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REVIEW

Effects of blood flow restriction training on aerobic capacity: a systematic review and meta-analysis

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Abstract

Background and purpose Numerous research studies have shown the effects of Blood Flow Restriction (BFR) training on muscle strength and hypertrophy, but there is still no comprehensive analysis of the effects on aerobic capacity. The purpose of this study was to conduct a systematic review with meta-analysis to evaluate the qualitative and quantitative results of BFR training on aerobic capacity.

Methods PRISMA guidelines were used to carry out the systematic review and meta-analysis. Five electronic databases were searched up to October 2020: PubMed, Web of Science, EBSCO, Scopus and Cochrane/Embase. Data selected for primary analysis consisted of post-intervention changes in VO2 values (VO_{2max}, VO_2peak). Case reports, acute studies and review studies were excluded. The protocol was registered on PROSPERO (CRD42020214919).

Results After the elimination of duplicates, 62 records were screened. Among these, 17 studies were included in the systematic review. Twelve of these were involved in the meta-analysis.

Discussion BFR training compared with exercise under normal blood flow conditions could positively influences both aerobic capacity and athletic performance. Differences in young and older subjects were discussed. BFR showed to be a promising and beneficial training to elicit improvements in aerobic capacity (measured in VO_2) and performances.

Level of evidence 1a.

Keywords Aerobic capacity · Blood flow restriction · BFR · Vascular occlusion training · VO_{2max} · VO_2peak

Introduction

The American College of Sports Medicine recommends adults to routinely perform moderate-intensity aerobic exercise 5–7 days a week (40–60% of VO_2 peak) or vigorous exercise 3 days a week (≥ 60% VO_2 peak) to improve cardiorespiratory fitness and reduce the risk of metabolic, cardiovascular and pulmonary diseases [1]. Maintaining a high degree of aerobic fitness may enhance sports performance [2–4] improve recovery capabilities [5] and have positive implications for health [6]. It has been suggested that a low maximal oxygen uptake (VO_{2max}) level could be a risk factor for developing cardiovascular diseases and all-causes of mortality among general population [7]. VO_{2max} and VO_{2peak} are usually used to assess aerobic capacity (AC). VO_{2max}, a concept first proposed by Hill et al. in 1923 [8, 9], is defined as the highest rate of oxygen uptake (VO_2) and utilization by the body during intense, maximal exercise that no further increases in work rate bring on additional rises in VO_2 (i.e., plateau) [10]. Peak VO_2 (VO_{2peak}), directly reflective of VO_{2max}, is the highest value of VO_2 attained upon an incremental or other high-intensity exercise test, designed to bring the subject to the limit of tolerance [11]. Exercise is considered a successful method for improving physical fitness in healthy individuals [12] as well as in individuals with special limitations [13]. Moreover, performing regular exercise help in preventing the decline of muscle strength and muscle mass, reducing VO_{2max} and VO_2 kinetics with advancing age [14]. Nevertheless, high-intensity exercise requires intense exertion and involves high mechanical stress, resulting more difficult and complex to perform by chronic physical illness patients. Thus, a possible alternative to high-intensity aerobic training is a method that

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combines aerobic exercise (walking or cycling) with blood flow restriction (BFR).

In recent years, research has demonstrated that combining of low-load resistance training with BFR to the active musculature may produce significant hypertrophy and strength gains [15–18] using loads as low as 30% 1RM [19]. In addition BFR training has been found to yield hypertrophy responses comparable to that observed with heavy-load resistance training [20]. BFR training involves exercising with an external constricting device (such as blood pressure cuffs, banded muscle wraps, or tourniquets) applied to the proximal limb musculature, whit the aim of partially restricting arterial blood flow, and totally occlude venous return [21]. The majority of BFR studies evaluated these effects on skeletal muscle strength and hypertrophy. Formiga et al. [22] have also studied the effects of BFR on AC, albeit only on young and physically active healthy subjects obtaining conflicting conclusions.

As discussed in a recent review [23], light-intensity exercise combined with BFR leads to improvements in AC and athletic performance in young adults when using occlusion pressures of 130 mmHg or higher. Proposed mechanisms for the improved VO_{2max} adaptations highlighted after BFR application, are the following: BFR can increase the central cardiovascular response during exercise [24] by elevating heartrates, systolic blood pressure and diastolic blood pressure compared to the same exercise under non-occluded conditions [25–27]. In recent times, Christiansen et al. [28] showed increases in muscle ancillary protein, peroxisome proliferator-activated receptor-γ co-activator 1α (PGC-1α mRNA) and phospholemman isoforms (FXYD1) during BFR exercise, which was related to increased oxidative stress and fiber type-dependent AMPK signaling. To speculate, it is possible argue that the described response elicited after BFR application might led to a greater training stimulus (compared to none BFR training), thus inducing VO_{2max}-related improvements. Recent data [29] indicate that the application of BFR may induce increases in VO_{2max} even in highly trained athletes, and this makes the results even more noteworthy.

Therefore, the goal of this review and meta-analysis was to systematically identify and assess studies combining training with BFR and to investigate the effectiveness of BFR on AC.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [30].

The protocol for this systematic review can be found on PROSPERO (ref. CRD42020214919), available from https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020214919.

Search strategy

A comprehensive literature review was performed through October 2020. A search for candidate studies published from early period up to 1st October 2020 was conducted using five relevant online databases (PubMed, Web of Science, EBSCO, Scopus and Cochrane/Embase) using the following search terms: ((VO2) OR (VO2max)) AND (("blood flow restriction") OR (bfr) OR (kaatsu) OR ("vascular occlusion")). The Rayyan QCRI Software [31] which is used for systematic reviews was used to read the titles and abstracts, remove duplicate articles and read the full texts; exercise training studies utilizing BFR were selected. The reference list of relevant papers was also examined.

Inclusion and exclusion criteria

No restrictions were applied to publication period, neither to the country in which the study was conducted. The search was limited to studies published in English. Restriction was applied on study designs. Only experimental studies were included, both Randomized Controlled Trials and Clinical Trials. Articles were considered eligible for inclusion when they included the pre-training and post-training assessments AC (i.e., VO_{2max} or VO_{2peak}), the training protocol consisted of exercise training with concurrent BFR, and the training protocol lasted a minimum of 2 weeks.

