The efficacy of blood flow restricted exercise: A systematic review & meta-analysis

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Review

The efficacy of blood flow restricted exercise: A systematic review & meta-analysis

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ABSTRACT

Objectives: To systematically search and assess studies that have combined blood flow restriction (BFR) with exercise, and to perform meta-analysis of the reported results to quantify the effectiveness of BFR exercise on muscle strength and hypertrophy.
Design: A systematic review.
Methods: A computer assisted database search was conducted for articles investigating the effect of exercise combined with BFR on muscle hypertrophy and strength. A total of 916 hits were screened in order based on title, abstract, and full article, resulting in 47 articles that fit the review criteria.
Results: A total of 400 participants were included from 19 different studies measuring muscle strength increases when exercise is combined with BFR. Exercise was separated into aerobic and resistance exercise. Resulting from BFR aerobic exercise, there was a mean strength improvement of 0.4 N m between the experimental group and control group, while BFR resistance exercise resulted in a mean improvement of 0.3 kg. A total of 377 participants were included in 19 studies measuring muscle size increase (cross sectional area) when exercise was combined with BFR. The mean difference in muscle size between the experimental group and control group was 0.4 cm^2.
Conclusion: Current evidence suggests that the addition of BFR to dynamic exercise training is effective for augmenting changes in both muscle strength and size. This effect was consistent for both resistance training and aerobically-based exercise, although the effect sizes varied. The magnitude of observed changes are noteworthy, particularly considering the relatively short duration of the average intervention.

1. Introduction

The maintenance of skeletal muscle mass is an important factor for health, longevity, and quality of life.[1] Skeletal muscle is a major contributor to glycemic control acting as the body's largest glucose sink by mass, which accounts for approximately 80% of non-insulin stimulated glucose uptake[2] and also plays an important role in oxidizing fatty acids.[3] Adequate skeletal muscle is crucial to maintaining the ability to undertake activities of daily living, ambulation, and fall avoidance. At the other end of the physical activity spectrum, skeletal muscle quantity and quality have a direct bearing on sport performance,[4] basal metabolic rate, caloric expenditure, strength, power, and somatotype. Disuse of skeletal muscle leads to relatively rapid and progressive atrophy, decreases in oxidative capacity, fiber shortening and reduced muscle compliance; all of which result in a reduced exercise capacity, impaired immune system and decreased sensitivity to insulin.[5] As such, muscle strength and mass has important implications for both health and fitness.

To enhance both muscle mass and strength, high-intensity resistance exercise with loads approximating 70–85% of one repetition maximum (1-RM) are typically recommended.[6] However, heavy-load resistance exercise is often challenging or even contraindicated for certain individuals, such as the elderly, persons with chronic disease, or rehabilitating and recovering athletes. As such, it is intriguing that several studies in recent years have suggested the potential for low load exercise (i.e. <25% maximal capacity) to stimulate significant muscular adaptations when the blood flow to a muscle or muscle group is restricted or fully occluded. For example, comparing blood flow restricted exercise to a non-occluded exercising control group, Takarada et al.[7] demonstrated a 14% increase in knee extensor strength of young subjects engaging in strength training at an intensity of 50% of 1 RM, while no change occurred using resistance training alone.

Blood flow restricted (BFR) training, also known as Kaatsu training, was pioneered by Yoshiaki Sato, of Japan in the 1970s and

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1980s.[8] This training method involves decreasing blood flow to a muscle by application of an external constricting device, such as a blood pressure cuff or tourniquet, to provide mechanical compression of the underlying vasculature. BFR is applied with the intent to promote blood pooling in the capillary beds of the limb musculature distal the tourniquet.[6] Although there have been isolated reports of adverse events (as would be expected with any form of exercise), on the whole there is little published evidence to suggest that this type of training offers any greater health risk than typical dynamic exercise training with high loads.[9]

BFR alone has been shown to attenuate the disuse of atrophy during periods of immobilization,[10] however, BFR must be combined with an exercise stimulus for enhanced muscular development. The exercise stimulus of resistance exercise appears to provide the most substantial muscular gains when combined with BFR. Yet interestingly, several investigations have reported that low-intensity aerobic exercise combined with BFR can facilitate improvements in muscular size and strength, even though strength and hypertrophy do not typically occur from aerobic mode of exercise.[11] The development of muscle size and strength using BFR-aerobic training may become a method of training for the wider population, including the frail and elderly.

