

Effect of Blood Flow Restriction on Cross-Education of Muscle Strength and Volume: A Systematic Review and Meta-Analysis

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Background: Cross-education (CE) involves strength and volume improvements in the untrained contralateral limb after unilateral training, with potential benefits in rehabilitation. Blood flow restriction training (BFR), using low-load exercises, may enhance CE effects, but its efficacy requires systematic evaluation.

Objective: To systematically assess the effects of low-load BFR on the CE of muscle strength and volume, providing evidence-based guidance for clinicians and rehabilitation therapists.

Design: Systematic review and meta-analysis.

Data Sources: PubMed, Web of Science, and Embase databases from inception through March 1, 2024.

Study Selection: Eligible studies investigated adults; included a synchronous training intervention for ≥ 4 weeks; compared ≥ 1 unilateral training group or a nonintervention control group; reported outcomes for ≥ 1 measure of maximal force, voluntary contraction, isometric strength, torque, or muscle cross-sectional area preintervention and postintervention; and had an experimental design.

Data Extraction: Two researchers extracted publication characteristics, participant grouping, participant characteristics, training characteristics, and outcome indicators after the exercise intervention.

Data Synthesis: We calculated standardized mean differences for muscle strength and mean differences for muscle volume, with heterogeneity assessed via the Higgins I^2 test.

We used the Cochrane Collaboration's randomized controlled trial bias evaluation tool for quality assessment.

Results: Of 1729 records retrieved, 6 articles ($N = 259$ young adults) were included in the meta-analysis. Results indicated a markedly enhanced CE effect in muscle-strength induction via BFR, with a combined effect size (standardized mean difference) of 0.59 (95% CI = 0.24, 0.94; $P = .001$) compared with the blank control group and 0.29 (95% CI = 0.06, 0.52; $P = .01$) compared with the unilateral resistance training group. Nonetheless, the CE effect on muscle-volume induction showed no notable variance between the BFR group and the blank control group (mean difference = -0.01 ; 95% CI = -0.06 , 0.04; $P = .60$) or the unilateral resistance training group (mean difference = 0.01; 95% CI = -0.04 , 0.06; $P = .64$).

Conclusions: Blood flow restriction effectively induced CE in muscle strength. Nevertheless, additional research is required to determine its effect on muscle-volume CE. Reduced exercise intensity with BFR may augment neural activation, implying possible advantages in rehabilitative training for individuals with neurological conditions, meriting additional investigation.

Key Words: neuromuscular adaptation, contralateral transfer, rehabilitation training, low-load resistance

Key Points

- Blood flow restriction training stimulated cross-education of muscle strength, but its effect on muscle volume has not been confirmed.
- Reduced exercise intensity during blood flow restriction training may enhance neural activation.
- Rehabilitation that combines neural mechanism-based and cross-education training for patients with neurological disorders should be studied.

Blood flow restriction training (BFR), also known as Kaatsu, was developed by Dr Yoshiaki Sato in Japan as a novel method to enhance muscle strength and exercise performance.¹ It involves partially restricting arterial blood flow and fully restricting venous return from the muscles to the heart during exercise without completely obstructing blood circulation.^{2,3} Using pressure cuffs on the limbs, clinicians can integrate BFR with diverse exercises, yielding substantial benefits in rehabilitation, muscle strengthening,

and hypertrophy. Blood flow restriction training is applied across a spectrum of individuals, including athletes, the generally healthy, and the middle-aged to older population.⁴ In controlled settings, BFR is considered a safe practice for the overall healthy population. However, individuals with cardiovascular conditions, such as heart disease and hypertension, should seek the guidance of their health care professional, who can carefully assess whether they can engage in BFR training and help formulate a training regimen.^{4–6} Researchers

have combined BFR with resistance exercise, aerobic exercise, or a blend of both; innovatively merged electromyographic with neuromuscular stimulation; and incorporated whole-body vibration.² Compared with isolated low-intensity load training, the integration of BFR has been shown to enhance muscle strength and hypertrophy more effectively.⁵