Only studies using mechanical BFR through external applied pressure on the proximal point of a limb (i.e., blood pressure cuff or tourniquet) were included. All other mechanisms (e.g., hyperbaric chamber and hypoxic environment) were excluded. Only studies about chronic adaptations after BFR were included in this review: any acute studies, case studies, single-arm studies or those not published in a scientific peer-reviewed journal in English were excluded from meta-analysis.

Risk of bias

Following the instructions in the Cochrane Handbook for Systematic Reviews of Interventions [32], risk of bias was assessed using six criteria that were individually rated for each study. Accordingly, selection bias, performance bias, detection bias, as well as attrition and reporting bias were considered by the reviewers.

Study selection and data extraction

Two independent researchers (authors PF and LB) screened the studies for inclusion, first based on titles and abstracts and then on full text. Disagreements were discussed and consensus was reached in all cases. After the first screening, the primary reviewer selected the relevant studies and assessed them against the inclusion criteria. A second reviewer then cross-checked the studies. After the second screening, studies that did not fit the inclusion criteria were systematically excluded and others that appeared pertinent were identified. A final list of eligible studies was compiled, and any disagreements were resolved by a third reviewer (AD) or by consensus. From the remaining eligible papers, data were recorded relating to (1) study design; (2) clinical population characteristics; (3) rehabilitation protocol: type, frequency, occlusion characteristics, training load and duration of BFR training and (4) outcome measure. Data regarding the safety of BFR implementation were obtained from the systematic analysis of the studies. Data were extracted using a custom spreadsheet composed by PF.

Strategy for data synthesis

A narrative synthesis of the findings of the included studies was provided, structured around the type of intervention, BFR characteristics, type of outcome, and intervention content. A quantitative synthesis of the benefits of BFR training concerning AC was discussed.

Meta-analysis

Data analysis was performed by one author (PF) and reviewed by the second author (LB). The quantitative analysis was conducted by comparing outcomes. Data were extracted in the form of mean, SD and sample size for the meta-analysis. Pooled data were analyzed with a fixed-effect model to determine heterogeneity between studies using the I^2 statistic, which determines the percentage of variability in effect estimates that is due to heterogeneity.

Results

Search results

A total of 138 records were identified. Seventy-seven duplicate records were excluded, and the remaining 62 were screened. After reading the titles and abstract, 23 studies were excluded. After the exclusion of 14 records for inappropriate research design (acute studies), of 7 records for the characteristics of the occlusion (pre or post exercise) and of 1 record for inappropriate BFR method, 17 studies [33–49] were included in the qualitative synthesis. Twelve [33–44] of the 17 studies examined were included in the quantitative synthesis. Figure 1 represents the selection process of the study. Table 1 contains information about the characteristics of included studies.

Study characteristics: clinical populations and BFR training interventions

The sample size in the studies varied from 10 [46] to 37 [41] participants. Mean ages ranging from 20.2 ± 3.3 [48] to 64.7 ± 4.1 years [47]. Subjects in the studies were all healthy except for one paper, [49] including post-infarction subjects. The samples included in the studies were different: subjects physically active [33–35, 37, 39, 43, 46, 48], and untrained or sedentary [36, 40, 44, 49]. In several papers, subject's physical condition was not described [41, 45, 47].

Considering the total number of subjects among the studies analyzed ($N=422$), most of the total were male ($M=268$, $F=129$). In one study [47], the sex of the subjects was not reported ($N=25$).

Among athletic subjects, various sports were described: football [39], rowing [43], netball [48] basketball [33]. BFR was applied using either pneumatic cuffs, practical cuffs, hand pumped blood pressure cuffs or elastic wraps ranging from 5 to 18 cm in width. Occlusive pressure ranged from 60 to 220 mmHg. Studies either selected a pressure based on previous research, on total limb occlusive pressure, on moderate perceived pressure, or on systolic blood pressure. The duration of the BFR training intervention ranged from 2 to 24 weeks, with a frequency of 2–5 training sessions per week.

Outcome measures

AC were measured by VO_{2max} [33–36, 39–43, 47, 48], VO_2 peak [37, 38, 44], VO_2 kinetic [45], peak VO_2/W [49], or difference between thigh O_2 delivery and O_2 uptake [46]. However, only VO_{2max} and VO_2 peak could be included in the meta-analysis.

Risk of bias

The main findings from the risk of bias assessment were that all the studies could not blind participants and no study included in this review specified the blinding of outcome assessment.

Nevertheless, the review authors judge the assessment of outcome is not likely to be influenced by knowledge of intervention received and, as indicated by the Cochrane handbook for systematic reviews of interventions [32], this is a criterion for a judgement of 'YES or LOW risk'.

Other main findings conceal group allocation, and sequence generation was largely unreported, while no attrition bias was observed. Reporting bias was not observed in the majority of studies. From the qualitative analysis, a small