There is a previous review[12] concerning BFR, however there has since been a fast growing evidence-base for BFR exercise training. Furthermore, the evidence has not been systematically reviewed. For these reasons, an up to date systematic review and meta-analysis of the BFR exercise training literature is needed for greater and more current understanding of the effects of blood flow restriction on training outcomes such as muscle strength and hypertrophic adaptations. This in turn will lead to the formulation of novel research questions and advance training methods for persons in both health and disease. At present, a variety of different BFR training methodologies are being employed and study designs have differed, making direct comparison challenging. Therefore, our objectives were: (1) to systematically identify and assess studies that have combined blood flow restriction with exercise (2) to perform a meta-analysis to quantify the effectiveness of BFR exercise on muscle strength and hypertrophy (3) identify which BFR training methods result in the greatest strength and muscle hypertrophy outcomes.

2. Methods

A computer assisted database search was used, targeting all articles published prior to the last week in June 2015. Databases searched included: PubMed, Medline, CAB abstracts, CINAHL, SPORT Discus, PSYCHinfo, and ScienceDirect. The search was conducted to find studies investigating the effect of exercise combined with BFR training on muscle hypertrophy and muscular strength. Search words included variations on words that were related to the restriction of blood flow to skeletal muscle, types of exercise used with BFR, and possible effects caused by BFR. The search terms used are included as a supplemental file to this article (Table 1, Supplemental material). Articles retrieved were examined for further relevant references.

All included articles were published in peer-reviewed English language scientific journals. Any investigation that focused on a BFR intervention combined with an exercise stimulus and compared to a matched exercise exposure without BFR was eligible for inclusion. At least one of two outcomes must have been considered: muscle strength or muscle size. Only studies using human adult (>18 yr) human participants in ostensibly good health were included. No modality of exercise was excluded but were classified as either an aerobic or resistance modality. Given the evidence relating to the differing physiological effects elicited by these two modalities (from both a clinical and performance standpoint), the authors believe this is a necessary division for interpretation. Article exclusion criteria included published supplements, abstracts, reports, reviews, opinion articles, commentaries, magazine articles, book chapters, case studies and presentations; however, relevant peripheral literature was collected and reference lists were searched. Only studies using mechanical blood flow restriction 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, hypoxic environment) were excluded. Mechanisms employing altered atmospheric pressure or reduced partial pressure of O_2 were excluded due to variability introduced from the physiologic adaptation happening via the lung or other components of the cardiorespiratory system, not related to a localized stimulus. The authors believe that the specificity and utility of the results for assessing BFR training are improved by the exclusion of such studies.

A total of 916 hits across all databases were saved in a reference management software program wherein exact duplicates were removed, leaving a total of 820 articles. Two of the authors (JS and JS) independently screened articles based on the title and abstract of each and the full article was retrieved for review when relevance was unclear from this information. In the event of a disagreement as to article's relevance by the primary reviewers the third authour's judgment was used as the sway vote. The reason for removal of studies, which were captured then culled were (1) improper controls or randomization to assess efficacy, and (2) not fully meeting our inclusion criteria (see above). This resulted in 47 articles that fit the inclusion criteria for the systematic review. All remaining articles were assessed for methodological quality using the Downs and Black checklist (1998)[13] (Table 2, Supplemental material). Articles that reported their results as a percentage change or only in graphical form could not be included in the meta-analysis due to an inability to accurately calculate an effect size. A total of 28 studies met the full inclusion criteria for the meta-analysis. The process of article retrieval is outlined in Fig. 1.

The extracted data included study identifying information, year of publication, research design, objectives, participant characteristics (age, sex, health status), sample size, intervention, FITT (frequency, intensity, time and type of exercise), methods of assessment, and physiological results.