Cross-education (CE) is characterized by a marked enhancement in strength and adaptability of the contralateral, untrained limb after unilateral limb training.⁷ The underlying mechanism of CE remains a focal point of research, with competing hypotheses including neural and myogenic mechanisms, but a consensus has not been reached. Although initial theories posited myogenic mechanisms as the cause of CE,⁸ subsequent research has indicated an absence of substantial size changes in contralateral homologous muscles, suggesting a neurogenic mechanism.^{9,10} Bilateral access and cross-activation represent 2 theoretical models explaining the neural mechanisms, wherein both the brain and spinal cord are implicated.¹¹ The bilateral-access model posits that the movement patterns in unilateral activities are mirrored by attempting to perform identical tasks on the opposite side of the body.¹² The cross-activation model demonstrates that adaptations from unilateral movements can transfer to the contralateral side of the body.¹³ Although consensus regarding the mechanism of CE is lacking, the characteristics and potential applications of CE have been extensively investigated. Cross-education can manifest in various muscle groups, including those of the upper limb, such as the rotator cuff, select elbow flexors, and wrist flexors,^{14–16} and the lower limb, such as certain ankle dorsiflexors and knee extensors.¹⁷ Several techniques effectively facilitate CE, such as neuromuscular electrical stimulation,¹⁸ targeted electroacupuncture,¹⁹ and independent muscle-contraction exercises.²⁰ The prevalent approach involves using conventional resistance training as a catalyst by modulating load intensities, training volumes, and contraction techniques.^{21,22} Nonetheless, investigations of BFR techniques for induction remain comparatively limited.^{23–28} In recent years, the application of CE in clinical settings has expanded, particularly in the early rehabilitation of unilateral neurological conditions such as stroke. Cross-education not only aids in preventing complications but also enhances muscle strength and function in the affected limb. Initiating contralateral training early after anterior cruciate ligament reconstruction may enhance the recuperation of quadriceps-muscle strength after the procedure.¹⁷ The clinical application of CE is progressively broadening, encompassing both neurological and orthopaedic conditions.

Although uncertainties about the mechanisms of CE effects exist, the indispensable role of CE in certain clinical rehabilitation populations is evident. Blood flow restriction training is simpler and more patient friendly than traditional methods used to induce CE effects. The nervous system serves as the conduit for CE effects, with substantial evidence pointing to the untrained hemisphere as the primary mediator, despite incomplete knowledge of the specific cortical and neurophysiological adaptations.²⁹ However, these cortical adaptations ultimately occur at the motor-unit level.³⁰ In general, the initial increase in muscle strength is greatly influenced by the activation patterns of motor units, whereas later stages are associated more with maximal muscle strength.^{31–33} Blood flow restriction can notably improve neuromuscular adaptability.^{34–39} However, experimental studies

are lacking on whether this enhanced adaptation can be transferred to the untrained side and the extent to which it can be preserved. Considering the test population, individuals without previous training experience, who have greater potential for neuromuscular improvement, may benefit more from BFR in enhancing motor-unit recruitment than from traditional resistance training. However, for elite professional athletes, the marginal gains offered by this method may appear insignificant. From a neural mechanism standpoint, the general population aligns well with the training principles of BFR and CE, presenting ample opportunity for enhancement. Injured athletes may find this training more suitable for preserving their skill level and decelerating the decline in muscle strength.

Cross-education effects are typically more pronounced after high-load exercise, with evidence indicating that high-load exercise at 70% of 1-repetition maximum (1RM) yields greater benefits than low-load exercise at 30% of 1RM.^{21,40,41} However, for certain populations, such as patients undergoing clinical rehabilitation or middle-aged and older patients, high-load lifting may be impractical. Therefore, identifying effective strategies to enhance the efficacy of low-load exercises is crucial for these individuals. Integrating BFR with low-load exercise could amplify CE benefits to match those achieved with high-load exercise.^{42,43} Blood flow restriction has demonstrated a more substantial increase in muscle size and strength compared with conventional equal-load exercise.⁴⁴ In conclusion, CE could potentially yield superior outcomes when coupled with BFR.

Investigation into whether BFR can augment CE benefits is still nascent. Current research on this topic typically involves small sample sizes, with approximately 10 participants per group, and lacks a systematic analysis.^{42,43} Therefore, the purpose of our study was to use a meta-analytic approach to systematically assess whether low-load BFR can facilitate CE of muscle strength and volume, offering empirical support for clinicians and rehabilitation specialists.

METHODS

Search Strategy

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for this systematic review.⁴⁵ The protocol was submitted at the International Platform of Registered Systematic Review and Meta-analysis Protocols (202090098; doi:10.37766/inplasy2024.4.0038).

We searched PubMed, Web of Science, and Embase databases for studies from inception through March 1, 2024, using a Boolean logic search for the following English terms: (blood flow restriction OR vascular occlusion OR kaatsu OR occlusion training) and (cross-education OR cross education OR cross transfer OR cross training OR interlimb transfer OR strength transfer OR unilateral strength training OR unilateral resistance training OR contralateral strength training OR resistance training OR strength training). Two researchers (L.S. and L.L.) independently screened the titles and abstracts of the retrieved articles, and a third researcher (C.W.) resolved disagreements.