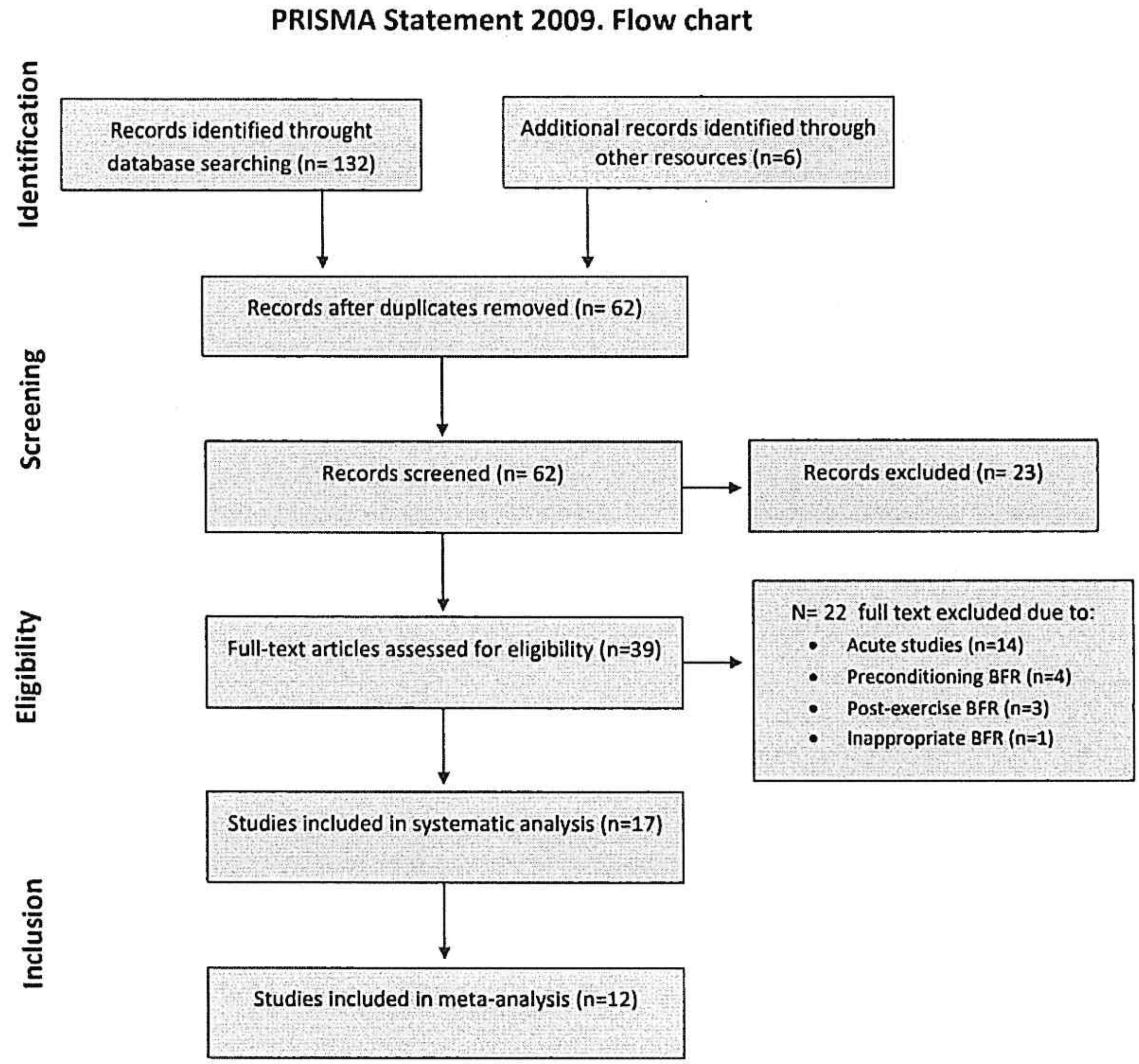

Fig. 1 Flow chart of study selection process

number of studies were found with a high level of quality [43, 46, 49] (Fig. 2).

Meta-analysis

The quantitative analysis was carried out by comparing outcomes and follow-ups. This pool was based on comparable outcomes and comparable subjects; this has allowed consideration of 12 studies in the meta-analysis. The values considered in this study are VO_{2max} and VO_2 peak. We decided to stratify the meta-analysis of the VO_{2max} value by separating athletic and well-trained subjects from sedentary or untrained subjects. Contrary because of the small number of studies reporting the VO_2 peak outcome, it was not possible to stratify the analysis for such parameter.

The meta-analysis and the stratification were structured as follows:

1. Comparison of exercise protocol + BFR vs. exercise protocol concerning VO_{2max} (ml/min/kg), in athletic or well-trained subjects. The studies of Abe et al. (2010), Amani et al. (2018), de Oliveira et al. (2015), Held et al. (2019), Park et al. (2010) and Paton et al. (2017) [33–35, 39, 41, 43] were considered. Meta-analysis revealed statistically significant results ($P < 0.0001$) in favor of the experimental group compared to the control group (mean difference = 4.92, 95% Confidence Interval (CI) = 2.69, 7.14). The I2 statistic of 11% represented very low heterogeneity in the results (Fig. 3.1).
2. Comparison of exercise protocol + BFR vs. exercise protocol concerning VO2 max (ml/min/kg), in sedentary or untrained subjects. The studies of Conceição et al. (2018), Ferreira Jr. et al. (2019) and Keramidas et al. (2011) [40–42]. The meta-analysis revealed results that were neither statistically nor clinically significant

Table 1 Characteristics of the included studies

References	Subjects Intervention group Control group	Exercise protocol	Frequency/duration	Cuff charateristics	Main findings
Abe 2010 [38]	Young physically active healthy man $n=19$ Gender male no. (%) = 19(100) Body mass (kg) = not reported Age = 23.0 ± 1.7 years Exercise protocol + BFR $n=9$ Exercise protocol $n=10$	40% of VO_{2max} and 15 min for IG 40% of VO_{2max} and 45 min for CG on an electrically braked bicycle ergometer	3 days a weeks, for 8 weeks	Pressure belts, width not reported, 160–210 mmHg	Significant improvements were observed in IG: ↑ MRI-measured thigh and quadriceps CSA and muscle volume increased by 3.4–5.1% ($P<0.01$) ↑ VO_{2max} (6.4%) ($P<0.05$) ↑ Exercise time until exhaustion (15.4%) ($P<0.05$) ↑ Isometric knee extension strength tended to increase by 7.7% ($P<0.10$) No changes in CG
Abe 2010 [35]	Elderly healthy active men and women $n=19$ Gender Male no. (%) = 4(21) Body mass (kg) = 54.1 ± 8.35 Age = 60–78 years Exercise protocol + BFR $n=11$ Non-exercise group $n=8$	20-min treadmill walking (67 m/min)	5 days a weeks, for 6 weeks	Pressure belts, width not reported, 160 – 200 mmHg	Significant (P < 0.05) improvements were observed in IG: ↑ Isometric (11%) knee extension and flexion torques ↑ Isokinetic (7–16%) knee extension and flexion torques ↑ muscle–bone CSA (5.8% and 5.1% for thigh and lower leg, respectively) ↑ ultrasound-estimated skeletal muscle mass (6.0% and 10.7% for total and thigh, respectively) ↔ No changes in Estimated VO_{2peak} No change in CG
Amani 2018 [39]	Young football players n = 28 Gender Male no. (%) = 28(100) Body mass (kg) = 73.04 ± 3.90 Age = 23.89 ± 2.26 years Exercise protocol + BFR n = 10 Non-exercising group $n=9$ Exercise protocol $n=9$	Aerobic interval at 400 m with maximum effort for 3 sets in per sessions (first week) and 4 set (second week)	4 days a weeks, for 2 weeks	Pressure belts, width not reported, 140 – 180 mmHg	↑ VO_{2max} (+3.66%) in IG ($P<0.05$) ↔ VO_{2max} in CG (+1.43%) ↓ VO_{2max} in non-exercise group (−3.82%) ↓ RPE in IG and CG ↑ RPE in non-exercise group