Descriptive statistics for each study and effect sizes (ES) were calculated using Comprehensive Meta-Analysis software (V.2.0, Biostat, Inc., Englewood, NJ). ES were analyzed and appropriately adjusted for potential sample bias using the methodology of Duval and Tweedie.[14] ES calculations were performed using unmatched groups and post data only; post data included means, SD, and sample size. A level of significance of $p = 0.05$ was selected a priori and the scale proposed by Rhea[15] was used for interpretation of effect size magnitude. Exercise was represented by both aerobic and resistance modalities. Almost uniformly, studies that tested aerobic exercise quantified BFR related increases in strength using Newton meters (N m); whereas studies that used resistance exercise quantified increases in strength using a measure of performance (i.e. weight lifted in kg). As such, exercise modalities were considered separately for both practical and theoretical reasons. Similarly, a mean difference for mixed modality training protocols could not be calculated, and the data is thus presented below separately.

3. Results

The 47 studies identified that fit the inclusion criteria for the systematic review included all healthy participants that had a mean age of 34 ± 18 yrs (18–70). There were 26 male only studies,

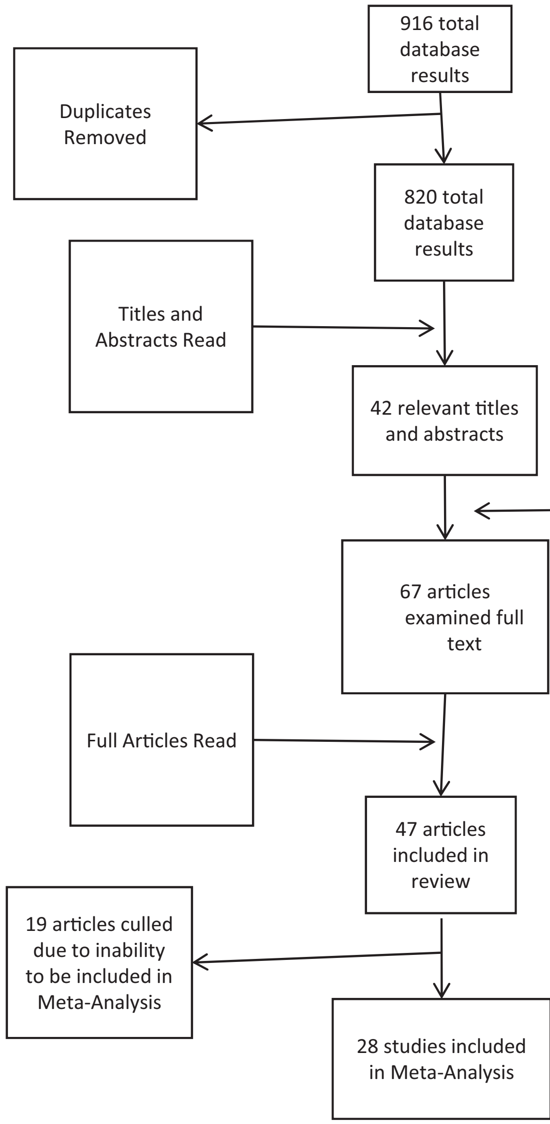

Fig. 1. Flowchart demonstrating the step-by-step process of article elimination to find the final articles to be included in the systematic review.

7 female only studies, and 14 studies that included both male and female.

3.1. Muscular strength

A total of 400 participants were included from 19 different studies (41 cases) measuring muscular strength increases and considering exercise combined with blood flow restriction.

Amongst the total of 72 subjects representing 4 independent studies (14 cases) that considered strength changes resulting from BFR aerobic exercise, the mean improvement in strength gains of the experimental group above changes in the control group was 0.4 N m [95% CI: 0.1, 0.6; $p = 0.04$] (Fig. 2A). Typically, when aerobic training was combined with BFR, muscle strength increased 5–8 N m. Training more than 6 weeks increased the mean difference in muscle strength between the experimental group and control group more than training less than 6 week, 0.6 N m [95% CI: 0.4, 0.9] versus 0.2 N m [95% CI: −0.5, 0.2], respectively ($p = 0.03$). The mean increase in muscle strength between the experimental group and the control group was larger when walking intensity was greater than 70 m/min compared to an intensity of less then 70 m/min, 1.9 N m [95% CI: 1.4, 2.3] versus −0.2 [95% CI: −0.5, −0.2], respectively ($p < 0.001$). There was inadequate data to analyze other training variables within aerobic-BFR training.

