Journal of Athletic Training 2022;57(4):402–417
doi: 10.4085/1062-6050-0603.20

www.natajournals.org

Low-Load Blood-Flow Restriction Exercise to Failure and Nonfailure and Myoelectric Activity: A Meta-Analysis

Mikhail Santos Cerqueira, MSc, PT*; Daniel Germano Maciel, MSc, PT*; Jean Artur Mendonça Barboza, MSc, PT*; Christoph Centner, PhD†; Maria Lira, PT*; Rafael Pereira, PhD, PT‡; Wouber Hérickson De Brito Vieira, PhD, PT*

*Department of Physical Therapy, Federal University of Rio Grande do Norte (UFRN), Natal, RN, Brazil; †Department of Sport and Sport Science, University of Freiburg, Germany; ‡Praxisklinik Rennbahn, Muttenz, Switzerland; §Department of Biological Sciences, Universidade Estadual do Sudoeste da Bahia (UESB), Jequié, Brazil

Objective: To compare the short- and long-term effects of low-load resistance training with blood-flow restriction (LL-BFR) versus low- (LL-RT) or high- (HL-RT) load resistance training with free blood flow on myoelectric activity and investigate the differences between failure (exercise performed to volitional failure) and nonfailure (exercise not performed to volitional failure) protocols.

Data Sources: We identified sources by searching the MEDLINE, PubMed, CINAHL, Web of Science, CENTRAL, Scopus, SPORTDiscus, and PEDro electronic databases.

Study Selection: We screened the titles and abstracts of 1048 articles using our inclusion criteria. A total of 39 articles were selected for further analysis.

Data Extraction: Two reviewers independently assessed the methodologic quality of each study and extracted the data. A meta-analytic approach was used to compute standardized mean differences (SMDs) $\pm$ 95% CIs. Subgroup analyses were conducted for both failure and nonfailure protocols.

Data Synthesis: The search identified 39 articles that met the inclusion criteria. Regarding the short-term effects, LL-BFR increased muscle excitability compared with LL-RT during nonfailure protocols (SMD = 0.61; 95% CI = 0.34, 0.88), whereas HL-RT increased muscle excitability compared with LL-BFR during failure (SMD = –0.61; 95% CI = –1.01, –0.21) and nonfailure (SMD = –1.13; 95% CI = –1.94, –0.33) protocols. Concerning the long-term effects, LL-BFR increased muscle excitability compared with LL-RT during exercises performed to failure (SMD = 1.09; 95% CI = 0.39, 1.79).

Conclusions: Greater short-term muscle excitability levels were observed in LL-BFR than in LL-RT during nonfailure protocols. Conversely, greater muscle excitability was present during HL-RT than LL-BFR, regardless of volitional failure. Furthermore, LL-BFR performed to failure increased muscle excitability in the long term compared with LL-RT.

Key Words: electromyography, muscle fatigue, vascular occlusion exercise, volitional failure, Kaatsu training

Key Points

- Low-load blood-flow restriction (LL-BFR) resistance training immediately increased muscle excitability compared with low-load resistance training with free blood flow only during exercises not performed to failure.
- Greater muscle excitability was identified during high-load resistance training compared with LL-BFR, regardless of muscle failure.
- Volitional failure should be considered a prescription variable interfering directly with myoelectric activation and indirectly with strength and muscle mass gains after LL-BFR.

Low-load resistance training (ie, 20%–50% of 1-repetition maximum [1RM]) with blood-flow restriction (LL-BFR) has gained increasing attention as an effective technique for enhancing muscle strength and hypertrophy,[1,2] with less mechanical demand than that of conventional high-load (70%–85% of 1RM) resistance training with free blood flow (HL-RT).[3] Previous evidence has suggested that LL-BFR was effective in individuals with joint pain, such as patients with knee osteoarthritis,[4] patients with anterior cruciate ligament reconstruction,[5] and athletes for facilitating muscle-strength and -hypertrophy gains.[6]

The underlying mechanisms responsible for muscle-strength and -hypertrophy gains after LL-BFR are mainly hypothetical and theoretical.[7,8] One proposed mechanism is increased metabolic stress due to a hypoxic muscular environment,[9] which may lead to increased myoelectric activity.[10] Indeed, authors[11] of previous LL-BFR studies found strong correlations between metabolic markers and muscle excitation. From a comprehensive perspective, increased myoelectric activity, assessed using surface electromyography (EMG), has been associated with strength and hypertrophy gains.[12,13]

