMI (kg.m^{-1})	Significant difference in weight, WC, AS, fat masse, % BF, BMI before and after training for EG ($p<0.05$, 0.05, 0.05, 0.01, 0.01, 0.05 respectively). For CG, no significant difference for all factors before and after training. A significant interaction (Group x time) was found in %BF, FM, and waist circumference ($p<0.05$, np2= 0.1, 0.194, 0.265 respectively)

Cintineo, 2024 (58) – R.C.T	54 reserve officers' training corps Age: 20.5±2.6 yrs Groups: **MIN+BFR:** minimal-equipment resistance training with BFR **MIN:** minimal-equipment resistance training **TRAD:** traditional-equipment resistance training	24 sessions, 4x/wk for 6 wks For all: full-body routine with an alternance between 2 different workouts MIN+BFR: rest periods lasted 1-3 min. BFR applied only during working sets MIN: rest periods lasted 1-3 min TRAD: rest periods lasted 2-3 min	Pneumatic cuffs (BStrong, Park City, UT) At the proximal portion of both arms and legs Cuffs were inflated to appropriate pressures relying on the manufacturer and existing guidelines Cuffs were adjusted throughout the 6-wk intervention based on subjective ratings as Borg's CR10	Body mass (kg) % BF FFM (kg)	All three groups significatively increased body mass and FFM and decreased % BF ($p<0.001$) for pre- to post- values. Body fat percentage decreased the most in TRAD group (TRAD: $d=-0.28$: MIN: $d=-0.15$; MIN+BFR: $d=-0.14$) No significant change ($p>0.31$ for time x group interaction) in body mass, body fat, FFM for none of the groups.
Corrêa, 2021 (84) – R.C.T.	90 male and female with chronic kidney disease Age: **CON**: 57 ± 6 yrs **RT**: 58 ± 9 yrs **RT+BFR**: 60 ± 8 yrs Groups: **CON**: control **RT**: resistance training **RT+BFR**: resistance training with BFR	3x/wk for 6 months CON: no intervention RT: 3 sets of 12 repetitions at 50% 1-RM in the first and second month, 3 sets of 10 repetitions at 60% 1-RM in the third and fourth month, and 3 sets of 8 repetitions at 70% 1-RM in the fifth and sixth month. RT+BFR: 3 sets of 12 reps at 30% 1-RM in the first and second month, 3 sets of 10 repetitions at 40% 1-RM in the third and fourth month, and 3 sets of 8 reps at 50% 1-RM in the fifth and sixth month.	No indications about the cuff and where they are located 50% of resting systolic blood pressure	Body weight (BW) (kg), BMI ($kg.m^{-2}$) Fat free mass (FFM) (kg), fat mass (kg)	No significant change for pre- to post-values for BW and BMI for CON, RT and RT+BFR groups ($p>0.05$). Significant change for pre- to post-intervention in RT and RT+BFR groups in FFM ($p<0.0001$) and fat mass ($p<0.0001$). No significant change for the CON group.

de Oliveira, 2016 (60) – R.C.T.	37 young adults Age: 23.8 ± 4 yrs Groups: **HIIT**: high intensity interval training **BFR**: low intensity interval training with BFR. **LOW**: low intensity interval training without BFR. **HIT+BFR**: combined HIT and BFR.	12 sessions, 3x/wk for 4 wks For both: cycling protocol, 2 sets of 5 reps for the first 3 sessions. Then one repetition per set was added each wk. Each rep lasted 2 min and was interspersed by 1-min passive rest. Rest interval 5-min between set. HIIT: each repetition began at 110% Pmax with a progressively 5% decrease in the intensity every 30 sec. BFR: applied intermittently: inflated during the 2-min rep and deflated during the 1-min rest period. LOW and BFR: training power output at 30% of Pmax.	Pressure cuff Proximal part of both thighs Belts inflated at 140 mmHg and then pressure increased by 20 mmHg every 3 sessions. Final pressure: 200 mmHg.	Body mass (kg) % body fat (BF)	No change for body fat and body mass among all groups.
Deus, 2022 (83) – R.C.T.	105 patients with chronic kidney disease Age: **RT:** 58 ± 6.22 yrs **RT+BFR:** 58 ± 6.51 yrs **CTL:** 57.51 ± 5.23 Groups: **RT:** resistance training **RT+BFR:** resistance training with the BFR **CTL:** control group	3x/wk for 6 months For both: 7 exercises, 1 min of rest between sets. The number of reps differed between the 3 training periods. Wks 1-8: 3 sets of 12 reps. Wks 9-16: 3 sets of 10 reps. Wks 17-24: 3 sets of 8 reps. RT: first period: 50% of 1 RM. Second period: 60% of 1 RM. Third period: 70% of 1 RM. RT+BFR: first period: 30% of 1 RM. Second period: 40% of 1 RM. Third period: 50% of 1 RM. The exercises performed with the BFR. CTR: non exercise training	The arm cuff: 7x80 cm (Clinic Arm Model) and thigh cuff: 10x80cm (Clinic Arm Model) On the proximal part of limbs. Pressure maintained at 50% of systolic blood pressure.	BMI (kg/m^2) BF (%) FFM (%)	Significant decrease in BMI in the RT+BFR compared with the CTL (p=0.0123). No significant difference in BMI between the two exercise groups. Significant decrease in % BF in RT+BFR compared with CTL (p=0.0038). No significant difference in body fat% between the two exercise groups. Significant increase in %FFM in the RT group compared with the CTL but did not differ from the RT+BFR (p=0.038).

