REVIEW

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Effects of Strength Training with and Without Blood Flow Restriction on Pain Reduction in Individuals with Knee Osteoarthritis: A Systematic Review with Meta-Analysis of Randomized Clinical Trials

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SUMMARY

Introduction. Blood flow restriction (BFR) training has been shown to be an effective strategy for improving morphology and increasing muscle strength in humans. However, there are still doubts about the mechanisms that lead BFR to promote these benefits in the musculoskeletal system.

Objective. To analyze the effects of strength training with and without blood flow restriction on pain reduction in individuals with knee osteoarthritis.

Methods. This study is characterized as a systematic review and meta-analysis. The PRISMA and PICOS criteria were followed. The databases used were MEDLINE (via PubMed), Scopus, Cochrane, Web of Science, PEDro. Bias risk assessment used the Rob 2.0 tool (Cochrane), methodological quality was assessed using the Testex tool, and the level of evidence quality was assessed using the Grade tool.

Results. 238 publications were found. After applying the selection criteria, a total of 6 RCTs were included in this systematic review and meta-analysis. The meta-analysis result showed a mean of -0.08 (95%CI -0.35 to 0.20) and a P-value of 0.59. There was no significant heterogeneity in the true results ($Q(5) = 3.03$, $p = 0.70$, $I^2 = 0\%$).

Conclusions. Of the 6 RCTs included in this meta-analysis, 4 showed a reduction in pain ($p < 0.05$) with the use of BFR training method in people with knee osteoarthritis, but the meta-analysis results did not confirm this significant difference.

KEY WORDS

Knee; osteoarthritis; blood flow restriction; strength training.

INTRODUCTION

Osteoarthritis (OA) is the predominant form of arthritis, characterized by inflammation and substantial structural changes in the joints. This condition causes considerable impairment due to pain and limited movement, resulting in a notable decrease in quality of life (1). The knee is particularly vulnerable to OA, with weakness in the quadriceps muscles being a significant risk factor for the development of this condition in this joint (2, 3).

Strength training with blood flow restriction (BFR) involves using a pressurized cuff applied to the limb, partially occluding blood flow. It is believed that the cumulative effects of fatigue, mechanical tension, metabolic stress, and reactive hyperemia contribute to promoting adaptation in the limb with minimal effort. Therefore, individuals are able to train with reduced loads and can receive the same benefits as conventional training using higher loads (4-7).

Strength training with blood flow restriction (BFR) has been

shown to be an effective strategy for enhancing morphology and increasing muscle strength in humans. However, there are still doubts about the mechanisms that enable BFR to promote these benefits in the musculoskeletal system (4,8,9). Low-intensity strength training (ST) with the application of BFR results in gains in hypertrophy and muscle endurance in the lower limbs (10). Currently, there is accumulating evidence on the practical value and benefits of strength training with blood flow restriction (STBFR) as a musculoskeletal rehabilitation tool in the clinical setting (8). This study is justified by the low number of meta-analyses (11-13) specifically investigating pain behavior comparing BFRST with conventional strength training in people with knee osteoarthritis. It is worth noting that only the studies by Grantham *et al.* (21) and Wang *et al.* (13) conducted meta-analysis of the pain variable, and with a smaller number of analyses than this meta-analysis. The BFRST can be an effective resource to alleviate the pain caused by knee osteoarthritis in the elderly, in addition to making it possible to perform with lower loads, reducing the risk of injury. The objective of the study was to analyze the effects of strength training with and without blood flow restriction on pain reduction in individuals with knee osteoarthritis.

METHODS

This study is characterized as a systematic review and meta-analysis. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed (14) (**figure 1**). The study was registered and approved by the international prospective register of systematic reviews (PROSPERO) under the number CRD42024530089.