Selection Criteria

In adherence to the Population, Intervention, Comparison, Outcome framework for systematic reviews, eligible studies

met the following inclusion criteria: (1) participants were aged ≥ 18 years; (2) interventions consisted of synchronous training for a minimum of 4 weeks; (3) comparisons included ≥ 1 unilateral training groups or nonintervention control groups; (4) outcomes were reported for ≥ 1 measure of maximal force, voluntary contraction, isometric strength, torque, or muscle cross-sectional area preintervention and postintervention; and (5) the research design was experimental.

Exclusion criteria were as follows: (1) absence of a strength-training group, (2) lack of muscle-strength-related indicators, (3) animal studies, (4) unpublished works, (5) duplicate publications, and (6) concurrent interventions such as diet control or cognitive training during the study period.

After the literature search was completed, 2 researchers (L.S. and K.W.) independently performed a double-blind screening of the literature according to the inclusion and exclusion criteria. First, they imported the literature into EndNote X9 software (Clarivate) for deduplication, and 2 researchers (L.S. and L.L.) conducted preliminary screening by reading the titles and abstracts and downloaded and screened the remaining literature in full. The 2 researchers compared the extracted literature, and if consensus was not achieved, a third researcher (C.W.) was consulted.

Data Extraction

Two researchers (L.S. and K.W.) read the full text of the included literature and extracted the required information according to a standardized process. The extracted information included the following: first author information, publication year, grouping, participant age, sample size, training characteristics (content, period, frequency, and intensity), and outcomes after exercise intervention (maximum strength, maximum voluntary contraction [MVC], maximum voluntary isometric contraction, rate of torque development, and cross-sectional area). When outcomes were repeatedly measured, the first measurement after intervention was extracted. Two researchers (L.S. and K.W.) resolved their differences through discussion, and when necessary, a third researcher (Y.Y.) was consulted. When data in the literature were missing, they contacted the author via email to provide the missing data and used WebPlotDigitizer software (version 4.1; automeris.io) to extract data reported only in graphical form (mean $\pm$ SD).

Statistical Analysis

Statistical analysis was conducted using RevMan software (version 5.4; Cochrane Collaboration). The outcome measures were continuous variables, and the strength data were categorical variables. To describe effect size, we used standardized mean differences (SMDs) with 95% CIs for muscle strength and mean differences (MD) with 95% CIs for muscle volume. We evaluated study quality using RevMan software.

Heterogeneity among studies was evaluated using the Higgins I^2 test. We interpreted ranges for I^2 according to the *Cochrane Handbook for Systematic Reviews of Interventions*: 30% to 60% indicated *moderate heterogeneity*; 50% to 90%, *substantial heterogeneity*; and 75% to 100%, *considerable heterogeneity*.⁴⁶ A fixed-effects model was used for all comparisons. If substantial or considerable

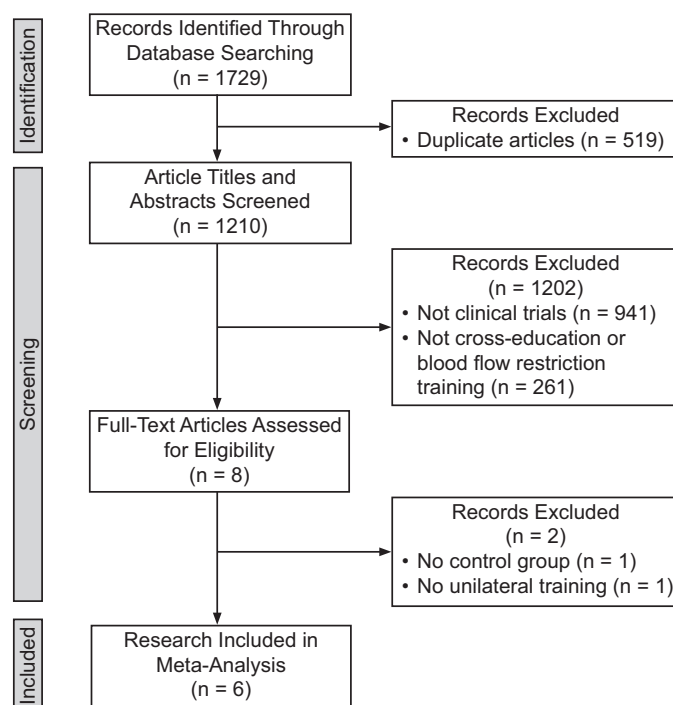


Figure 1. Literature selection process.

heterogeneity was detected, a random-effects model was adopted. Values of $P < .05$ were considered different.