There were 15 studies (27 cases) with a total of 328 subjects, that considered strength changes resulting from BFR resistance exercise, and these revealed a mean augmentation of muscle strength gains between the experimental group and control group of an additional 0.3 kg [95% CI: 0.1, 0.5, $p < 0.01$] (Fig. 2B). Only a minor variation was apparent in the mean difference in gains comparing the experimental and control group considering 2 day versus 3 day/week training, 0.4 kg [95% CI: −0.2, 1.0] versus 0.3 kg [95% CI: 0.01, 0.4], respectively ($p > 0.05$). Gains in muscle strength were significantly greater when the intensity of the workout was >20% 1 RM versus < 20% 1 RM or lower. Importantly, when comparing gains in muscle strength between training at 20% 1 RM and 30% 1 RM, training at 30% 1 RM resulted in a much greater improvement in muscle strength ($p < 0.001$). Training programs of greater than 8 wk were approximately 60% as effective as those less than 8 wk (0.2 kg versus 0.3 kg, $p = 0.05$), but it should be noted that the mean difference between the experimental and control group were relatively small and despite statistical significance, practical significance may be of more questionable value. Cuff pressure of ≥150 mmHg caused an increase in strength comparing the

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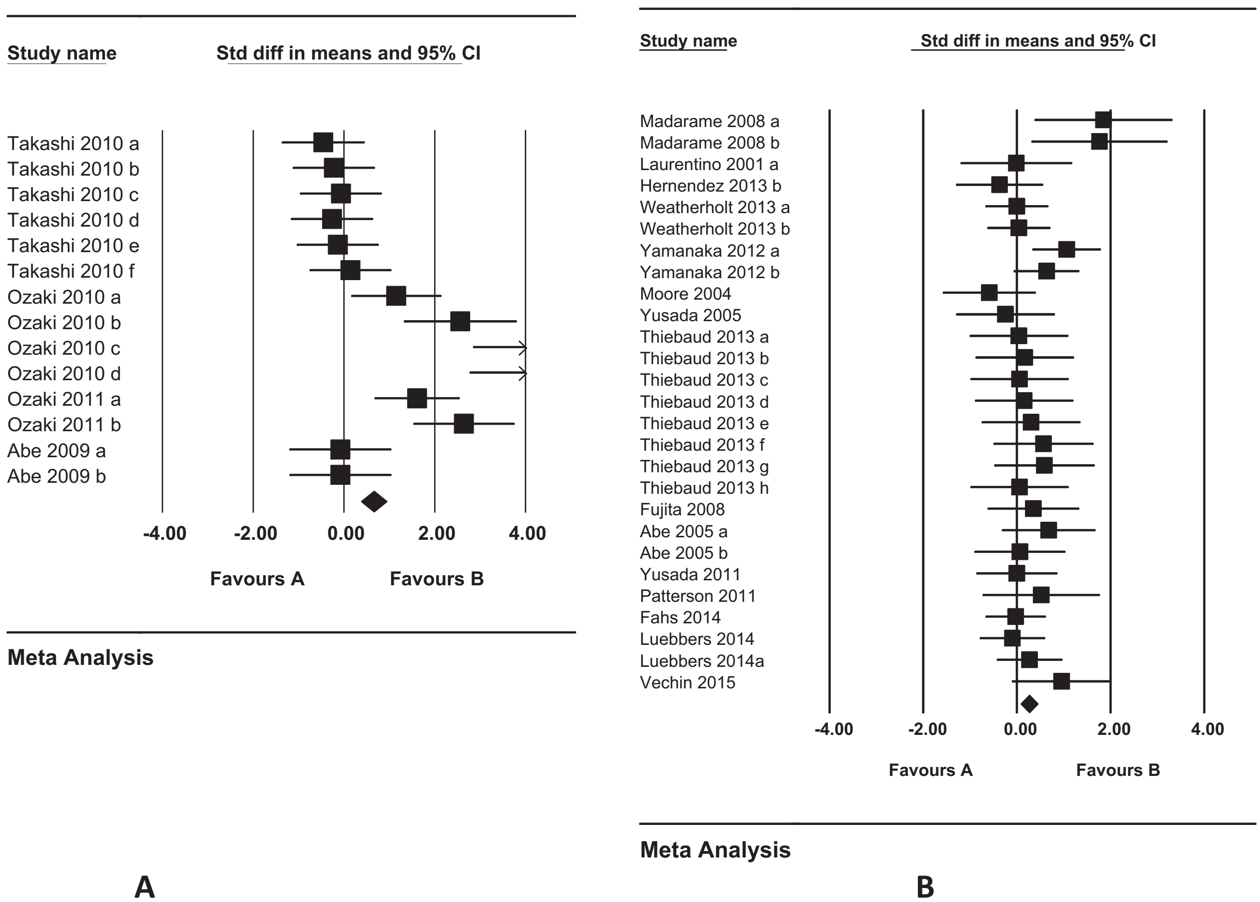