However, the capacity of LL-BFR to increase muscle excitability is controversial.[14] Some researchers[15–17] have shown higher myoelectric activity during LL-BFR compared with low-load resistance training with free blood-flow (LL-RT) protocols, whereas others[18,19] noted similar myoelectric activity during both protocols. In addition, despite similar muscle hypertrophy induced by LL-BFR and HL-RT,[1] the former seemed to induce less muscle excitation than HL-RT.[20] These controversies are likely due to the high level of heterogeneity in LL-BFR prescription, especially concerning whether exercise is performed to volitional failure.[19] Interestingly, in a recent study, Morton et al[21] demonstrated that muscle-fiber activation was unaffected by exercise load when the task was performed to failure. This highlights the need to consider this factor while examining changes in muscle excitation. In terms of blood-flow restriction training, the authors[8,10,12,14,17] of several narrative reviews discussed myoelectric activity as a pivotal mechanism for LL-BFR adaptations. However, no authors of systematic reviews have summarized this topic quantitatively or included volitional failure as a potential moderating factor. Thus, the purpose of our systematic review and meta-analysis was to investigate whether short- or long-term LL-BFR altered myoelectric activity in individuals (healthy or unhealthy, active or sedentary) of any age compared with HL-RT or LL-RT. Additionally, we examined differences between failure (exercise performed to volitional failure) and nonfailure (exercise not performed to volitional failure) protocols.

METHODS

Study Design

This systematic review was developed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. The review protocol was prospectively submitted to the PROSPERO platform (ID: 150824).

Identification of Studies

The electronic database searches included MEDLINE, PubMed, CINAHL, Web of Science, CENTRAL, Scopus, SPORTDiscus, PEDro, and the trial register in the ClinicalTrials.gov website (ie, gray literature). A systematic literature search was carried out with no language restriction between database inception (April 1978) and September 2019. The search terms were derived from *blood flow restriction*, *blood flow restriction exercise*, *blood flow restriction training*, *kaatsu*, *vascular occlusion exercise*, *muscle fatigue*, *electromyography*, *emg*, *muscle activation*, and *clinical trial* (see Supplementary Table, available online at http://dx.doi.org/10.4085/1062-6050-0603.20.S1). We also manually checked the reference lists of the identified studies, previous systematic reviews, and forward citations (to August 2020) for potentially relevant studies.

Eligibility Criteria

All studies were screened and assessed for eligibility according to inclusion and exclusion criteria based on the PICOTS principle (ie, extracting population, intervention, comparison intervention, outcome measures, time point measure, and study design information). Those involving participants (healthy or unhealthy, active or sedentary) aged $\geq$18 years were included. We considered interventions that compared LL-BFR ($\leq$50% of 1RM/maximal voluntary contraction [MVC]) with LL-RT ($\leq$50% of 1RM/MVC) or HL-RT ($\geq$70% of 1RM/MVC).[1,2] The LL-BFR protocol needed to follow the same resistance-exercise modality (ie, isometric or dynamic) used in the LL-RT and HL-RT protocols, and LL-BFR and LL-RT needed to follow a matched number of repetitions (in nonfailure protocols) and load. Similar protocols have been deemed essential for drawing conclusions about the additional effects of BFR and enabling comparability. Surface EMG variables measured in time or frequency domains during MVC or exercise bouts were considered outcome measures. Only randomized crossover trials, randomized within-participant trials, or randomized controlled trials assessing short-term or acute responses, long-term adaptations, or both were included in this review. Studies involving a single exercise section for each intervention group were considered *short term*, and those involving at least 4 weeks of intervention were considered *long term*.

Those studies without available full text (short version) or without both LL-BFR and LL-RT conditions were not included. Studies involving only intermittent BFR or aerobic exercise as the intervention group, assessing only individual motor-unit characteristics with no EMG evaluation, or lacking the EMG signal in at least 1 agonist muscle of the movement performed were excluded.

Study Selection

The searches, data collection, risk-of-bias assessment, and data extraction were performed separately by 2 independent reviewers (D.G.M., J.A.M.B.), and when a consensus was not reached, the differences were discussed with a third evaluator (M.S.C.). The reviewers initially judged the relevance of the studies by reading the titles and abstracts. Those that did not match the inclusion criteria and duplicates were excluded. Articles with abstracts that presented the potential for eligibility or raised questions were retained for careful full-text analysis.