Risk-of-Bias Assessment

The risk of bias in the included literature was assessed using the Cochrane Collaboration's randomized controlled trial bias evaluation tool.⁴⁷ A rating of low risk for all items in the Cochrane tool indicates *overall low bias risk* for the study; if 1 or 2 items are rated as high risk or uncertain risk, the study is deemed to have *moderate overall bias risk*; and an assessment of high risk or uncertain risk for ≥ 2 items classifies the study as having *high overall bias risk*. The risk of bias was evaluated independently by 2 researchers (L.S. and S.L.), and disagreements were resolved via negotiation or discussion with a third researcher (H.L.).

RESULTS

Study Selection

A total of 1729 articles were retrieved, and 519 duplicate records were excluded. After reading the titles and abstracts of 1210 studies, we excluded 1202 studies and downloaded the full text of 8 articles. Six articles were included in the meta-analysis.^{42,43,48–51} The literature screening process is shown in Figure 1.

Study Characteristics

Study characteristics are provided in the Table. The sample size of 306 individuals comprised 154 men and 152 women. Three studies exclusively involved men,^{42,48,51} 1 focused solely on women,⁴³ and 2 encompassed both sexes.^{49,50} The average age of participants ranged from 21.5 to 24.8 years. All studies quantified variable resistance, with the BFR group consistently using a low load

Table. Study Characteristics

Study	Sample		Intervention				
	Characteristics	Experimental (BFR) Group	Control Group	Method	Occlusion Pressure	Duration	Factors
Colomer-Poveda et al ⁴² (2017)	Healthy young men with no training or injury experience within 6 mo	n = 7; age = 23.8 ± 2.5 y	n = 8; age = 24.8 ± 2.9 y (blank control group) n = 7; age = 21.5 ± 3 y (non-BFR group)	Dominant legs were used to perform 4 sets of unilateral soleus isometric training (25% MVC, 4 sets: 1 × 30 repetitions, 3 × 15 repetitions). Left leg was used as the untrained control, and a blank control group was included.	150–210 mm Hg	4 wk (3 times/wk)	Soleus: MVC, CSA
Hill ⁴³ (2020)	Healthy young women with no training or injury experience within 6 mo; age = 22 ± 2 y	n = 12	n = 12 (blank control group) n = 12 (non-BFR group)	Randomly assigned dominant or non-dominant arms used to perform 4 sets of isokinetic training (30% peak torque, 4 sets: 1 × 30 repetitions, 3 × 15 repetitions). Opposite arm was used as the untrained control, and a blank control group was included.	40%	4 wk (3 times/wk)	Biceps: MVIC, CSA
May et al ⁴⁸ (2018)	Healthy young men with no training or injury experience within 6 mo	n = 12; age = 22.6 ± 3.3 y	n = 12; age = 22.1 ± 2.5 y (non-BFR group)	Dominant arms of experimental and control groups were used to perform unilateral biceps curling (50% of 1RM, 3 × 10 repetitions). Nondominant arm was used as control.	60%	7 wk (3 times/wk)	Biceps: 1RM, CSA
Wong et al ⁴⁹ (2023)	Healthy young volunteers (102 women, 77 men) with no training or injury experience within 6 mo	n = 41; age = 21 ± 3 y	n = 47 (non-BFR group); age = 21 ± 3 y n = 44 (blank control group); age = 21 ± 3 y n = 47 (maximal effort group); age = 21 ± 3 y	Dominant hands were used to perform 4 sets of handgrip training (30%/50% of 1RM, 4 × 2 min; 4 × 5 s of 100% MVC). Nondominant hand was used as the untrained control, and a blank control group was included.	50%	6 wk (3 times/wk)	Forearm: 1RM, CSA
Mendonca et al ⁵⁰ (2021)	Healthy young volunteers (16 men, 14 women) training <2 times/wk	n = 15; age = 22.3 ± 2.9 y	n = 15; age = 21.9 ± 3.3 y (high-intensity non-BFR group)	Perform 4 sets of plantarflexion training (20% of 1RM/75% of 1RM, 4 × 10 repetitions) on right leg. Left leg was used as the control.	60%	4 wk (5 times/wk)	Soleus: MVC, RTD, CSA
Madarama et al ⁵¹ (2008)	Healthy men without previous experience of regular resistance training	n = 8; age = 21.6 ± 2.4 y	n = 7; age = 21.9 ± 2.9 y (non-BFR group)	Randomly selected dominant or nondominant side was used to perform 4 sets of unilateral dumbbell curling (30% of 1RM, 3 × 10 repetitions) and knee-extension and knee-bending training (50% of 1RM, 2 × 15 repetitions), with opposite side serving as the control.	160–260 mm Hg	10 wk (2 times/wk)	Arm and thigh: equidistant torque, 1RM, CSA