Search strategies

The EndNote Online 20.0.1 reference management software was used in the bibliographic search. Then, the inclusion criteria were applied according to the theme researched and the descriptors used. The databases used were MEDLINE (via PubMed), Scopus, Cochrane, Web of Science, PEDro from March 5 to 18, 2024. The electronic search was carried out by two independent and experienced evaluators, without language or time filters. , and any conflicts were resolved by a third reviewer. The search terms used were grouped into a single Boolean phrase separated by the operators "AND", "OR" (**supplement 1**). Keywords related to the topic were selected based on a literature review and verified by the Medical Subject Headings (MeSH) and Health Sciences Descriptors (Decs) metadata systems.

Selection criteria

The PICOS strategy was used for data inclusion criteria: 1) Population: adults of both sexes with knee osteoartitis; 2) Intervention: TFRFS; 3) Comparison: TFRFS *versus* conventional TF; 4) Outcome: pain; 5) Study design: randomized controlled trials (RCT). The exclusion criteria were as follows: 1) Systematic reviews and meta-analyses; 2) Participants aged > 18 years; 3) Studies that did not use TFRFS as the main intervention.

Risk of bias assessment

The Cochrane Collaboration tool (ROB 2.0), available at: https://www.riskofbias.info/welcome/rob-2-0-tool/current-version-of-rob-2 was used to analyze the risk of bias in the eligible RCTs in this study. To ensure the reliability of the results, two experienced authors evaluated independently and a third author was responsible for possible discrepancies. The domains evaluated were: 1: Randomization; 2: Deviations from intended interventions; 3: Outcome measures; 4: Missing outcome data; 5: Deviations from intended interventions; 6: Randomization process (15) (**table I**).

Methodological quality assessment

TESTEX is a specific scale related to physical exercise, designed to assess methodological quality. It is a 15-point scale, which is divided into two blocks: 5 points for the methodological quality of the study and 10 points for the quality of the report. One point is assigned for each criterion defined on the scale and zero in the absence of these indicators. The scale presents the following parameters: 1) specification of inclusion criteria; 2) random allocation; 3) allocation secrecy; 4) similarity of groups in the initial or baseline phase; 5) assessor blinding (for at least one key outcome); 6) measurement of at least one primary outcome in 85% of allocated subjects (up to three points); 7) intention-to-treat analysis; 8) comparison between groups of at least one primary outcome (up to two points); 9) report measures of variability for all reported outcome measures; 10) monitoring activities in control groups; 11) the relative intensity of the exercise remained constant; and 12) characteristics of exercise volume and energy expenditure (16) (**table II**).

Data extraction

The following study characteristics were extracted: authors, year of publication, country, study population characteristics (age, sex, and sample size), study design, intervention data including general and specific exercises, interven-

tion duration (weeks), training volume (training duration in minutes and training frequency per week), assessment method, and outcomes.

Meta-analysis

The Jamovi 2.3.21.0 program was used to analyze study variables. The standardized mean difference (SMD) was used according to the inverse variance method due to the studies presenting different units of measurement in the pain variable. SMD values in each study were pooled using a random (if heterogeneity was significant) or fixed-effects (if heterogeneity was due to chance) model. SMD values were interpreted as: < 0.2: weak; 0.2-0.79: moderate; ≥ 0.8: strong (17). A statistically significant effect was indicated by $p < 0.05$.

Evaluation of the level of evidence

Two authors independently assessed the certainty of the evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach with the GRADE PRO website, available at https://gradepro.org. GRADE specifies four categories: "high", "moderate", "low", and "very low", applied to a set of evidence. RCTs start with high-quality evidence. Five aspects can decrease the quality of evidence: methodological limitations, inconsistency, indirect evidence, imprecision, and publication bias. On the other hand, three aspects can increase the quality of evidence: effect size, dose-response gradient, and confounding (18). Heterogeneity among studies was analyzed using the I2 statistic. I2 values are interpreted as low heterogeneity (0–50%), moderate heterogeneity (50–74%), and high heterogeneity (≥ 75%) (19, 20) (**table III**).