Fig. 2. Forrest plot displaying the difference in muscle strength between the experimental group and control group for each individual case, when undergoing aerobic exercise (A) and resistance exercise (B).

experimental group and control group than when the cuff pressure was lower than 150 mmHg, 0.2 kg [95% CI: −0.1, 0.5] versus 0.1 kg [95% CI: −0.2, 0.4], respectively ($p > 0.05$).

3.2. Muscular hypertrophy

A total of 377 participants were included in 19 studies (40 cases) measuring muscle size increase (cross sectional area (CSA)) considering both modalities of exercise when combined with blood flow restriction. Most often, the change in muscle size ranged from an increase of 2–5 cm^2 when exercise was combined with BFR. The mean increase in post-training muscle size between the experimental group and the control group was 0.36 cm^2 [95% CI: 0.16, 0.46, $p < 0.001$]. Training programs that were 8 weeks or longer caused a 0.7 cm^2 [95% CI: 0.34, 0.964] size increase between experimental and control group, compared to training programs 8 weeks or less that only caused a 0.2 cm^2 (95% CI: −0.10, 0.37) size difference ($p < 0.001$). Muscle size differences between the experimental group and control group did vary when training took place 3 days a week compared to a training 2 days a week, 0.34 cm^2 [95% CI: 0.11, 56] versus 0.29 cm^2 [95% CI: 0.031 0.55], respectively ($p > 0.05$).

A total of 131 participants were included in 7 studies (11 cases) measuring CSA increase when aerobic exercise is combined with blood flow restriction. Aerobic training had a mean increase of post-training muscle size between the experimental group and control group of 0.32 cm^2 $p = 0.03$ [95% CI: 0.03, 0.61] (Fig. 3A). There were insufficient studies to analyze further dose–response training variables within aerobic-BFR training.

A total of 246 participants were included in 12 studies (29 cases) measuring CSA increase when resistance exercise was combined with blood flow restriction. The mean increase in muscle size as a result of BFR training was 0.41 cm^2, $p = 0.001$ [95% CI: 0.12, 0.58] (Fig. 3B) greater than that seen in the control groups.

4. Discussion

Current research suggests that the addition of BFR to low load dynamic exercise training is effective for augmenting changes in both muscle strength and size. This effect was true for both resistance-training exercises and aerobically based exercise, although the degree of increase varied. Importantly, research suggests that low load resistance exercise (20–30% 1 RM) and low load aerobic exercise (<70 m/min walk training), which would not be expected to cause considerable increases in muscular quantity or quality under normal circumstances, when combined with BFR produced an exaggerated response for maximizing muscle strength and hypertrophy. This analysis offers a quantified description of the strength increase produced by various training variables including intensity, frequency, volume, and cuff pressure. At present, there remain a number of further variables such as age, sex, fitness level, training status, baseline strength and muscular size that lack a sufficient evidence base to be included in meta-analysis. This highlights the need for further work in this area to clarify the dose–response relationship of this perturbation of typical exercise training; however, the results of this analysis give insight into variables and methodological considerations that could be important to consider