Abbreviations: BFR, blood flow restriction training; CSA, cross-sectional area; MVC, maximum voluntary contraction; MVIC, maximum voluntary isometric contraction; 1RM, 1-repetition maximum; RTD, rate of torque development.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
May et al ⁴⁸ (2018)	?	+	+	+	+	+	+
Colomer-Poveda et al ⁴² (2017)	?	+	+	+	+	+	+
Hill ⁴³ (2020)	?	+	+	+	+	+	+
Mendonca et al ⁵⁰ (2021)	+	+	+	+	+	+	+
Madarame et al ⁵¹ (2008)	?	+	+	+	+	+	+
Wong et al ⁴⁹ (2023)	?	+	+	+	+	+	+

Figure 2. Analysis of the risk of bias in accordance with the Cochrane Collaboration Guidelines.

between 20% and 50% 1RM. In 2 studies, the control group used loads varying from low (75% of 1RM) to high (100% of MVC).^{49,50} Three studies^{42,43,49} included a blank control group, 3 studies^{48,50,51} included a non-BFR unilateral training control, and 3 studies^{42,43,49} implemented both control types concurrently. Intervention duration ranged from 4 to 10 weeks, with sessions held 2 to 5 times weekly postintervention. Muscle strength and volume were assessed in all studies.

Study Quality and Reporting

Using the Cochrane risk-of-bias assessment tool, we rated all 6 articles as having a high risk of bias. Figure 2 illustrates the results of the evaluation.

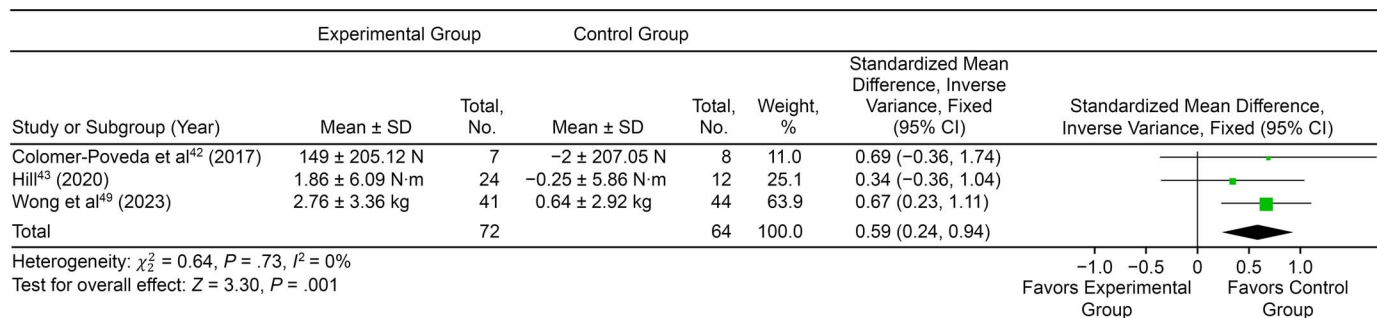


Figure 3. Forest plot of meta-analysis of the effectiveness of blood flow restriction training in inducing muscle-strength cross-education benefits.

Meta-Analysis

We included 3 intervention studies in the meta-analysis of CE benefits of BFR versus a blank control group on contralateral muscle strength.^{42,43,49} All studies tested muscle strength at different times, with a total of 3 comparisons. The meta-analysis results showed no heterogeneity ($I^2 = 0\%$, $P = .73$), with a combined effect size of $SMD = 0.59$ (95% CI = 0.24, 0.94), indicating a difference ($P = .001$; Figure 3).

In the meta-analysis of CE benefits of BFR versus unilateral resistance training on contralateral muscle strength, 5 intervention studies were included and tested muscle strength at different times, with a total of 8 comparisons.^{42,48-51} The meta-analysis results showed no heterogeneity ($I^2 = 36\%$, $P = .14$), with a combined effect size of $SMD = 0.29$ (95% CI = 0.06, 0.52), indicating a difference ($P = .01$; Figure 4).

We included 3 intervention studies in the meta-analysis of CE benefits of BFR versus a blank control group on contralateral muscle volume.^{42,43,49} All studies tested muscle strength at different times, with a total of 3 comparisons. The meta-analysis results showed no heterogeneity ($I^2 = 0\%$, $P = .98$), with a combined effect size of $MD = -0.01$ (95% CI = -0.06, 0.04), which was not different ($P = .60$; Figure 5).