Table 1 (continued)

References	Subjects Intervention group Control group	Exercise protocol	Frequency/duration	Cuff charateristics	Main findings
Conceiçao, 2018 [40]	Healthy sedentary young men $n=30$ Gender Male no. (%) = 30(100) Body mass (kg) = 78.93 ± 10.6 Age = 22.6 ± 2.6 years Endurance Training group + BFR (ET-BFR) $n=10$ Endurance training group $n=10$ Resistance training group $n=10$	ET-BFR ($n=10$, 4 d°wk-1, 30-min cycling at 40% of VO_{2max}) RT ($n=10$, 4°wk-1, 4 sets of 10 repetitions leg press at 70% of one-repetition maximum with 60-s rest) ET ($n=10$, 4°wk-1, 30-min cycling at 70% of VO_{2max})	8 weeks	Pressure belts, width 18 cm, inflated to 80% LOP	↑ Leg-press 1-RM ($P<0.05$) in ET-BFR e RT ↔ No changes in leg press 1-RM in ET ↑ VO_{2max} ($P<0.05$) in ET-BFR e ET ↔ No changes in VO_{2max} in RT ↔ No changes in RPE in All groups ↑ VEGF mRNA ($P<0.05$) in ET and ET-BFR
Corvino 2019 [45]	Healthy participants $n=24$ Gender Male no. (%) = 17(71) Body mass (kg) = 70.4 ± 11.6 Age = 25 ± 6 years Low-intensity BFR interval training (BFR, $n=8$) Low-intensity interval training without BFR (LOW, $n=7$) High-intensity interval training without BFR (HIT, $n=9$)	2 sets of incremental reps on a stationary cycle ergometer. Rep = 3 + (n.weeks + 1) Each rep 2 min of cycling with 1-min passive rest, 5-min rest interset 30% Ppeak for LOW and BFR 110% Ppeak with a progressive 5% decrease in HIT	3 days a weeks, for 4 weeks	Pressure cuff belts (18 cm wide) 140–200 mmHg	↑ CO2p and VEp kinetics were speeded only in HIT (38.5 ± 10.6% $P<0.001$ and 31.2 ± 24.7% $P=0.004$) ↑ O2p kinetics speeded in HIT and BFR ↔ No changes in LOW

Table 1 (continued)

References	Subjects Intervention group Control group	Exercise protocol	Frequency/duration	Cuff charateristics	Main findings
Christiansen 2020 [46]	Healthy male physically active $n=10$ Gender Male n°(%) = 10(100) Body mass (kg) = 84 ± 14 Age = 25 ± 4 years Exercise protocol + BFR one limb $n=10$ Exercise protocol + no BFR contralateral limb (CONleg) $n=10$	5-min warm-up followed by 3 sets of three 2-min bouts with 1 and 5 min of active recovery between bouts and sets, respectively.. The intensity was 61 ± 3% in the first, 72 ± 4% in the second, and 81 ± 10% of maximal aerobic power	3 days a weeks, for 6 weeks	Pneumatic tourniquet, 13-cm wide inflated to ~ 180 mmHg	In BFR-leg, during exercise at 25% iPPO (Ex1) ↑ oxygen delivery and uptake (vs. CONleg; $P<0.05$) ↓ net lactate release (vs. CON-leg; $P<0.05$) In BFR-leg, during exercise at 90% iPPO (Ex2) ↑ oxygen delivery ↓ oxygen extraction ↔ oxygen uptake (vs. CON-leg; $P>0.05$) In CONleg, at both intensities, oxygen delivery, extraction, uptake, and lactate release, remained unchanged ($P>0.05$) Resting femoral artery diameter increased with intervention only in BFR-leg (~4%; $P<0.05$)
de Oliveira, 2015 [41]	Young adults = 37 Gender Male no. (%) = 22(59) Body mass (kg) = 70 ± 11 Age = 23.8 ± 4 years Low-intensity interval training with BFR ($n=10$) Low-intensity training without BFR (low, $n=7$) High-intensity interval training (HIT, n = 10), • Combined HIT and BFR (BFR + HIT, $n=10$ every session performed 50% as BFR and 50% as HIT)	5-min warm-up at 30% of Pmax 2 Sets of 5–8 reps of 2-min + 1-min passive Between Sets: 3-min at 30%Pmax + 2-min passive rest on a stationary cycle ergometer HIT ($n=10$): 110/105/100/95% Pmax HIT + BFR ($n=10$): Random order 1st set HIT or BFR and 2nd set HIT or BFR LOW ($n=7$): 30%Pmax BFR ($n=10$): 30%Pmax + 140–200 mmHg	3 days a weeks, for 4 weeks	Pressure cuff belts (18 cm wide) 140–200 mmHg, deflated during the 1-min rest periods	↑ VO_{2max} in BFR (5.6 ± 4.2%), HIT (9.2 ± 6.5%), and HIT + BFR (6.5 ± 5.5%) ↔ VO_{2max} in LOW (0.4 ± 4.7%) ↑ OBLA in all groups BFR = 16 ± 13%; HIT = 25 ± 13%; HIT + BFR = 22 ± 12%; LOW = 6 ± 4%) ↑ *P*max in BFR (11.7 ± 4.7%), HIT (15.0 ± 4.5%), and HIT + BFR (10.9 ± 4.5%) ↔ *P*max in LOW (1.6 ± 3.9%) ↑ Isometric strength only for the BFR group (11.4 ± 7.3%) ↔ Isometric strength unchanged in HIT (−0.7 ± 9.9%), HIT + BFR (−3.5 ± 6.8%), LOW (−2.6 ± 6.7%)

Table 1 (continued)