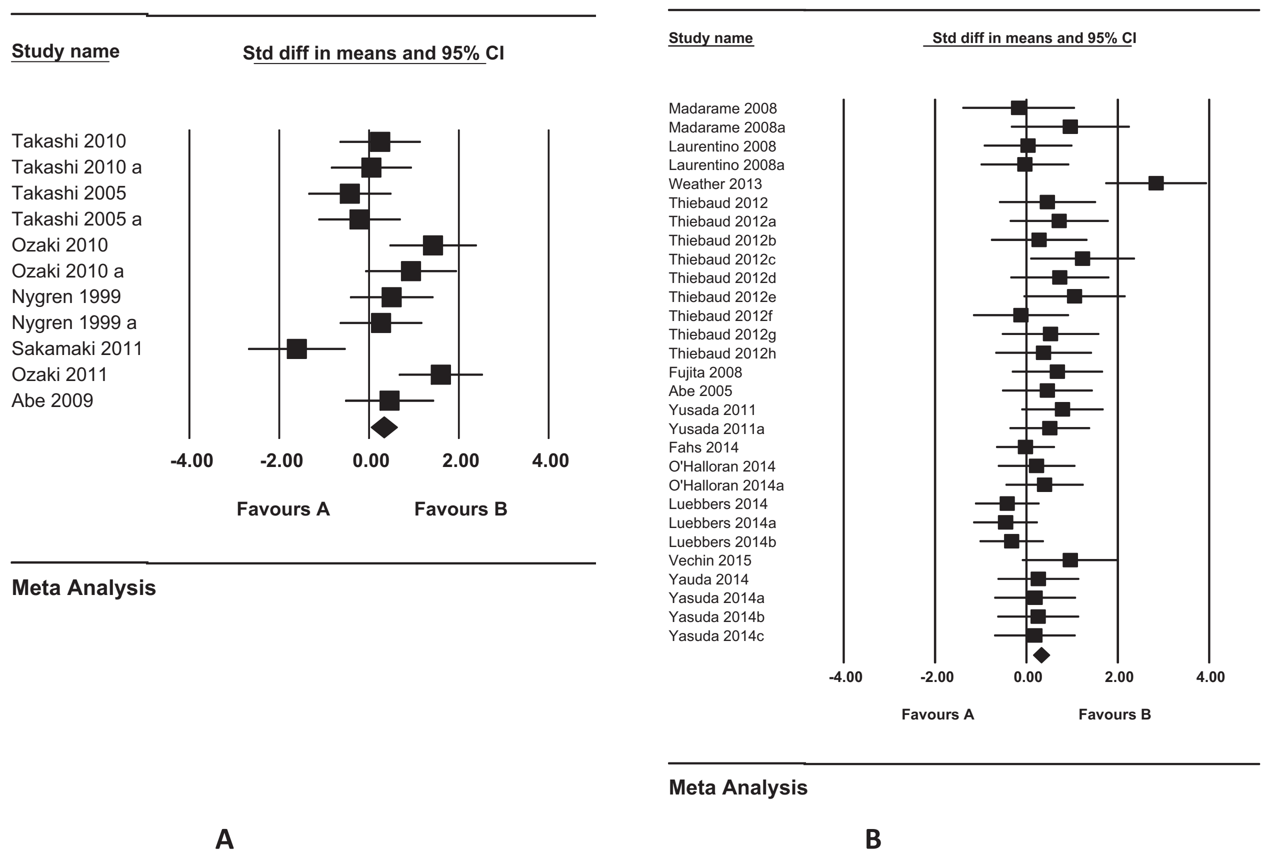

Fig. 3. Forrest plot displaying the difference in muscle size between the experimental group and control group for each individual case, when undergoing aerobic exercise (A) resistance exercise (B).

in future research design. Furthermore, the authors highlight that the identification and analysis of these variables is based on limited research, using specific equipment, and should be interpreted with caution.

4.1. Muscular strength

Owing to a methodological difference in the reporting of units of strength between aerobic and resistance modalities of exercise, we were unable to calculate an "overall" effect for exercise irrespective of the stimulus. However, since both aerobic and resistance modalities revealed a positive mean difference between the experimental and control group, it seems acceptable to conclude that, regardless of the unit of measure, overall muscle strength would also have a mean increase.

Our analysis suggests that when performing BFR aerobic exercise, training durations >6 weeks produced greater strength increases compared to training <6 weeks. This is in agreement with the generally accepted adaptation period for standard resistance training, and the work of Loenneke et al.[12], who have suggested that with BFR training, muscle strength does not significantly increase until the 10th week.