From the remaining eligible papers, the following data were extracted: (1) study design; (2) participant characteristics (sample size, sex, age, and training status); (3) exercise protocol (number of series and repetitions, frequency of training [number of days per week], training length [number of weeks], exercised muscle, muscle action mode [isometric, isokinetic, concentric, or eccentric], and exercise load); (4) cuff settings (pressure and width); (5) outcome measures (surface EMG variables extracted from time or frequency domain [assessed muscles and normalization method]); and (6) main study results. Data were extracted using a custom spreadsheet built by the third evaluator (M.S.C.).

Given the limited and heterogeneous data regarding frequency-domain measures, long-term studies comparing LL-BFR with HL-RT and studies assessing EMG time-domain variables immediately pre-exercise and postexercise bouts were analyzed only qualitatively. Thus, for the meta-analysis, the following comparisons were performed: (1) short-term LL-BFR versus LL-RT, (2) short-term LL-BFR versus HL-RT, and (3) long-term LL-BFR versus LL-RT effects. For these comparisons, time-domain variables (ie, muscle excitation) were extracted during submaximal exercise bouts and MVC in short- and long-term studies, respectively. For each comparison, subgroup analyses were conducted for both failure and nonfailure protocols.

Quality Assessment of the Studies

The quality assessment was conducted using the Cochrane risk-of-bias tool, which classifies the risk of bias as high, low, or unclear. The risk of bias is considered *high* if a methodologic procedure is not described, *unclear* if the description is unclear, or *low* if the entire procedure is described in detail. Information from the studies was independently extracted by both reviewers and stored in Review Manager (RevMan) software (version 5.3; The Nordic Cochrane Center, The Cochrane Collaboration) for subsequent data crossing and discussion of possible discrepancies. Potential biases were assessed via visual inspection of funnel plots (Supplementary Figures 1 and 2).

Statistical Analyses

We used the random-effects model in the meta-analysis to evaluate standardized mean differences (SMDs) ± 95% CIs. Those SMD outcomes between ≥0.2 and <0.5 were considered *small*, those between ≥0.5 and <0.8 were considered *medium*, and those ≥0.8 were considered *large*.[22,23] A random-effects meta-analysis was conducted because of data heterogeneity from different EMG variables.[24] Mean, SD, and sample-size data were extracted. Regarding the meta-analyses performed for studies assessing short-term responses at multiple time points, only the last time point was considered, because the variables were normalized for MVC or the beginning of the exercise. In studies assessing the long-term effects, the mean and SD difference values between pretraining (SD_{pre}) and posttraining (SD_{post}) were used. Given that we partially observed differences between time points (ie, between SD_{pre} and SD_{post}), we defined the SD_{change} as follows: square root $([SD_{pre}^2/N_{pre}] + [SD_{post}^2/N_{post}])$, where N was sample size.[25] We either contacted authors when essential data were not comprehensively reported in the manuscript or estimated data from graphs using the ImageJ software (National Institutes of Health). If any information regarding SDs was missing, these values were calculated from SEs or CIs if available.

Heterogeneity was assessed using the I^2 statistic, which describes the true variation among studies as a percentage, and values were interpreted as *low* (25%), *medium* (50%), or *high* (75%) *heterogeneity*.[24] For those studies evaluating several muscles, only 1 muscle was included in the meta-analysis to avoid including the same study population multiple times (ie, double counting), which would have inherently increased the statistical weight.[2]

Given high EMG data variability, the following data-extraction order was prioritized for the meta-analysis[2]: vastus lateralis > vastus medialis > rectus femoris > soleus > tibialis anterior > fibularis longus in the lower extremity and biceps brachii > triceps brachii > brachioradialis > forearm flexors in the upper extremity. Lower limb muscles were prioritized in studies involving both upper and lower limb exercises to minimize outcome variability.[2] For studies performed with several muscle-action modes, the order was prioritized as isometric > isokinetic > concentric > eccentric, and priority was given to the open kinetic chain in studies of both open and closed kinetic chains. For those studies involving loads <20% of 1RM or MVC and several occlusion pressures, the highest BFR pressure (up to 80%) was considered. Moderate pressures (ie, 40% to 60% of total occlusion pressure) were prioritized in studies using several BFR levels and loads >20% of 1RM or MVC. In all analyses, multiple comparisons were included from several studies (eg, dynamic and isometric exercise, muscles of upper and lower limbs) to increase accuracy and thus the generalization of our results.[26]

All statistical analyses were performed using the Cochrane Review Manager (RevMan) software. The α level was set a priori at $P < .05$.