Kargaran, 2021 (86) – R.C.T.	24 healthy older women Age: 62.9 ± 3.1 yrs Groups: **C:** no training **DT**: dual task without BFR **DTBFR**: dual task with BFR	24 sessions, 3x/wk for 8 wks For both: 20-min walk on a treadmill at 45% heart rate reserve while performing cognitive tasks DTBFR: the cuff pressure was applied throughout 20 min of walking	Pneumatic cuffs (5 cm, Ghamat Pooyan, Tehran, Iran) At the proximal portion of the legs Pressure was set at 50% of arterial occlusion pressure and was increased by 10% every 2 wks	Total fat (kg)	A significative interaction was found between group and time. ($p = 0.022$, $\eta p2 = 0.30$)
				Body mass (kg), BMI ($kg.m^{-2}$),	Changes in body mass and BMI in both experimental groups after training were significantly greater than those in the C group ($p<0.001$). Significative interaction was found for body mass ($p<0.001$, np2 = 0.66) and BMI ($p<0.001$, np2= 0.66)
				%BF	Changes in % BF in the DTBFR group were more significant than both DT ($p=0.007$) and C groups ($p=0.001$). %BF change in the DT group was also greater than in the C group ($p=0.017$). Significant difference in %BF after training in both experimental groups. Significative interaction was found ($p<0.001$, $\eta p2=0.61$)
				Visceral fat (kg),	A decrease significantly greater in visceral fat ($p = 0.003$) in DTBFR than in the C group ($p<0.05$) but there was no significant difference with the DT group ($p>0,05$). Significative interaction was found ($p=0.044$, $\eta p2=0.26$).

Lan, 2022 (68) – R.C.T.	56 students <u>Age</u>: 18 - 25 yrs <u>Groups:</u> **LICT-BFR**: low-intensity continuous training with the BFR **MICT**: moderaite intensity continuous training **HITT**: hifh-intensity interval training **CON**: to maintain the same lifestyle	3x/wk for 8 wks <u>For both</u>: a standardized 5 min warm-up. A 10 min resting phase followed. All sessions were performed on the treadmill. <u>LICT-BFR</u>: 15 min at 57-63% HRmax <u>MICT</u>: 45 min at 64-76% HRmax with the cuff <u>HITT</u>: 4x4min at 85-95%HR max followed by 3min active resting to 64-76% between the interval training	Elastic cuffs (B Strong, USA, width 5-8cm) At the proximal ends of the thighs Pressure set at 200 mmHg and increased by 20 mmHg for each wk (200 to 360 mmHg)	Fat mass (kg)	Significant reduction and non-significant increase in fat mass after training in MICT and CON respectively ($p<0.05$, $p = 0.075$, respectively). Significant decreasing effects on fat mass in LICT-BFR and MICT compared with CON ($p<0.05$).
				Muscle mass (kg)	Significant increase in muscle mass after training for LICT-BFR and MICT ($p<0.05$). Non-significant changes in muscle mass for HITT and CON. Significant increase in muscle mass for all exercise groups compared with CON ($p<0.01$)
				% BF	Significant decrease in body fat percentage after training for all exercise groups ($p<0.05$). Significant increase in % BF for CON ($p<0.001$). Significant decrease in % BF for all exercise groups compared with CON.
				Waist to hip ratio	No significant change in waist to hip ratio for all groups.
				Visceral fat area (cm^2)	Significant decrease in visceral fat area after training for MICT ($p<0.01$). Significant increase in visceral fat area after training for CON ($p<0.05$). Significantly decreasing effect of visceral fat surface area in groups 1 and 2 compared with the con group.