References	Subjects Intervention group Control group	Exercise protocol	Frequency/duration	Cuff charateristics	Main findings
Ferreira Jr, 2019 [42]	Middle aged men $N=26$ Gender Male no. (%) = 26(100) Body mass (kg) = 80.4 ± 10,9 Age = 51.9 ± 3.5 years Training + BFR $n=14$ Training $n=12$	For each session, 5 walking bouts of 3 min, 1-min rest interset Training on treadmill, 6 km/h, 5% grade	3 times a week, for 6 weeks	Standard sphygmomanometer, width 18 cm, length 80 cm, 80–100 mmHg	↑ VO_2 only in BFR group (P < 0.01) ↑ VO_2 on-kinetics only in BFR group ($P<0.01$) ↑ Muscle strength only in BFR group ($P<0.01$) ↑ VO_2 OFF-kinetics in BOTH groups ($P<0.01$)
Held, 2019 [43]	Elite Rowers n = 31 Gender Male no. (%) = 23(74) Body mass (kg) = 73.05 ± 11.5 Age = 21.8 ± 3.45 years Training + BFR $n=16$ Training $n=15$	Rowing (low, moderate and high intensity), cross (running and cycling) and strength training—at low intensities (< 2 mmol/L)	3 times a week, for 5 weeks	Elastic knee wraps, 200 × 13 cm, with moderate perceived pressure (7 on a scale of 0–10)	↑ VO_{2max} (+9.1 ± 6.2%) in IG ↔ SQ1RM
Keramidas, 2011 [36]	Untrained individuals $N=20$ Gender Male no (%) = 6(30) Body mass (kg) = 64.25 ± 14.35 Age = 23 ± 4.3 years Training + BFR (CUFF) group n = 10 Training, no BFR, (CON) $n=10$	2-min work, 2-min active recovery bouts at 90% and 50% of VO_{2max} for CON group 90% of VO_{2max}PRESS and 50% of VO_{2max} for CUFF group	3 times a week, for 6 weeks	Thigh cuffs pressure of + 90 mmHg	NO change in VO_{2max} Significantly increased peak power output (CON: 12%, CUFF: 20%) that was accompanied by higher deoxygenation (DStO2) measured with near-infrared muscle spectroscopy. These changes were more pronounced in the CUFF group Both groups reduced VO2 during the Sub80 test without concomitant changes in DStO2 TF150 was enhanced in both groups
Kim, 2016 [37]	Physically active subjects $N=31$ Gender Male no. (%) = 31(100) Body mass (kg) = 75.16 ± 12.16 Age = 22.4 ± 3.0 years Low-intensity cycling with BFR (LI-BFR) $N=11$ Vigorous intensity (VI) cycling ($N=10$) No exercise control ($n=10$)	VI: 20 min of cycling at 60% HRR for the initial 3 weeks followed by cycling at 70% HRR for remaining 3 training weeks LI-BFR: 20 min of cycling at 30% HRR for 6 weeks	3 times a week, for 6 weeks	elastic cuffs, width 5 cm, 160–180 mm Hg	↑ Knee flexion strength BOTH in VI and LI-BFR ↑ Leg lean mass LI-BFR NO change in VO_{2max} in LI-BFR

Table 1 (continued)

References	Subjects Intervention group Control group	Exercise protocol	Frequency/duration	Cuff charateristics	Main findings
Libardi, 2015 [47]	Healthy older adults $N=25$ Gender Male no. (%) = not described Body mass (kg) = 69.33 ± 10.8 Age = 64.7 ± 4.1 years Exercise protocol + BFR (BFR-CT) $n=10$ CT (endurance training (ET) $n=8$ No exercise group $n=7$	CT = endurance training (ET), 2 days/week for 30–40 min, 50–80% VO_{2peak} and RT, 2 days/week, leg press with 4 sets of 10 reps at 70–80% of 1-RM with 60-s rest BFR-CT = endurance training (ET), 2 days/week for 30–40 min, 50–80% VO_{2peak} and RT 2 days/week, leg press with 1 set of 30 and 3 sets of 15 reps at 20–30% 1-RM with 60-s rest	4 times a week, for 16 weeks	Standard blood pressure cuff (175 mm (width) 920 mm (length), at 50% of LOP	↑ CSAq post-test in CT and BFR-CT (7.3%, $P<0.001$; 7.6%, $P<0.0001$) ↑ 1-RM post-test in CT and BFR-CT (38.1%, $P<0.001$; 35.4%, $P=0.001$) ↑ VO_{2peak} post-test in CT and BFR-CT (9.5%, $P=0.04$; 10.3%, $P=0.02$)
Manimmanakorn, 2013 [48]	Netball players $n=30$ Gender Male no. (%) = 0 (0) Body mass (kg) = 65.2 ± 6.5 Age = 20.2 ± 3.3 years Exercise protocol + BFR $n=10$ Exercise protocol $n=10$ Exercise protocol + intermittent hypoxic training $n=10$	Three sets of knee extension followed by three sets of knee flexions to failure (total of 6 sets) with a 30-s rest between sets and a 2-min rest between exercises using an isotonic leg extension and flexion machine	3 times a week, for 5 weeks	Pneumatic cuff, 5 cm width, 160–230 mmHg	Relative to CG: ↑ MVC3 (11.0 ± 11.9%) ↑ MVC30 (10.2 ± 9.0%) ↑ Reps201RM (28.9 ± 23.7%) ↑ CSA (6.6 ± 4.5%) ↑ Vertical jump (4.8 ± 10.0%) ↑ 20-MST (11.7 ± 7.4%) ↑ MAS (3.3 ± 2.0%) ↑ VO_{2max} (5.1 ± 3.9%) ↓ 5 m Sprint (− 16.3 ± 14.4%) ↓ 10 m Sprint (− 3.3 ± 5.2%) ↓ 505 Agility (− 9.0 ± 6.7%)
Ozaki, 2010 [44]	Elderly sedentary women $n=18$ Gender Male no. (%) = 0 (0) Body mass (kg) = 53.45 ± 2.1 Age = 64 ± 1 years Exercise protocol + BFR $n=10$ Exercise protocol $n=8$	20 min of treadmill walking at a predetermined exercise intensity of 45% of heart rate reserve (HRR)	4 times a week, for 10 weeks	Elastic cuff, 5 cm width, 160–200 mm Hg	↑ MRI-measured thigh muscle CSA in BFR group (3.1%, $P<0.01$) ↑ muscle volume in BFR group (3.7%, $P<0.01$) ↑ maximal isometric strength in BFR group (5.9%, $P<0.05$) ↑ maximal isokinetic strength in BFR group (up to 22%, $P<0.01$) ↔ No differences in Control Group ↑ Estimated VO2peak in both groups ($P<0.05$)