RESULTS

Identification and Selection of Studies

A total of 1678 articles were retrieved from database searches. After removing duplicates, we submitted the remaining articles to title and abstract analyses, and 54 articles were considered eligible. Of these, 16 were excluded for the following reasons: no EMG assessment,[27–32] no free–blood-flow group,[33] no LL-BFR group,[34] lack of resistance training,[35,36] individual motor-unit assessment,[37] intermittent BFR,[38] collapsed data regarding LL-BFR and LL-RT,[39,40] lack of EMG assessment in the agonist muscle,[41] and total BFR.[42] The remaining 39 studies,[15,16,18,19,43–77] published between 2006 and 2020, were included in the systematic review. Thirty-two studies[15,16,18,19,43–70] were included in meta-analyses (Figure 1). An overview of the studies is in Table 1.

Risk of Bias

Most of the included trials presented a high risk of performance bias and other bias. In addition, most of the studies presented an unclear risk of bias for random sequence generation, allocation concealment, blinding of outcome assessment, incomplete outcome data, selective reporting, and group similarity at baseline (Table 2).

Participants

A total of 548 participants were enrolled in the 39 included trials,[15,16,18,19,43–77] and data from 411 participants were included in the meta-analyses.

Exercise Protocol

The short-term effects of BFR were verified in 33 studies,* and the long-term effects of BFR on myoelectric activity were verified in 6 studies.[68,69,72,73,75,77] In the long-term studies, the training program duration ranged from 5 to 12 weeks, with a frequency of 2 or 3 times per week.

The training load ranged between 10% and 50% of 1RM or MVC for both LL-BFR and LL-RT and between 60% and 80% for HL-RT. The load was imposed using elastic resistance in 2 studies.[48,62] In 15 studies,† repetitions were applied to failure, and in 24 studies,‡ a predetermined number of repetitions was performed.

Outcome Measures

Myoelectric activity was assessed in the time domain in 31 studies,§ in the frequency domain in 1 study,[76] and in both domains in 7 studies.[19,44,53,69–71,74] The surface EMG variables assessed in the time domain were the root mean square (RMS), integrated EMG (iEMG), peak of the EMG

*References 15, 16, 18, 19, 43–67, 70, 71, 74, 76.
†References 18, 19, 46, 49, 50, 54, 56, 57, 59–61, 68, 69, 71, 75.
‡References 15, 16, 43–45, 47–49, 51–53, 55, 58, 62–67, 70, 72–74, 77.
§References 15, 16, 18, 43, 45–52, 54–68, 72, 73, 75, 77.