Li, 2022 (82) – R.C.T.	72 obese adults Age: **C**: 21.5 ± 1.5 yrs **H**: 21.8 ± 1.8 yrs **I**: 21.6 ± 1.9 yrs **E**: 22.1 ± 2.0 yrs Groups: **C**: control, no training **H**: high intensity interval training **I:** high intensity interval training with BFR during interval **E:** high intensity interval training with BFR during exercise	24 sessions, 2x/wk for 12 wks For all: A 10 min warm-up followed by 4 repetitions of 3 min sprint at an intensity of 85% VO_2max with a resting phase of 3 min between each repetition. A 10 min cool-down at the end of the session. All sessions were performed on a cycle ergometer I: BFR was applied during the resting phases E: BFR was applied during the sprints	Inflatable 7-cm wide cuffs (The Occlusion Cuff, Belfast, Britain) At the inguinal folds of both legs Pressure maintained at 40% of limb arterial occlusive pressure	% BF, total body fat mass (kg), android fat mass (kg), gynoid fat mass (kg), trunk fat mass (kg), abdominal visceral fat area (AVFA) and abdominal subcutaneous fat area (ASFA)	Significant decreased ($p<0.05$) for all body composition measures in the three exercise groups (H, I and E) for pre- to post-intervention and also compared with the C group. Significant decrease difference ($p<0.05$) in BF, trunk fat mass in both I and E groups compared with the H group but only for the I group in total body fat mass, android fat mass. The reduction of AVFA in the I group was significatively ($p<0.05$) superior to the H and E groups.
Lopes, 2022 (85) – R.C.T.	32 older adults Age: 72 ± 7 years Groups: **RT-BFR**: low intensity with BFR **RT-HI:** high intensity without BFR **RT-CON**: low intensity	3x/wk for 12 wks For all: 30 min of strength exercises for the lower and upper limbs in a precise order. 3 sets of 10 reps. 1-min rest between sets. RT-BFR: 30% of 1-RM with the BFR. During leg exercises, only the leg cuffs were inflated and vice versa. RT-HI: 70% of 1-RM RT-CON: 30% of 1-RM without the BFR	A nylon cuff (11x85 cm) connected to a pneumatic cuff (Holanson modèle TD312, Bellevue, WA, USA) On the proximal third of the arms and legs Inflated to 50% of resting arterial occlusion pressure	Fat % Fat mass (kg) Lean mass (kg) FFM (kg) Bone mineral content (kg) Appendicular muscle mass(kg) Skeletal muscle mass (kg)	Significant increase in AMS and SMM in the RT-BFR compared with the RT-CON group ($p<0.05$ and ES = 0.18). No significant changes in the other measures.

Tangchaisuriya, 2022 (73) – R.C.T	50 males masters road cyclists <u>Age:</u> **BFRIT**: 39.6 ± 3.8 yrs **CON**: 41.5 ± 4.5 yrs **HIIT**: 41.7 ± 3.8 yrs <u>Groups</u>: **BFRIT**: high intensity interval training with BFR **CON:** continuous training **HIIT:** high intensity interval training	2x/wk for 12 wks <u>For all:</u> a standardized 6 min warm-up. A 10 min cool-down after the session. All sessions were performed on a cycle ergometer <u>BFRIT</u>: 2x4 min at 80% PPO and 2x4 min at 60% alterned with 2 min at 30% PPO. BFR during all training session after the war-up. <u>CON:</u> 75 min 65-70% PPO <u>HIIT</u>: 4x4 min at 80% PPO alternated with 2 min at 30% PPO	Pneumatic cuff (SC10 segmental pressure cuff; Hokanson, Bellevue, WA) At the proximal portion of both tights Pressure maintained at 30% of arterial occlusion pressure	BW (kg) %BF Fat mass (kg) Total lean mass (kg)	No significant changes pre- to post values in BW, BF and fat mass for all three groups ($p>0.05$). Significant increase for pre- to post-x between groups values in total lean mass for BFRIT ($p<0.001$).