In the meta-analysis of CE benefits of BFR versus unilateral resistance training on contralateral muscle volume, 5 intervention studies were included and tested muscle volume at different times, with a total of 5 comparisons.^{42,48-51} The meta-analysis results showed no heterogeneity ($I^2 = 0\%$, $P = .93$), with a combined effect size of $MD = 0.01$ (95% CI = -0.04, 0.06), indicating no difference ($P = .64$; Figure 6).

DISCUSSION

Few researchers have comprehensively evaluated the effects of BFR on CE of muscle strength and volume using quantitative analysis. We analyzed the effects of BFR by comparing a BFR training group with a blank control group and a unilateral resistance training group, focusing on changes in muscle strength and cross-sectional area. The aim was to optimize clinical rehabilitation prescriptions and enhance muscle function in patients undergoing rehabilitation and middle-aged or older individuals.

After comparing the growth of contralateral muscle strength between the BFR group and the blank control group in 3 studies, we concluded that BFR induced CE of

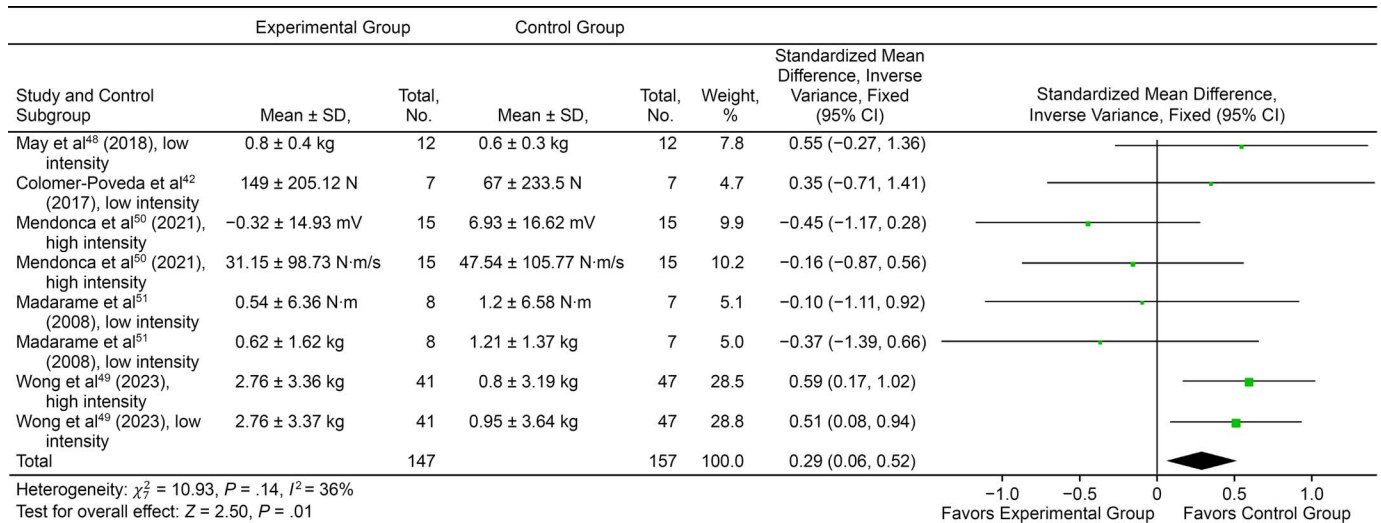


Figure 4. Forest plot of meta-analysis of muscle-strength cross-education benefits of blood flow restriction versus unilateral resistance training.

muscle strength.^{42,43,49} Therefore, we need to explore whether BFR has an advantage over unilateral resistance training in increasing contralateral muscle strength and is worth choosing over conventional unilateral resistance training despite certain risks.

Of the 5 studies included in the meta-analysis comparing the BFR group with the unilateral resistance training group, 3 studies^{42,48,49} indicated a notably greater CE of muscle strength with BFR, and 2 other studies^{50,51} yielded contrasting findings. Previous systematic reviews demonstrated that high-load exercises induce greater CE effects compared with low-load-intensity exercises.^{52,53} In our study, only Mendonca et al used high-intensity resistance training in the control group.⁵⁰ This could explain why they reported contrary findings; they compared the growth of contralateral muscle strength between low-intensity BFR (20% of 1RM) and high-intensity unilateral resistance training (75% of 1RM). Their findings indicated that although low-load unilateral training may exhibit greater CE compared with low-load unilateral training, it may not be as effective as high-intensity unilateral training. In their 2017 meta-analysis, Hughes et al reported that BFR led to improvements in muscle strength, muscle cross-sectional area, and physical function in older adults compared with a blank control group, with average strength gains ranging from 2.9% to 35.6%, increases in muscle cross-sectional area ranging from 3.1% to 8.0%, and improvements in functional testing ranging

from 12% to 28%.⁵ However, they also indicated that, although BFR effectively enhances strength in older adults as demonstrated by Cook et al, this increase is not as great as that achieved through high-intensity unilateral resistance training.⁵⁴ This conclusion does not necessarily affect the use of unilateral BFR in clinical rehabilitation. Blood flow restriction training can effectively enhance muscle strength in individuals who cannot tolerate high-load training or for whom it is contraindicated; relieve pain; and prevent muscle atrophy and strength decline in patients who are bedridden and older adults.