Table 1 (continued)

References	Subjects Intervention group Control group	Exercise protocol	Frequency/duration	Cuff charateristics	Main findings
Park, 2010 [33]	Collegiate Basketball players $n=12$ Gender Male no. (%) = 12 (100) Body mass (kg) = 88.15 ± 6.65 Age = 20.45 ± 1.25 years Exercise protocol + BFR $n=7$ Exercise protocol $n=5$	5 sets of 3-min walking (4 km/h at 5% grade) on a motorized treadmill and a 1-min rest between walk-sets (19 min of total time). The walking speed was increased up to 6 km/h in the OCC-walk group while it remained constant throughout the training period in the NOR-walk group	2 times a DAY, 6 days a week, 2 weeks	Pneumatic cuff, 11 cm width, 160 to 220 mmHg	↑ VO_{2max} (+11.6%: $P=0.005$) ↑ VE max (+10.6%: $P=0.003$) ↑ Anaerobic capacity (Wingate test) (+2.5%: $P=0.022$) ↔ No difference in muscular strength
Paton, 2017 [34]	Recreational Athletes $n=16$ Gender Male no. (%) = 10 (62) Body mass (kg) = 75 ± 14 Age = 25 ± 7 years Running training + BFR $n=8$ Running training $n=8$	Running at 80% of PRV on a treadmill. Repeated bouts of 30-s efforts interspersed with 30-s of passive rest, from 2 sets of 5 rep to 3 sets of 8 rep. 150-s rest interset	2 times a week, for 4 weeks	Elastic knee wraps, width 7.5 cm, with moderate perceived pressure (7 on a scale of 0–10)	↑ VO_{2max} (+6.3 ± 3.5%) in IG vs (+4.0 ± 3.3%) in CG—(ES = 0.18 in favor of IG) ↑ TTE (+27 ± 9%) in IG vs (+17 ± 6%) in CG—(ES = 0.31 in favor of IG) ↑ Running economy only in IG (ES = 0.4 in favor of IG) ↑ PRV and Incremental time, both in IG and CG, (ES = 0.3 in favor of IG)
Tanaka, 2018 [49]	Patients with post-infarction heart failure $N=30$ Gender Male no. (%) = 30 (100) Body mass (kg) = 70.6 ± 11.7 Age = 60.7 ± 11.1 years Exercise protocol + BFR (IG; $n=15$) Exercise protocol (CG; $n=15$)	cycle ergometer at an intensity of 40–70% of the peak VO_2/W for 15 min	3 times a week, for 6 months	Pneumatic tourniquets (width: 90 mm; length: 700 mm), with appropriate pressure resulting in a 40–80 mmHg increase in the systolic blood pressure that is required for vascular occlusion (208.7 ± 7.4 mmHg)	Peak VO_2/W in the IG significantly increased compared with that in the CG Change in the serum BNP levels was significantly larger in the IG than in the CG

CG control group, *IG* intervention group, VO_{2max} maximum oxygen uptake, *CSA* cross-sectional area, *RPE* rate of perceived exertion, 1RM one-repetition maximum, *VEGF mRNA* vascular endothelial growth factor mRNA abundance, *Ppeak* peak incremental power, *CO2p* CO2 output, *ET-BFR* Endurance Training group with BFR, *VEp* ventilatory kinetics, *O2p* pulmonary oxygen kinetics, *iPPO* incremental peak power output, *Pmax* maximal power output, OBLA onset blood lactate accumulation, SQ1RM one-repetition maximum squat test, *Sub80* 6-min constant-power test at 80% of VO_{2max}, *DStO2* changes in oxygen saturation, *TF150* timed ride to fatigue—150-s maximal constant-power test to exhaustion, *CSAq* Quadriceps cross-sectional area, *MCV3* 3-s maximal voluntary contraction, *MCV30* 30-s maximal voluntary contraction, *Reps20IRM* number of repetitions at 20% 1RM, *20-MST* maximal multistage 20-m shuttle run test, *MAS* maximal attained speed, *VE max* maximal minute ventilation, *TTE* time to exhaustion, *PRV* peak running velocity, *BNP* brain natriuretic peptide