RESULTS

A total of 238 publications were found from the database search following the proposed search methodology (MEDLINE via PubMed = 10; Scopus = 180; Cochrane = 18; Web of Science = 9; PEDro = 21). After applying the selection criteria, a total of 6 RCTs were included in the present systematic review. Of these studies, 4 provided data for meta-analysis (**figure 1**).

Table I presents the results of the bias risk analysis of randomized studies using the Cochrane Collaboration tool (RoB 2.0). The studies by Bryk *et al.* (21), Segal N. *et al.* (24), and Segal NA *et al.* (25) showed a low risk of bias,

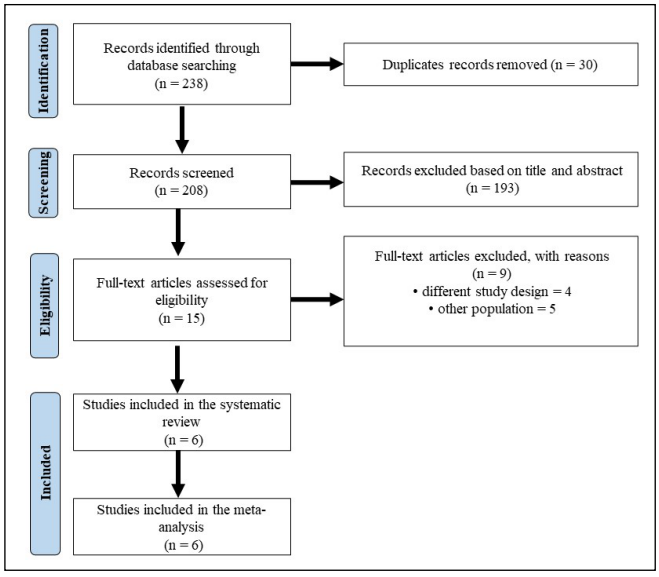


Figure 1. Flowchart of included studies following PRISMA recommendations.

Table I. Bias risk analysis of randomized studies (RoB 2.0).

Studies/Year	1	2	3	4	5	6	Total
Bryk *et al.* (18)	Low	Low	Low	Low	Low	Low	Low
Branco Ferraz *et al.* (19)	Low	Some Concerns	Low	Low	Low	Some Concerns	Some Concerns
Sari *et al.* (20)	Low	Some Concerns	Low	Low	Low	Some Concerns	Some Concerns
Harper et al. (21)	Low	Low	Low	Low	Low	Low	Low
Segal *et al.* (22) (a)	Low	Low	Low	Low	Low	Low	Low
Segal *et al.* (23) (b)	Low	Low	Low	Low	Low	Low	Low

1: Randomization; 2: Deviations from intended interventions; 3: Outcome measurements; 4: Missing outcome data; 5: Deviations from intended interventions; 6: Randomization process.

Table II. Assessment of methodological quality using the TESTEX tool.

Studies	Study quality					Sub-Total	Study report										Sub-Total (0 to 10)	Total (0 a 15)
	1	2	3	4	5		6a	6b	6c	7	8a	8b	9	10	11	12		
Bryk *et al.* (18)	1	1	1	1	1	4	1	0	1	1	1	1	1	1	1	1	9	14
Branco Ferraz *et al.* (19)	1	1	1	1	0	3	1	0	1	1	1	1	1	1	1	1	9	12
Sari *et al.* (20)	1	1	1	1	0	3	1	0	1	1	1	1	1	1	1	1	9	12
Harper *et al.* (21)	1	1	1	1	0	4	1	1	1	1	1	1	1	1	1	1	10	14
Segal *et al.* (22) (a)	1	1	1	1	1	4	1	0	1	1	1	1	1	1	1	1	9	14
Segal *et al.* (23) (b)	1	1	1	1	1	4	1	0	1	1	1	1	1	1	1	1	9	14