Legend: %BFt=percentage of body fat, BFR=blood flow restriction, BMI=body mass index, min=minute, Pmax=maximal power, sec=second, vVO$_2$max=speed at VO$_2$max, wk=week, wks=weeks, yrs=years, BW=body weight, FFM=fat free masse, TG=triglyceride, LDL-C= low-density lipoprotein, HDL-C=high-density lipoprotein, 1RM= one repetition maximum, PPO= peak power output, HRmax = maximum heart rate

Table 6: RCT's studies studying non-localized effects on blood homeostasis.

Author – article type	Sample, age and groups	Training program	BFR material, cuff site(s) and occlusion pressure	Measures	Results for non-localized effects
Chen, 2022 (87) – R.C.T.	37 obese male students (>25% body fat or >28kg/m2 BMI Age: **EG**: 20.3 ± 1.07 yrs **CG**: 20.1 ± 1.08 yrs Groups: **EG:** training at low intensity with BFR **CG**: training at low intensity without BFR	24 sessions, 2x/wk for 12 wks For both: 3 sets of 15 minutes cycling on a cyclo-ergometer at 40% of VO_2 max 1-min rest between sets. EG: BFR for the entire training period	Air pressure belts (Kaatsu-Master, Sato Sports Plaza, Tokyo) On the proximal thighs Pressure maintained at 200 mmHg	Glucose, total cholesterol, TG, HDL-C cholesterol, LDL-C	Significant decrease in glucose, total cholesterol, LDL-C,for EG compared to CG ($p<0.05$). Significant increase in HDL-C for EG compared to CG ($p<0.05$) Significant difference in glucose, total cholesterol, TG, HDL-C, LDL-C before and after the training in the EG ($p<0.05$ and $p<0.001$). Significant difference in glucose, total cholesterol, and LDL-C before and after the training in the CG ($p<0.05$)

Corrêa, 2021 (84) – R.C.T.	90 male and female with chronic kidney disease Age: **CON**: 57 ± 6 yrs **RT**: 58 ± 9 yrs **RT+BFR**: 60 ± 8 yrs Groups: **CON**: control **RT**: resistance training **RT+BFR**: resistance training with BFR	3x/wk for 6 months CTRL: no intervention RT: 3 sets of 12 repetitions at 50% 1-RM in the first and second month, 3 sets of 10 repetitions at 60% 1-RM in the third and fourth month, and 3 sets of 8 repetitions at 70% 1-RM in the fifth and sixth month. RT+BFR: 3 sets of 12 repetitions at 30% 1-RM in the first and second month, 3 sets of 10 repetitions at 40% 1-RM in the third and fourth month, and 3 sets of 8 repetitions at 50% 1 -RM in the fifth and sixth month	No indications about the cuff and where they are located 50% of resting systolic blood pressure	Blood pressure reactivity to stress (3-minutes static handgrip exercise at 30% MVC) Blood collection Blood pressure monitoring Estimated glomerular filtration rate (eGFR)	Exercise pressor response attenuated in RT and RT+BFR when compared to pre-intervention values and CTRL ($p<0.0001$ for group × time interaction). Blood collection: Ang1-7 increased and vasopressin decreased after both RT programs ($p<0.0001$ for group × time interaction), but the decrease in vasopressin was greater for the conventional RT when compared to RT+BFR. Significant decrease in blood pressure for RT and RT+BFR for pre- to post-intervention values ($p<0.001$). No significant change for the CTRL group. Significant difference between RT and RT+BFR groups versus CTRL ($p<0.001$) at 6 months. Significant decrease of eGFR for RT, CTRL and RT+BFR for pre- to post-intervention values ($p<0.001$). Decrease was less marked for RT and RT+BFR versus CTRL ($p<0.001$) at 6 months.