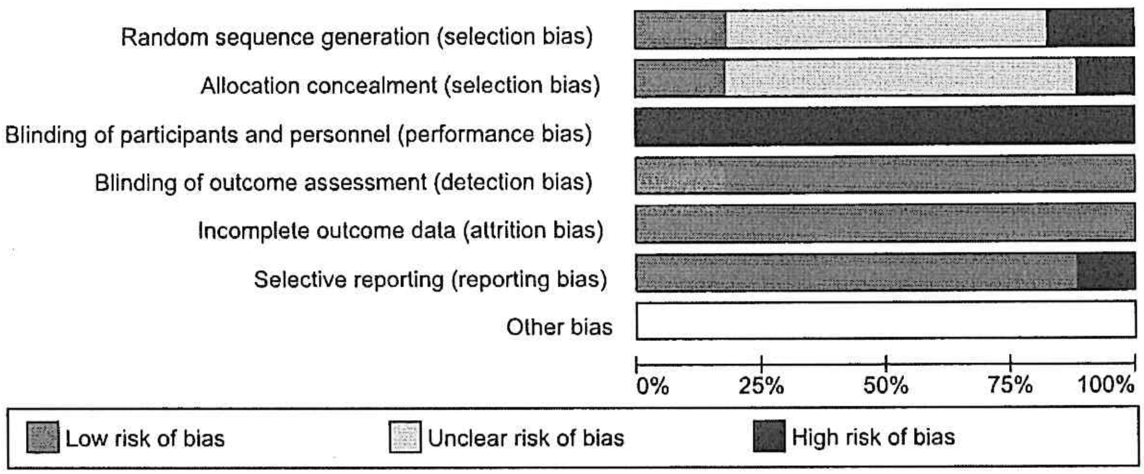

Fig. 2 Risk of bias graph

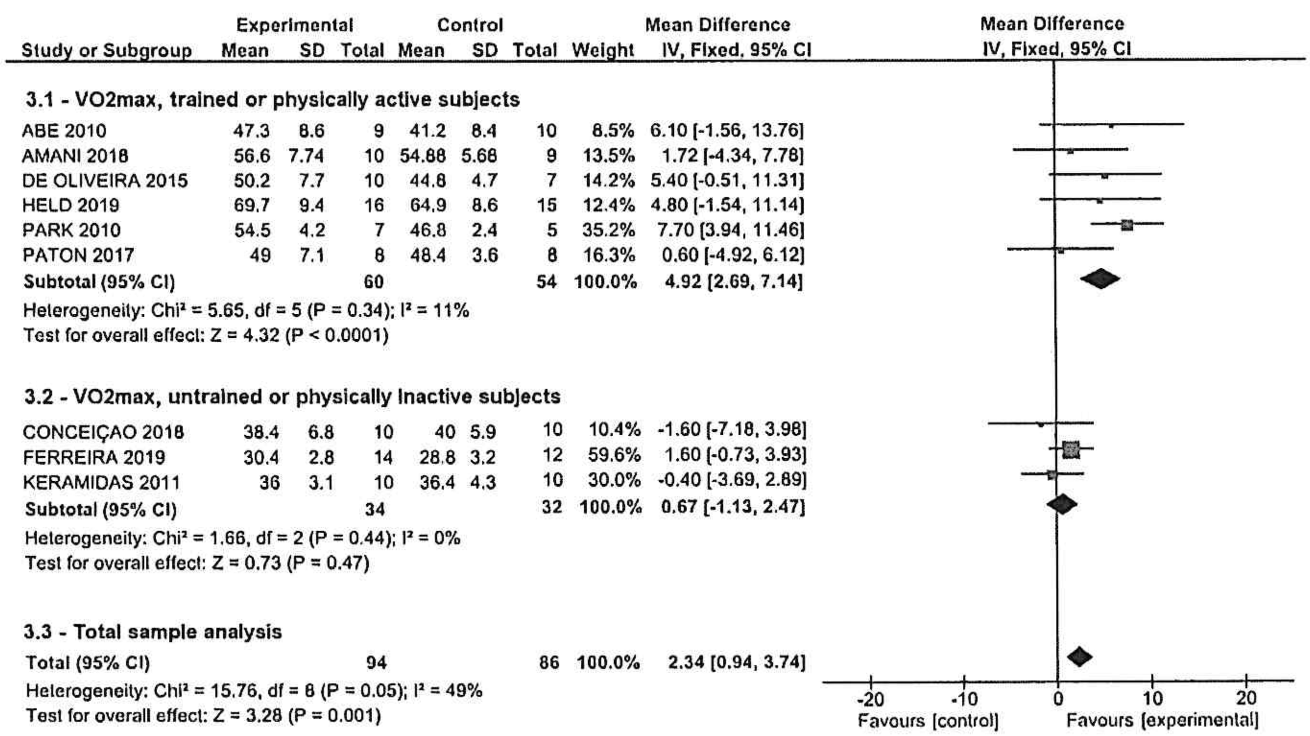

Fig. 3 Forest plot of the overall and subgroup effects of blood flow-restricted training on VO_{2max}

($P = 0.47$), showing a negligible impact on Vo2max in favor of the experimental group compared with the control group (mean difference = 0.67, 95% Confidence Interval (CI) = − 1.13, 2.47). The I^2 statistic revealed minimal heterogeneity in the results (0%) (Fig. 3.2).

3. Comparison of exercise protocol + BFR vs. exercise protocol concerning VO_2 peak (mL(kg/min). The studies of Abe et al. (2010–1), Kim et al. (2016) and Ozaki et al. (2010–1) [37, 38, 44] were considered. Meta-analysis revealed results statistically significant ($P = 0.01$) in favor of the control group compared to the experimental group (mean difference = − 1.67, 95% Confidence Interval (CI) = −2.97, −0.37). The I^2 statistic revealed minimal heterogeneity in the results (0%) (Fig. 4).

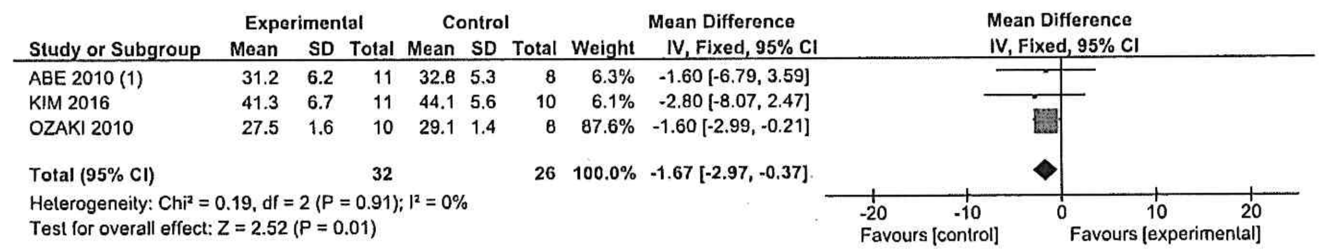

Fig. 4 Forest plot of the overall effects of blood flow-restricted training on VO_2 peak

Discussion

There is a growing interest in the use of BFR as a clinical rehabilitation tool as well as for athletic preparation training in sportsmen; however, the effectiveness of this novel training modality on AC is still unclear. A systematic search of the literature revealed 17 publications regarding the effects of BFR exercise on AC. Among them, 10 showed improving in VO_{2max} [33–35, 39–43, 46, 48] and one [45] showed improvements in O_2p kinetics, CO_2 output and ventilatory kinetics. In particular, the effects of low-to-moderate-intensity exercise with BFR demonstrated significant and consistent improvements in AC compared to low-to-moderate-intensity exercise without BFR in physically active healthy individuals. The Fick equation [$VO_2 = HR \times SV \times$ (a-vO_2 difference)] could be responsible for the changes observed in this meta-analysis and provides a framework to understand the effects of training with BFR. As suggested by Silva et al. (2019) [50], improvements on AC may be referred to adaptations in muscle oxidation capacity (arterial and mixed venous blood oxygen (a-VO_2) difference and systolic volume). Moreover, increased muscle mass in the lower body, capillary density, and citrate synthesis activity may be associated with improvements in VO_{2max} in the BFR training group. According to Formiga [22], during BFR, hypoxia's effects on vascular endothelial growth factor (VEGF), the increase in endothelium-dependent vasodilation from increased shear stress and the nitric oxide production during cuff release and reperfusion after BFR, can explain the mechanism of how BFR may help improving AC. Conceição et al. in a recent paper found that VEGF mRNA abundance improved after BFR training [40]; increased VEGF and endothelium-dependent vasodilation from BFR training have the capacity to improve oxygen delivery and uptake [23]. Another factor that may help in the understanding of the significant improvement in AC during training with BFR is the effect that BFR training appears to have on ventilation/minute. Furthermore, the study by de Oliveira et al. (2015) included in this meta-analysis [41], examined the effects of training with and without BFR on the onset of blood lactate accumulation and found that the BFR group improved 16% compared to the 6% improvement in the non-BFR group.