Quality of the study: 1 = specific eligibility criteria; 2 = specified type of randomization; 3 = concealed allocation; 4 = similar groups at the start of the study; 5 = assessors were blinded (for at least one primary outcome); 6 = outcomes assessed in 85% of participants (6a = 1 point if more than 85% completed; 6b = 1 point if adverse events were reported; 6c = if exercise frequency was reported); 7 = intention-to-treat statistical analysis; 8 = statistical comparison between groups reported (8a = 1 point if between-group comparisons are reported for the primary outcome variable of interest; 8b = 1 point if statistical comparisons between groups are reported for at least one secondary measure); 9 = point estimates and variability measures for all reported outcome measures; 10 = monitoring of activities in the control group; 11 = relative exercise intensity remained constant; 12 = exercise volume and energy expenditure were reported.

Table III. Characterization of the sample from the selected studies.

Studies/Country	Age (mean and SD)	BMI	Sex	Groups (n)
Bryk *et al.* (18)/Brazil	CG: 60.4 ± 6.7 EG: 62.3 ± 7.0	CG: 30.8 ± 3.7 EG: 28.9 ± 3.7	♀	CG: 17 EG: 17
Branco Ferraz *et al.* (19)/Brazil	CG: 59.9 ± 4.0 EG: 60.3 ± 3.0	CG: 30.3 ± 5 EG: 30.2 ± 3	♀	CG: 16 EG: 16
Sari *et al.* (20)/USA	CG: 69.1 ± 7.1 EG: 67.2 ± 5.2	CG: 29.8 ± 5.3 EG: 31.7 ± 5.9	♂♀	CG: 19 EG: 16
Harper *et al.* (21)/Indonesia	CG: 61.42 ± 5.70 EG: 57.71 ± 5.25	NI	♂♀	CG: 14 EG: 14
Segal *et al.* (22) (a)/USA	CG: 54.6 ± 6.9 EG: 56.1 ± 5.9	CG: 32.1 ± 5.2 EG: 28.7 ± 4.4	♀	CG: 21 EG: 19
Segal *et al.* (23) (b)/USA	CG: 56.1 ± 7.7 EG: 58.4 ± 8.7	CG: 30.4 ± 4.2 EG: 31.3 ± 5.3	♂	CG: 22 EG: 19

EG: experimental group; CG: control group; ♂: Men; ♀: Women.

while the studies by Branco Ferraz *et al.* (22) and Sari *et al.* (27) presented "some concerns" of bias. The domains downgraded were "deviations from intended interventions" and "randomization process".

Table II presents the assessment of methodological quality using the TESTEX tool. The domains that showed bias to a greater extent were "Reporting of adverse events" and "Blinding of assessors".

Table IV. Data extracted from the included studies.