De Deus, 2021 (88) – R.C.T.	105 patients with chronic kidney disease <u>Age</u>: **CTL:** 57.60 ± 5.22 yrs **RT:** 58.09 ± 6.26 yrs **RT+BFR**: 58.06 ± 6.47 yrs <u>Groups</u>: **CTL**: control **RT:** resistance training without BFR **RT+BFR**: resistance training with BFR	3x/wk for 6 months <u>For RT and RT+BFR</u>: 8 exercises (upper and lower body) per session with a training load adjusted every 2 months. For the first 2 months: 1-3 sets of 12 repetitions at 50% 1-RM. For the third and fourth months: 2-3 sets of 10 repetitions at 60% 1-RM. For the last 2 months: 3 sets of 8 repetitions at 70% 1-RM <u>RT+BFR</u>: cuffs were applied on each arm only during upper body exercises and on each thigh only during lower body exercises	7.0x80.0cm cuffs for the upper limbs and 18cm wide cuffs for the lower limbs Cuffs were applied to both arms and inguinal fold areas Pressure was maintained at 50% of systolic blood pressure at rest	eGFR	The eGFR decreased in all groups from baseline values but it was significatively less pronounced ($p<0.0001$) in both RT and RT+BFR groups in comparison to the CTL group.
Deus, 2022 (83) – R.C.T.	105 patients with chronic kidney disease <u>Age:</u> **RT:** 58 ± 6.22 yrs **RT+BFR:** 58 ± 6.51 yrs **CTL:** 57.51 ± 5.23 <u>Groups:</u> **RT:** resistance training **RT+BFR:** resistance training with BFR **CTL:** control group	3x/wk for 6 months <u>For both:</u> 7 exercises, 1 min of rest between sets. The number of reps differed between the 3 training periods. Wks 1-8: 3 sets of 12 reps. Wks 9-16: 3 sets of 10 reps. Wks 17-24: 3 sets of 8 reps. <u>RT:</u> first period: 50% of 1 RM. Second period: 60% of 1 RM. Third period: 70% of 1 RM. <u>RT+BFR:</u> first period: 30% of 1 RM. Second period: 40% of 1 RM. Third period: 50% of 1 RM. The exercises performed with the BFR. <u>CTR:</u> non exercise training	The arm cuff: 7x80 cm (Clinic Arm Model) and thigh cuff: 10x80cm (Clinic Arm Model) On the proximal part of limbs. Pressure maintained at 50% of systolic blood pressure.	eGFR Albumin (g/dL) Blood glucose (mg/dL)	Significant decrease in eGRF in all three groups between the start and end of training ($p<0.001$). Significantly lower decrease between RT, RT-BFR and CRT ($p<0.001$). No significant difference between the decrease in eGRF for the two exercise groups. No significant difference in serum albumin levels for all groups between the beginning and end of training. A significant change was demonstrated in the delta analyses for the exercise groups. This change was an increase in albumin levels ($p<0.001$). Significant reduction in blood glucose levels for RT and RT+BFR between the start and end of training ($p<0.001$). No significant difference between these two groups. Blood glucose levels were

	significantly lower in the exercise groups compared to the CRT group (p<0.001).
HbA1c (%)	Significant reduction in HbA1c in RT and RT-BFR between the start and end of training (p<0.001). No significant difference between these two groups. HbA1c was significantly lower in the exercise groups compared with the CRT group (p<0.001).
TG (mg/dL)	Significant decrease in TG between the start and end of training for RT (p<0.05). Significantly greater decrease in TG in RT compared with the CTL (p<0.01). No time effect or group effect on TG for the RT+BFR. The changes in TG levels were significantly higher in the RT and RT+BFR compared to the CTL (p<0.001).
HDL-C (mg/dL), LDL-C (mg/dL), total cholesterol (mg/dL)	No time effect or group effect on HDL-C, LDL-C and total cholesterol for all groups.