The current evidence base suggests that as a result of BFR resistance training, greater strength gains may be expected when employing intensities ≥20% 1 RM. Such an effect mirrors what would be expected for traditional resistance training, albeit at a greatly reduced percentage of 1 RM. Despite a greater overall efficacy with higher loads, however, it is important to highlight that measurable effects were still consistently observed even when training employed these very low intensities, which would not be expected to illicit adaptation in the absence of BFR. It is entirely possible that efficacy may change further using higher intensities, or that risk may appreciably increase, but at present this remains speculation.

From our analysis, BFR training trended toward greater efficacy for increasing muscle strength when cuff pressure >150 mmHg, but the 95% confidence interval crosses zero thus this should be interpreted cautiously. Within the literature there are many different cuff pressures used for BFR training. It has been found that there is no single pressure that produces equal BFR between subjects, and different types of cuffs and limb circumferences occlude arterial blood flow at much different inflation pressures.[16] Therefore, there is a need for more investigation into a model that will result in equal occlusion for all subjects. We do not believe the above cut-points to represent hard-fast thresholds, but rather these apparent divides in common methodologies were the only points at which an analysis could be performed between variables. Nonetheless, this may represent important information when selecting application methods to use with BFR training.

4.2. Muscular hypertrophy

Perhaps not surprisingly, the evidence suggests that resistance training causes greater increases in muscle size than aerobic training. This difference is likely related to the purposeful isolation and increased muscular work performed by a given muscle group in resistance training.

Overall, ≥8 wk of training has a greater effect on muscle size than training <8 wk. In agreement with muscle strength, a cuff pressure >150 mmHg appeared more effective at increasing muscle size than pressures <150 mmHg, but further investigation into the optimization of cuff pressure and the relationship with other training variables (and safety) is again suggested. There were insufficient studies to further breakdown and analyze the training variables of resistance and aerobic exercise.

5. Conclusion

This systematic review provides meta-analytic evidence of greater increases in muscle size and strength when exercise is combined with BFR, compared with low load exercise alone. Given that the training intensity typically required to maximize increases in strength and hypertrophy ranges from 45 to 60% 1 RM in untrained individuals, or 80–85% 1 RM in trained athletes, the accumulated evidence showing alterations in strength and hypertrophy with low loads (20–50% 1 RM), is convincing verification that BFR contributes substantially to these adaptive processes. This type of training offers potential benefits to various practitioners ranging from clinical to human performance applications. Low load training may offer benefit to those recovering from orthopaedic or other conditions requiring rehabilitative care, but for which higher load training is contraindicated. Similarly, the practitioner working with athletes may find application in progressing strength while reducing loads on the associated tissues including muscular, tendinous and bony. Finally, it is worth stressing that the current findings regarding optimal training methods should be interpreted with the understanding that few studies have specifically sought to determine these factors as targeted study outcomes. A strength of the systematic reviewing process is the ability to highlight knowledge gaps and this has revealed that, at present, there is a relative dearth of specific research in this area; thus, more targeted studies are required before concrete statements regarding methodological optimization can be made. Again, the above cut-points chosen were apparent divides in common methodologies of the literature and were the only cut-points at which an analysis could be performed between variables, which we offer as a starting point. We do not believe these cut-points represent hard-fast thresholds; however, this investigation has established a path for future research and highlights important areas of concentration.

6. Practical implications

- These results suggest lighter load BFR training to stimulate increases in muscle size and strength effects may be effective, and could potentially be used when traditional high-load training may be inappropriate or unattainable.
- Current evidence suggests that within the range of low load stimulus, adaptation may still be associated with intensity (i.e. at 30% 1 RM could offer much more strength gaining benefit than training at 20% 1 RM).
- Quantifiable muscular adaptations present quickly; however, training durations >6 weeks seem to offer greater returns in strength adaptation.
- BFR training has a potential benefit to those recovering from orthopaedic or other conditions requiring rehabilitative care, but for whom training with higher loads is contraindicated.
- BFR training has applicability to a range of populations who may seek to progress strength while reducing loads on the associated tissues including muscular, tendinous, connective, and bony.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jsams.2015.09.005.

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