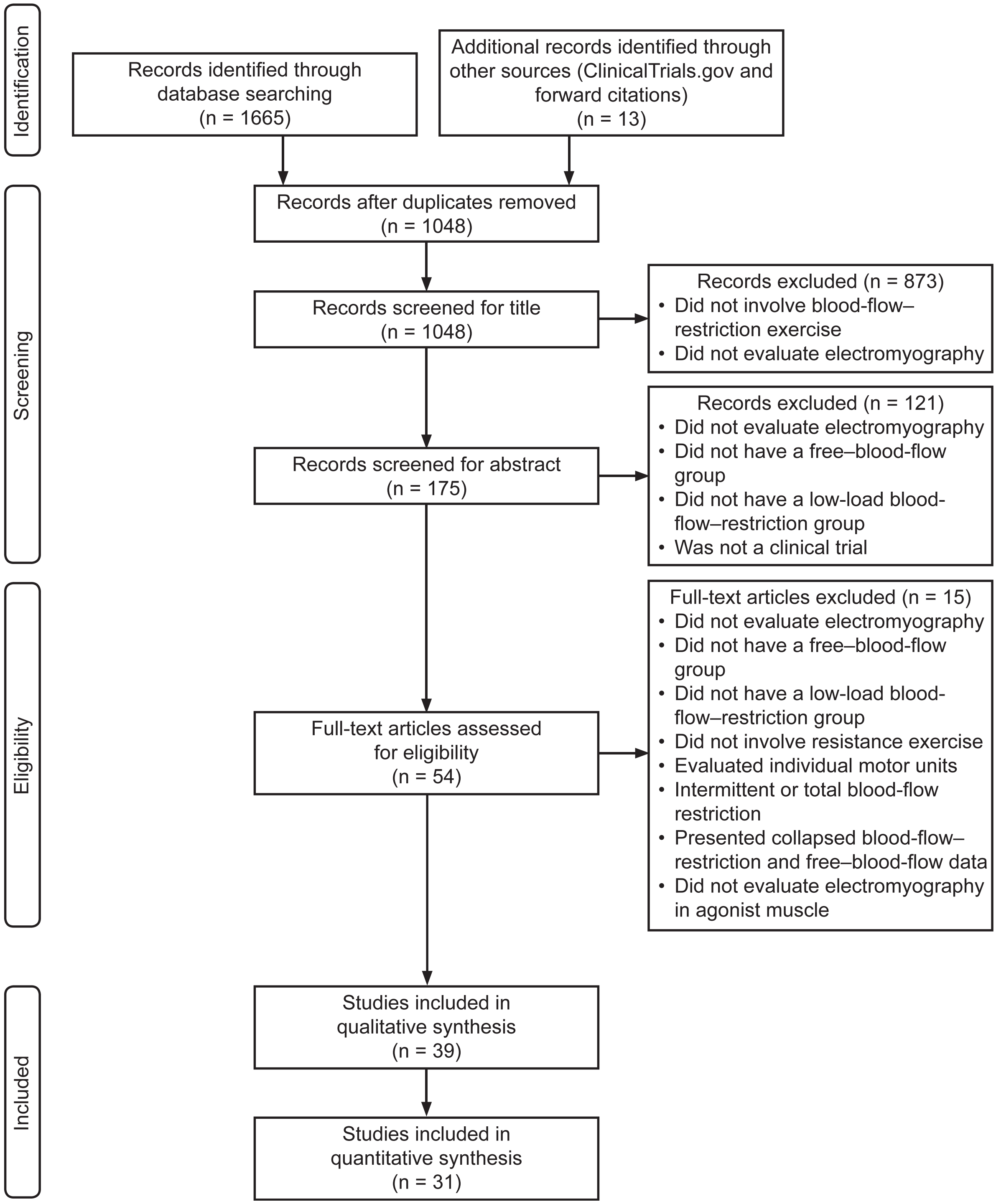

Figure 1. Flow diagram of article selection process according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

signal (EMGpeak), EMG amplitude, and average EMG, whereas mean power frequency (MPF), median frequency (Fmed), and central frequency (CF) were assessed in the frequency domain.

Short-Term Effects of LL-BFR on Myoelectric Activity

Comparison: LL-BFR and LL-RT. Based on 18 studies,[‖] LL-BFR presented a moderate effect in increasing muscle excitability when exercises were not performed to failure compared with LL-RT (SMD = 0.61; 95% CI = 0.34, 0.88; $Z = 4.41$; $P < .001$). Heterogeneity was low ($I^2 = 39\%$, $P = .04$). When exercise was performed to failure (n = 10 studies[¶]), no differences were observed in muscle excitation between LL-BFR and LL-RT (SMD = –0.14; 95% CI = –0.38, 0.10; $Z = 1.17$; $P = .24$). The I^2 statistic of 0% ($P = .60$) represented very low heterogeneity for this