Madarama et al randomly selected the dominant or non-dominant side for intervention training in the experimental group, whereas other researchers focused solely on the dominant hand.⁵¹ However, the hemisphere function of the brain is asymmetrical, with researchers noting higher corticospinal excitability⁵⁵ and shorter transcallosal conduction delay in the dominant hemisphere.⁵⁶ During unilateral movement, the inhibitory effect of the dominant hemisphere on the nondominant hemisphere outweighs the reverse.^{56–58} The dominant hemisphere exhibits greater involvement in nondominant movement and tends to interfere with mirror movements generated by the excitatory output of the nondominant hemisphere.^{56–58} Therefore, although both limbs bear equal loads during unilateral training, the dominant limb is disproportionately stimulated, leading to increased limb asymmetry, particularly evident during complex multijoint exercises.

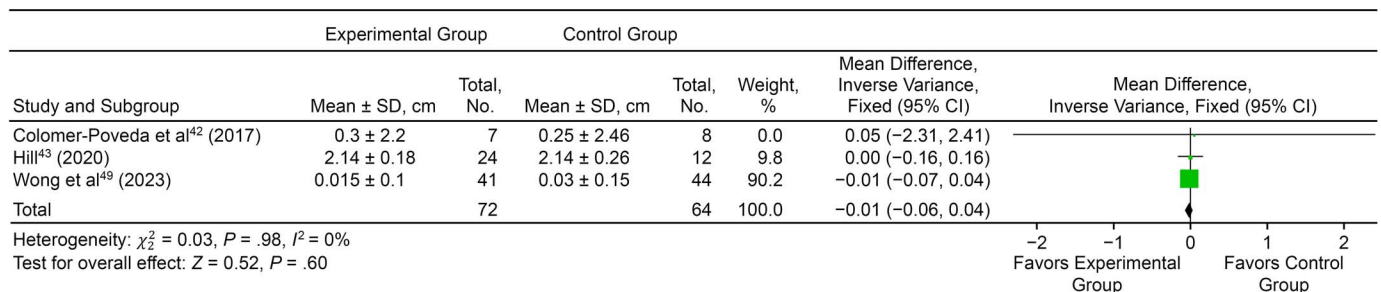


Figure 5. Forest plot of meta-analysis of the effectiveness of blood flow restriction training for inducing muscle-volume cross-education benefits.

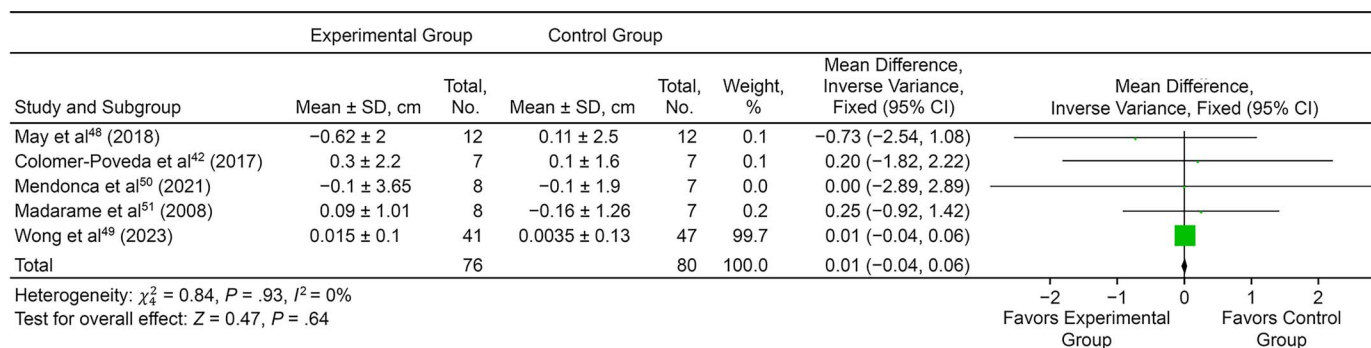


Figure 6. Forest plot of meta-analysis of muscle-volume cross-education benefits of blood flow restriction versus unilateral resistance training.