Studies	Intervention	VT	Evaluation	Results (p < 0.05)
Bryk *et al.* (18)	CG (70% 1RM CST) e EG (30% 1RM STBFR - 200 mmHg): Stretching; CORE training (3 x 30s); Hip abduction with weights (3 x 10 reps); Calf raises (3 x 10 reps); Elastic band exercises (3 x 10 reps); Sensorimotor training (3 x 30s); Knee extension on the machine (3 x 10 reps).	3 x week; 6 weeks	Numerical Pain Rating Scale (NPRS)	GC: ↓ GE: ↓
Branco Ferraz *et al.* (19)	CG (CST) AND EG (STBFR): 1st week: 4 sets of 10 reps at 50% 1RM progressing to 80% 1RM in the 2nd week, from the 5th week onwards, 5 sets of each exercise were performed; The resistance training program consisted of bilateral leg press and knee extension exercises on the machine; TFRFS: 70% pressure relative to total vascular occlusion.	2 x week; 12 weeks	Womac pain scale	GC: ↔ GE: ↓
Sari *et al.* (20)	CG (60% 1RM CST) and EG (20% 1RM STBFR): The exercises performed were Leg Press, knee extension, calf raise, and leg curl.	3 x week; 12 weeks	Womac pain scale	GC: ↔ GE: ↔
Harper *et al.* (21)	CG (CST) and EG (STBFR): 20% of 1-RM for weeks 1-2 and 30% of 1-RM for weeks 3-6, 4 sets x 15 reps in week 1, and 5 sets x 15 reps in weeks 2-6 using knee extension machine; TFRFS: Occlusion of 50 mmHg.	2 x week; 6 weeks	Womac pain scale	GC: ↓ GE: ↓
Segal *et al.* (22) (a)	CG (CST) and EG (STBFR): 4 sets at 40% of 1RM for 4 seconds on the Leg Press; TFRFS: Occlusion ranged from 100 mmHg to 200 mmHg according to the intervention time, with weekly increments.	3 x week; 4 weeks	Knee Osteoarthritis Outcome Score (KOOS)	GC:↔ GE:↔
Segal *et al.* (22) (a)	CG (CST) and EG (STBFR): Four sets at 40% 1RM for 4 seconds on the Leg Press for both groups. In the TFRFS, occlusion varied from 100 mmHg to 200 mmHg according to the intervention time, with weekly increments.	3 x week; 4 weeks	Knee Osteoarthritis Outcome Score (KOOS)	GC: ↓ GE: ↓

VT: volume training; STBFR: Strength Training with Blood Flow Restriction; CST: Conventional Strength Training; WOMAC: Western Ontario and McMaster Universities OA Index; KOOS: Knee injury and Osteoarthritis Outcome Score; s: seconds; RM: Repetition Maximum; Reps: Repetitions; CG: control group; EG: experimental group; ↑: increase; ↔: no change.

In **table III**, the study variables are organized by author and year, country of origin, age, BMI, sex, and sample size.
Table IV contains the data extracted from the studies included in this review. The type of intervention, training volume, assessment instrument, and statistical results were detailed.
In **figure 2**, a total of 6 studies were included in the analysis. The observed standardized mean differences ranged from -0.55 to 0.31, with the majority of estimates being negative (100%). The estimated standardized mean difference (SMD) based on the fixed-effects model was -0.08 (95%CI -0.35 to 0.20). Therefore, the average result did not differ significantly from zero ($z = -0.54$, $p = 0.59$). According to the Q-test, there was no significant heterogeneity in the true results ($Q(5) = 3.03$, $p = 0.70$, $I^2 = 0\%$).

DISCUSSION

The aim of the present study was to analyze the effects of strength training with and without blood flow restriction on reducing pain in individuals with knee osteoarthritis.
Thus, the analysis of the 6 studies included in this systematic review revealed an average age of 60 years for both the

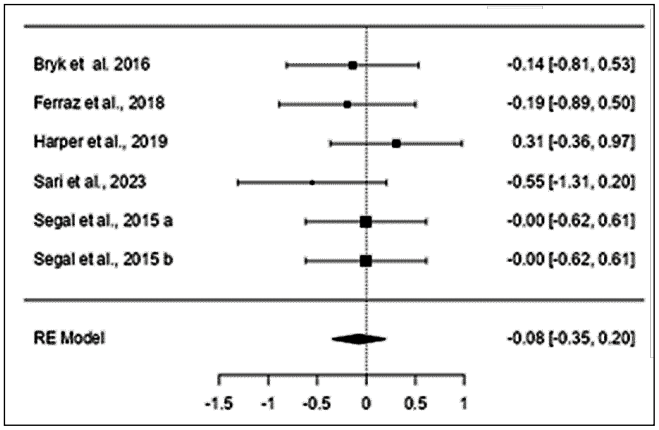


Figure 2. Forest plot (pain analysis).

experimental group (EG) and control group (CG). The BMI presented an average of 30.7 kg/m^2 (grade 1 obesity) in the CG and 30,1 kg/m^2 (overweight) in the EG. Furthermore, the total number of participants was 210, with 109 in the CG and 101 in the EG. Among the included studies, the oldest was published in 2015 and the most recent in 2023, with an interval of 8 years between publications. Additionally, 2 studies were conducted in Brazil (21, 22), followed by 3 studies conducted in the USA (23-25) and only 1 study (26) was conducted in Indonesia. Moreover, the total intervention time ranged from 4 to 12 weeks, with the number of sessions occurring 2 to 3 times per week.