‖ *References 15, 16, 43–45, 47, 48, 51–53, 55, 58, 62–67.*

¶ *References 18, 19, 46, 50, 54, 56, 57, 59–61.*

Table 1. Summary of the Included Studies Continued on Next Page

Study	Design	Patient Characteristics and Training Status	Muscle Action Mode and Assessed Muscle	EMG Variables (Normalization Method)	Study Intervention: Exercise Measures[a]	BFR Pressure and Cuff Width[b]	Main Results
Short-term studies (lower limbs)							
Karabulut et al[70] (2006)	RWP	12 men; age = 23.7 ± 4.1 y; active and not engaged in RT	Intermittent isometric; vastus lateralis	RMS and MPF pre-exercise, during exercise, and postexercise (MVC)	LL-BFR: 5 sets (20 repetitions/set) at 20% MVC LL-RT: similar to LL-BFR	183.3 mm Hg; 5 cm	No differences pre-exercise, during exercise, or postexercise between LL-BFR and LL-RT
Kinugasa et al[67] (2006)	RCO	7 men; age = 24.7 ± 1.5 y; engaged in RT	Concentric and eccentric; vastus lateralis, vastus medialis, and rectus femoris	iEMG pre-exercise, during exercise, and postexercise (MVC)	LL-BFR: 5 sets (10 repetitions/set) at 50% 10RM LL-RT: similar to LL-BFR	87.9% arterial occlusion pressure; 10 cm	No differences pre-exercise, during exercise, or postexercise between LL-BFR and LL-RT
Wernbom et al[18] (2009)	RWP	11 men and women; age range = 20–39 y; engaged in RT	Eccentric; vastus medialis and vastus lateralis	RMS during exercise (MVC)	LL-BFR: 3 sets to failure at 30% 1RM LL-RT: similar to LL-BFR	100 mm Hg; 13.5 cm	LL-BFR did not increase RMS versus LL-RT
Karabulut et al[44] (2010)	RWP	14 men; age = 23.9 ± 0.9 y; not engaged in RT	Concentric and eccentric; vastus lateralis	RMS and MPF pre-exercise, during exercise, and postexercise (MVC)	LL-BFR: 5 sets (20 repetitions/set) at 20% MVC LL-RT: similar to LL-BFR	1.44 × Systolic blood pressure; 5 cm	No differences between groups in RMS and MPF during exercise Reduced RMS postexercise in LL-BFR versus LL-RT; no differences in MPF
Cook et al[46] (2013)	RCO	8 men; age = 22 ± 2 y; recreationally active and not engaged in RT	Concentric and eccentric; vastus lateralis, vastus medialis, and rectus femoris	RMS during exercise (MVC)	LL-BFR: 3 sets to failure at 20% 1RM LL-RT: similar to LL-BFR at 20% 1RM HL-RT: similar to LL-BFR at 70% 1RM	180 mm Hg; 5 cm	Increased RMS during HL-RT versus LL-RT and LL-BFR
Labarbera et al[59] (2013)	RCO	20 men and women; age range = 18–25 y; not engaged in RT	Concentric and eccentric; vastus lateralis, vastus medialis, and rectus femoris	RMS during exercise (MVC)	LL-BFR: 3 sets to failure at 20% 1RM LL-RT: similar to LL-BFR	180 mm Hg; 5.4 cm	LL-BFR did not increase RMS versus LL-RT
Wilson et al[45] (2013)	RCO	12 men; age = 21 ± 3 y; engaged in RT	Concentric; vastus lateralis	RMS during exercise (NR)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 30% 1RM LL-RT: similar to LL-BFR	Elastic wraps; 7.6 cm	Increased RMS during LL-BFR versus LL-RT
Fahs et al[60] (2015)	RWP	17 men and women; age range = 40–64 y; not engaged in RT	Concentric and eccentric; vastus lateralis	RMS during exercise (MVC)	LL-BFR: 2 sets to failure at 30% 1RM LL-RT: similar to LL-BFR	50%–80% Arterial occlusion pressure; 5 cm	Increased RMS during LL-RT versus LL-BFR
Loenneke et al[49] (2015)	RCO	40 men; age range = 18–35 y; physically active	Concentric and eccentric; vastus lateralis	RMS during exercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 20% or 30% 1RM LL-RT: 4 sets to failure at 20% or 30% 1RM HL-RT: 4 sets (10 repetitions/set) at 70% 1RM	40%, 50%, or 60% Arterial occlusion pressure; 5 cm	Increased RMS during HL-RT versus LL-RT and LL-BFR
Cayot et al[51] (2016)	RCO	7 men; age = 24.8 ± 1.4 y; recreationally active	Isometric; vastus lateralis and vastus medialis	RMS during exercise (MVC)	LL-BFR: 1 set of 4 repetitions at 20% or 40% MVC LL-RT: similar to LL-BFR HL-RT: similar to LL-BFR at 60% or 80% 1RM	130% Systolic blood pressure; 6 cm	No differences in RMS between groups during any exercise intensity
Lauver et al[66] (2017)	RCT	16 participants; age = 22.8 ± 2.3 y; NR	Isokinetic eccentric; vastus lateralis and vastus medialis	RMS during exercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 30% MVC LL-RT: similar to LL-BFR	130% Systolic blood pressure; 6 cm	Increased RMS during LL-BFR versus LL-RT