Minimal clinically important difference in aerobic capacity

It is important to interpret the change in AC from exercise with and without BFR presented in this meta-analysis with the minimal clinically important difference (MCID).

Hays and Woolley [51] suggest that the threshold for a MCID corresponds to a small effect size (0.20) and a more recent study [52] pointed out that a 3.4% increase in AC may be considered as a MCID in healthy adults. The data presented in Fig. 3 show that the effect size (std. mean difference) among trained subjects is 4.92, among trained subjects 0.67 and the total value is 2.34, far exceeding improvement of 0.20. In view of the results of this meta-analysis regarding the percentage variation, as showed in Table 2, all the included studies but the work by Keramidas et al. [36] had an increase in AC in the BFR group that exceeded 3.4% and only two of the nine studies (Paton and Conceição et al.) [34, 40] observed an improvement in AC in the non-BFR group that exceeded 3.4%. The change in AC of the non-BFR groups in the seven other studies ranged from −4.21% to+2.69%. [33, 35, 36, 39, 41–43]. Finally, the one study in which the BFR group did not exceed a 3.4% improvement in AC (a high-intensity study) did observe a decrease in AC that was less than the non-BFR group (−2.17% versus −4.21%, respectively) [36].

The forest plot in Fig. 3.3 relative to the total sample (180 subjects) regarding VO2max shows that BFR training has both statistically and clinically significant effects mean difference= +2.34, 95% confidence interval (CI)=0.94, 3.74). Regarding the percentage variation of the BFR group regarding the VO_{2max} value, with an increase of 6.97% it is possible to conclude that BFR training appears to facilitate an improvement in VO2max with a MCID.

Impact of BFR training on VO_2 peak

From analysis of the studies, unlike VO_{2max}, VO_2 peak did not significantly improve in any group. Potential reasons for the discrepancy could be several. One plausible reason might be that of the three studies considered, two had older subjects

Table 2 Summary of VO_{2max} % changes from the included studies

Author, year	VO2max % change, BFR-group	VO2max % change, nonBFR-group
Abe, 2010	5,11	0,73
Amani, 2018	3,66	1,42
de Oliveira, 2015	5,46	0,45
Held, 2019	10,63	2,69
Park, 2010	11,45	-1,27
Paton, 2017	6,29	3,86
Conceicao, 2018	11,30	18,69
Ferreira Jr, 2019	10,95	1,41
Keramidas, 2011	-2,17	-4,21

as their sample. In elderly populations measures of athletic performance improved; however, measures of AC remained unchanged. These findings could potentially suggest different mechanisms of adaptation between older and younger individuals, according with Bennet et al. [23]. Kim et al. among young subjects [37] used heart rate reserve (HRR) to set the intensity of exercise, but HRR might not be appropriate for BFR exercise. In fact, was observed an increase in HR with the application of BFR despite the absence of exercise due to the decrease in venous return [53]. Another reason could be that the 30% HRR of intensity was lower than other BFR cycle training study (average 59% HRR) resulting in improvement of AC [38]. As declinations in muscle quality are observed with increase in age [54], it could be hypothesized that BFR aerobic exercise in older adults stimulates peripheral adaptations first. As these peripheral deficits are not typically observed in younger individuals, it would be reasonable to suggest that exercise with BFR is, therefore, more likely induce more central cardiovascular adaptations in this population. This would help explain the improvements in athletic performance measures observed in older individuals, without the same improvements in AC.

Study limits

There are some limitations in the present meta-analysis that should be mentioned. This meta-analysis includes a variety of exercise regimens and methods to employ BFR as well as the limited number of studies comparing the effects of exercise with and without BFR on AC in untrained or sedentary healthy subjects. Regarding studies with trained or athletic subjects, another limitation is that the subjects practiced very different sports: the physiological responses of aerobic capacity could change depending on the sport practiced. Moreover, it should be taken into account that the training and BFR modalities (2–6 sessions per week; 2–24 weeks duration of intervention; 60–220 mmHg BFR cuff pressure, width of the cuff 5–18 cm) have varied greatly among studies, and the lack of a standardized protocol might create difficulties on directly comparing results. Uniformity of outcome measures and better quality of studies would also be desirable.

Further research in the above areas is needed to fully understand the effects of exercise with BFR on AC.

Conclusion

Exercise plays a key role to the maintenance of cardiovascular health and function, while also is integral to enhancing athletic performance. This review demonstrates that BFR training results in improvements in AC and athletic performance in various populations, regardless of training intensity, although some considerations are necessary. BFR training, even at light intensities has been shown to elicit improvements in both AC and athletic performances in young adults; conversely, BFR combined with exercise seems to strictly enhance athletic performance in older adults, without improving physiological measures of AC. It is reasonable to argue that BFR training could elicit predominantly peripheral adaptations in older individuals, where a combination of central and peripheral adaptions may be more likely to occur in young adults. This could be a plausible hypothesis to explain the difference in the effects of BFR training depending on the age of the subjects. Despite the limitations of the included studies, BFR training could have potential applications in settings where high-intensity training is not appropriate, although more high-quality research would be desirable. This technique seems to provide a promising and beneficial training stimulus when used in a controlled environment supervised by trained and experienced personnel and elicit improvements in AC and athletic performances.

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Declarations

Conflict of interest The authors declare that they have no competing interests.

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