Thus, all studies included in this systematic review presented both a control group (CG) and an experimental group (EG) that underwent strength training (ST), with the CG performing conventional ST while the EG underwent blood flow restriction strength training (BFRST). For the analysis of results, the studies by (21-23, 27) utilized knee extension on a machine, while the studies by (23-25) used the Leg Press equipment. The randomized controlled trial (RCT) conducted by (28) corroborates these findings by analyzing 40 middle-aged women with osteoarthritis. The sample was divided into BFRST and conventional ST groups, with 3 training sessions per week for 4 weeks. The results showed benefits in functional mobility for the group of women who underwent training with the BFRST method.

Similarly, the pain variable was investigated using different tests. Three studies (22, 23, 27) used WOMAC, the study by Bryk *et al.* (21) used the NPRS test, and the studies number 24, and 25 used the test KOOS. The studies numbers 21, 22, 24 and 27 showed a significant reduction ($p < 0.05$) in pain in the EG compared to the CG, while the studies 23 and 25 did not show significant differences between the groups.

A study by Schwiete *et al.* (29) conducted an RCT with 19 participants undergoing intermittent BFRS and continuous BFRS, aiming to assess discomfort rate, perceived effort, degree of hypertrophy, maximum strength, and muscle thickness. The results indicated a significant increase ($p < 0.05$) in maximum strength, hypertrophy, and muscle thickness, but the perception of pain was lower in the group that underwent intermittent BFRS. In a systematic review conducted by Pitsillides *et al.* (30), the findings favored the use of BFRS compared to high-intensity training for muscle strengthening and pain reduction in patients with knee osteoarthritis. Similarly, another systematic review conducted by Bobes Álvarez *et al.* (31) suggests that BFRS could provide similar benefits to high-intensity training and with the advantages of low-intensity training.

Therefore, it is worth noting that the results presented by this meta-analysis showed no reduction in pain with the use of the BFRST method compared to conventional strength training.

Thus, the main limitation of the study was the total intervention time found in the RCTs. The hypothesis is that possibly a greater number of weeks may yield better results in pain reduction. Another limitation is the small number of studies involving BFRST according to the inclusion criteria established in this study. A greater number of RCTs with a significant sample could provide more robustness to the results found.

CONCLUSIONS

Based on the results found in the present systematic review and meta-analysis, of the 6 RCTs included in this meta-analysis, 4 studies (21, 22, 24, 27) showed a significant reduction ($p < 0.05$) in pain with the use of the BFRST method in individuals with knee osteoarthritis. However, the results of the meta-analysis did not confirm this significant difference. It is hoped that more RCTs can be developed and that their results may differ from those found in this study.

Additionally, other studies using BFRST should investigate and suggest an analysis of specific biomarkers (bone remodeling) and behavioral (self-esteem) in individuals with knee osteoarthritis. Thus, knowledge of possible effects on different physical variables may help professionals using the BFRST method to achieve positive and safe outcomes in patients with the pathological condition of osteoarthritis.

FUNDINGS

None.

DATA AVAILABILITY

All data used in this review is appropriately cited.

CONTRIBUTIONS

DGL: conceptualization, data extraction, data analysis and writing – original draft. BGL, RGSV: supervision, writing – review & editing. CJBP, GCPSMS, ASM: data analysis, writing – review & editing.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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