Table 1. Continued From Previous Page

Study	Design	Patient Characteristics and Training Status	Muscle Action Mode and Assessed Muscle	EMG Variables (Normalization Method)	Study Intervention: Exercise Measures[a]	BFR Pressure and Cuff Width[b]	Main Results
Barnes et al[55] (2018)	RCO	10 men; age = 22.5 ± 2.1 y; engaged in RT	Concentric and eccentric; vastus lateralis	Average EMG during exercise (first set)	LL-BFR: 5 sets (15 repetitions/set) at 30% 1RM LL-RT: similar to LL-BFR HL-RT: 3 sets (10 repetitions/set) at 75% 1RM	30% Arterial occlusion pressure; 6 cm	Increased average EMG during HL-RT versus LL-BFR and LL-RT
Fatela et al[53] (2018)	RCO	10 men; age range = 19–34 y; not engaged in RT or aerobic training	Concentric; vastus medialis and rectus femoris	RMS and median frequency pre-exercise, during exercise, and postexercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 20% 1RM LL-RT: similar to LL-BFR HL-RT: 4 sets (10 repetitions/set) at 75% 1RM	80% Arterial occlusion pressure; 13 cm	Increased RMS during HL-RT versus LL-BFR and LL-RT No differences postexercise among LL-BFR, LL-RT, and HL-RT
Husmann et al[52] (2018)	RCO	17 men; age = 25 ± 4 y; physically active and engaged in RT	Concentric; vastus lateralis, vastus medialis, and rectus femoris	RMS during exercise (first 3 repetitions)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 30% 1RM LL-RT: similar to LL-BFR	60% Arterial occlusion pressure; 10 cm	Increased RMS during LL-BFR versus LL-RT
Ilett et al[16] (2019)	RCO	13 men; age = 25 ± 6 y; not engaged in RT	Intermittent isometric; vastus lateralis	RMS pre-exercise, during exercise, and postexercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 20% 1RM LL-RT: similar to LL-BFR HL-RT: similar to LL-BFR at 80% 1RM	40%, 60%, or 80% Arterial occlusion pressure; 10.5 cm	Increased RMS during HL-RT versus LL-BFR and LL-RT; RMS was higher during LL-BFR versus LL-RT No differences postexercise among LL-BFR, LL-RT, and HL-RT
Ishizaka et al[63] (2019)	RCO	7 men and women; age range = 25–75 y; patients with cardiomyopathy	Concentric and eccentric; vastus lateralis, vastus medialis, and rectus femoris	EMG amplitude during exercise (MVC)	LL-BFR: 3 sets (30 repetitions/set) at 10% or 20% 1RM LL-RT: similar to LL-BFR	180 mm Hg; 6 cm	LL-BFR did not increase EMG amplitude compared with LL-RT
Jessee et al[56] (2019)	RCO	23 men and women; age = 22 ± 2.7 y; engaged in RT	Concentric and eccentric; rectus femoris and vastus lateralis	RMS during exercise (MVC)	LL-BFR: 4 sets to failure at 15% 1RM LL-RT: similar to LL-BFR HL-RT: similar to LL-BFR at 70% 1RM	40% or 80% Arterial occlusion pressure; 10 cm	Increased RMS during HL-RT versus LL-BFR and LL-RT
Kjeldsen et al[62] (2019)	RCO	17 men and women; age = 35 ± 10 y; NR	Concentric and eccentric; tibialis anterior	RMS during exercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) with elastic resistance LL-RT: similar to LL-BFR	60% Arterial occlusion pressure; 22–26 cm	Increased RMS in LL-BFR versus LL-RT
Freitas et al[65] (2020)	RCO	14 men; age range = 18–30 y; not engaged in RT	Concentric and eccentric; vastus lateralis and vastus medialis	RMS during exercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 20% 1RM LL-RT: similar to LL-BFR HL-RT: 4 sets (10 repetitions/set) at 70% 1RM	50% Arterial occlusion pressure; 13.5 cm	Increased RMS during HL-RT versus LL-BFR and LL-RT
Killinger et al[15] (2020)	RCO	19 men and women; age = 21.8 ± 2.8 y; chronic ankle instability patients	Isometric; tibialis anterior and fibularis longus	RMS during exercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 30% MVC LL-RT: similar to LL-BFR	80% Arterial occlusion pressure; NR	Increased RMS in LL-BFR versus LL-RT
Short-term studies (upper limbs)							
Yasuda et al[58] (2006)	RCO	12 men and women; age = 24.1 ± 3.5 y; not engaged in RT	Concentric and eccentric; triceps brachii and pectoralis major	iEMG during exercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 30% 1RM LL-RT: similar to LL-BFR	100% Systolic blood pressure; 3 cm	Increased iEMG during LL-BFR versus LL-RT
Yasuda et al[43] (2008)	RCO	10 men; age = 22.3 ± 1 y; physically active and not engaged in RT	Concentric and eccentric; biceps brachii	iEMG pre-exercise, during exercise, and postexercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 20% 1RM LL-RT: similar to LL-BFR	100% Systolic blood pressure; 3 cm	Increased iEMG during exercise with LL-BFR versus LL-RT No differences postexercise between LL-BFR and LL-RT