Li, 2022 (82) – R.C.T.	72 obese adults Age: **C**: 21.5 ± 1.5 yrs **H**: 21.8 ± 1.8 yrs **I**: 21.6 ± 1.9 yrs **E**: 22.1 ± 2.0 yrs Groups: **C:** control, no training **H:** high intensity interval training **I:** high intensity interval training with BFR during interval **E:** high intensity interval training with BFR during exercise	24 sessions, 2x/wk for 12 wks For all: A 10 min warm-up followed by 4 repetitions of 3 min sprint at an intensity of 85% VO_2max with a resting phase of 3 min between each repetition. A 10 min cool-down at the end of the session. All sessions were performed on a cycle ergometer was selected during the exercise. I: BFR was applied during the resting phases E: BFR was applied during the sprints	Inflatable 7-cm wide cuffs (The Occlusion Cuff, Belfast, Britain) At the inguinal folds of both legs Pressure maintained at 40% of limb arterial occlusive pressure	Blood sampling (TG, glucose, insulin, total cholesterol)	Significant decreased ($p<0.05$) for TG, glucose, insulin, total cholesterol in the three exercise groups (H, I and E) for pre- to post-intervention values and also compared with the C group. Both the I and E groups showed significantly greater improvements in blood glucose and insulin levels compared to the H group ($p<0.05$).
Tanaka, 2018 (72) – R.C.T.	30 men with post-infarction heart failure Age: 60.7 ± 11.1 Groups: **CG**: control **IG**: exercises with BFR	3x/wk, 6 months For both: 15 min of cycling on a cycle ergometer at 40-70% of the VO_2peak CG: no BFR applied IG: BFR applied during the training session	Pneumatic cuff (width: 90 mm; length: 700 mm) On the proximal ends of the thighs 40–80 mmHg over the systolic blood pressure that is required for vascular occlusion	Blood sampling (serum TG, HDL-C, LDL-C, total cholesterol, glucose, and HbA1c)	No significant difference in serum TG, HDL-C, LDL-C, total cholesterol, glucose, and HbA1c for CG and IG group for pre- to post-test values and no significant difference between groups at the end of the intervention

Tangchaisuriya, 2022 (73) – R.C.T	50 males masters road cyclists Age: **BFRIT:** 39.6 ± 3.8 yrs **CON**: 41.5 ± 4.5 yrs **HIIT**: 41.7 ± 3.8 yrs Groups: **BFRIT:** high intensity interval training with the BFR **CON:** continuous training **HIIT:** high intensity interval training	2x/wk for 12 wks For all: a standardized 6 min warm-up. A 10 min cool-down after the session. All sessions were performed on a cycle ergometer BFRIT: 2x4 min at 80% PPO and 2x4 min at 60% alterned with 2 min at 30% PPO. BFR during all training session after the war-up. CON: 75 min 65-70% PPO HIIT: 4x4 min at 80% PPO alterned with 2 min at 30% PPO	Pneumatic cuff (SC10 segmental pressure cuff; Hokanson, Bellevue, WA) At the proximal portion of both tights Pressure maintained at 30% of arterial occlusion pressure	Blood sampling (TG, total cholesterol, HDL-C, LDL-C, glucose and creatine phosphokinase)	No significant difference for pre- to post-intervention values in total cholesterol, TG, HDL-C, glucose, creatine phosphokinase for all three groups and also no significant difference between groups at the end of the intervention. Significant decrease in LDL-C for the BFRIT group (p=0.012).

Footnote legend: 1-RM =one repetition maximum, BFR=blood flow restriction, HbA1c= glycosylated hemoglobin, LDL-C= low-density lipoprotein, HDL-C= high-density lipoprotein, TG= triglyceride, eGFR= Estimated glomerular filtration rate, VO2peak= highest value of oxygen attained upon an incremental or other high-intensity exercise test, PPO= peak power output, wk=week, wks=weeks, yrs=years,

ABSTRACT

BACKGROUND: The BFR training has been stated as a safe strengthening technique used and a safe rehabilitation tool if it's properly applied but to the best of our knowledge, there are only some articles that reported the non-localized chronic adaptations of BFR training. The main objective of this scoping review is to assess the current literature on the non-localized effects of chronic use of the BFR technique. Secondly, this review will identify gaps in the existing research that could be addressed in future studies.

METHODS: The search equations were entered into three scientific databases: Embase, PubMed, and Scopus. The "Grey literature" was screened by searching on Google Scholar and through several websites. The studies had to meet the eligibility criteria to be included. The scoping review was drafted following the PRISMA guidelines.

RESULTS: A total of 56 articles were included in this exploratory review following the selection process. The results show a trend towards improvement in anaerobic and aerobic capacities, mainly for VO_2max and PPO. Adaptations were also observed for certain measures of body composition, such as percentage of fat mass and lean mass, as well as for certain blood homeostasis data: glucose levels, cholesterol (total and LDL-C), eGFR and triglycerides. Finally, neuromuscular effects were also observed in the EMG amplitude. Few and some conflicting results were found for BFR's cross-transfer effect, either in proximal cuff muscles or unrestricted limbs.

CONCLUSION: The use of BFR seems to lead to non-localized effects. However, further research is needed to confirm some of these effects. In the future, these non-localized effects could be advantageous in the management of pathological populations such as patients with chronic kidney disease, chronic heart failure or obesity.

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