This discrepancy may account for the lack of difference in CE observed between the BFR group and the unilateral resistance training group.

Based on the above content, we conservatively conclude that in clinical settings, BFR can be prioritized to induce contralateral muscle strength. For individuals who cannot undergo high-intensity unilateral resistance training to promote contralateral muscle-strength recovery, BFR is a more suitable and effective choice.

In practical applications, the magnitude of CE is correlated with the muscle-strength increment on the trained limb, with the strength increase on the opposite side being approximately 60% of that on the same side.^{59–61} Therefore, in assessing the CE phenomenon, one can gauge enhancement in muscle strength on the contralateral side by monitoring the strength increase on the ipsilateral limb, facilitating a prompt and convenient evaluation of the therapeutic effect. Furthermore, this evaluation allows for a scientific determination of training volume for the advantaged limb, enhancing the overall efficacy of the rehabilitation plan, thereby increasing the strength of the contralateral muscle and achieving the desired rehabilitative outcome.

Regarding muscle volume, the results of the meta-analysis indicated no difference between experimental and control groups. Of the 3 studies^{42,43,49} including a blank control group for comparison, 2 studies^{42,43} showed an increase in or maintenance of contralateral muscle volume (Figure 5). Four of 5 studies including a unilateral resistance training group for comparison reached the same conclusion (Figure 6).^{42,49–51}

Hortobágyi et al indicated that the maintenance of muscle volume relies on a delicate balance between muscle protein synthesis and degradation.⁶² Muscle atrophy occurs when protein degradation surpasses synthesis, and CE has been proven effective in reducing muscle atrophy.⁶² Researchers have suggested that the protective effect of CE on skeletal muscle mass depends on synergistically activating protein synthesis pathways, inhibiting protein degradation pathways, or both.¹¹ Another hypothesis is that training the contralateral limb inhibits protein degradation pathways instead of activating protein synthesis pathways. This effect may not be detected under stable conditions of basic protein degradation but can be substantial in severe muscle atrophy, thus preventing disuse-induced muscle atrophy. The mechanism underlying increased strength and muscle hypertrophy during BFR remains unclear. Evidence in multiple studies has suggested that it could be due to indirect effects, including the response of muscle cells to swelling and the accumulation of metabolites, possibly triggered by

the biochemical stress response and metabolite buildup during exercise.^{63–65} These effects may lead to the recruitment of more type 2 muscle fibers, enhancing muscle activation through fatigue and improving training efficiency. Concurrent metabolic stress response and tissue hypoxia also promote the expression of hypoxia inducible factor-1 α and vascular endothelial growth factor.^{35,38} Furthermore, muscle-fiber swelling facilitates cell protein synthesis via mechanistic target of rapamycin/ribosomal protein S6 kinase 1–mediated mammalian targeting pathways and satellite cell migration to muscle fibers.^{36,37} The augmentation of these responses ultimately leads to muscle hypertrophy and increased skeletal muscle capillaries.^{34,39} Therefore, based on previous evidence regarding the effects of CE or BFR on muscle volume, a BFR-induced CE phenomenon could mitigate or prevent muscle-volume atrophy on the disused side.

LIMITATIONS AND FUTURE DIRECTIONS

This study has limitations. The included literature is publicly available, omitting theses, possibly introducing publication bias. All participants were healthy, which limits generalization to those with major or chronic diseases. The focus on adults aged 18 to 30 years may not represent muscle adaptability in an older population. Cross-education induced by BFR is intricate, influencing body adaptations differently. Future research including robust randomized controlled trials is needed for comprehensive investigation.

Currently, no clear standard definition is available for the pressure-intensity limit of BFR. Variation in pressure among patients in the literature hinders the establishment of an optimal range. In addition, BFR variables, including automatic pressure regulation, occlusion time, deflation during rest, and methods for calculating total limb occlusion pressure, require ongoing exploration. Blood flow restriction training offers advantages through neural mechanisms, enhancing motor-unit recruitment and facilitating muscle hypertrophy and strength gains. However, its direct effect on muscle strength and quality is limited, potentially leading to slower progress after initial gains. Future research should be done to investigate CE and BFR mechanisms to enhance theoretical understanding and clinical efficacy in rehabilitation populations.

CONCLUSIONS

Our meta-analysis showed that BFR can stimulate CE of muscle strength, yet confirmation is pending regarding its

effect on muscle volume. Reduced exercise intensity during BFR may enhance neural activation. Coupled with neural mechanism-based training, CE rehabilitation training holds distinctive exploratory value for patients with neurological disorders.

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