Table 1. Continued From Previous Page

Study	Design	Patient Characteristics and Training Status	Muscle Action Mode and Assessed Muscle	EMG Variables (Normalization Method)	Study Intervention: Exercise Measures[a]	BFR Pressure and Cuff Width[b]	Main Results
Yasuda et al[74] (2009)	RCO	10 men; age = 24.1 ± 3.2 y; physically active and not engaged in RT	Concentric and eccentric; biceps brachii	iEMG and MPF pre-exercise, during exercise, and postexercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 20% 1RM LL-RT: similar to LL-BFR	160 mm Hg; 3 cm	Increased iEMG and reduced MPF during exercise in LL-BFR versus LL-RT No differences postexercise between LL-BFR and LL-RT
Hotta and Ito[76] (2011)	RCO	4 men; age range = 20–29 y; NR	Isometric; biceps brachii	Central frequency during exercise (NR)	LL-BFR: 8 min at 20% MVC LL-RT: similar to LL-BFR	200 mm Hg; NR	Reduced central frequency in LL-BFR versus LL-RT
Yasuda et al[47] (2013)	RCO	8 men; age = 25 ± 2 y; physically active and not engaged in RT	Concentric; biceps brachii	iEMG during exercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 20% 1RM LL-RT: similar to LL-BFR	160 mm Hg; NR	Increased iEMG during LL-BFR versus LL-RT
Thiebaud et al[64] (2014)	RCO	9 men; age = 22.4 ± 3.2 y; not engaged in RT	Eccentric; biceps brachii and brachioradialis	RMS during exercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 30% 1RM LL-RT: similar to LL-BFR	35–120 mm Hg; 3.3 cm	LL-BFR did not increase RMS versus LL-RT
Yasuda et al[48] (2014)	RCO	9 men; age range = 23–41 y; engaged in RT	Concentric and eccentric; biceps brachii and triceps brachii	iEMG during exercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) with elastic resistance LL-RT: similar to LL-BFR	170–260 mm Hg; 3 cm	Increased iEMG during LL-BFR versus LL-RT
Fahs et al[60] (2015)	RWP	17 men and women; age range = 40–64 y; not engaged in RT	Concentric and eccentric; vastus lateralis	RMS during exercise (MVC)	LL-BFR: 2 sets to failure at 30% 1RM LL: similar to LL-BFR	50%–80% Arterial occlusion pressure; 5 cm	Increased RMS during LL-RT versus LL-BFR
Farup et al[61] (2015)	RWP	10 men and women; age = 25.5 ± 3 y; not engaged in RT	Concentric; biceps brachii	iEMG during exercise (EMGpeak)	LL-BFR: 4 sets to failure at 40% 1RM LL-RT: similar to LL-BFR	100 mm Hg; 8 cm	LL-BFR did not increase iEMG versus LL-RT
Loenneke et al[49] (2015)	RCO	40 men; age range = 18–35 y; physically active	Concentric and eccentric; vastus lateralis	RMS during exercise (MVC)	LL-BFR: 4 sets (30, 15, 15, 15 repetitions) at 20% or 30% 1RM LL-RT: 4 sets to failure at 20% or 30% 1RM HL-RT: 4 sets (10 repetitions/set) at 70% 1RM	40%, 50%, or 60% Arterial occlusion pressure; 5 cm	Increased RMS during HL-RT versus LL-RT and LL-BFR
Yasuda et al[50] (2015)	RCO	10 men; age = 27 ± 5 y; recreationally active	Concentric and eccentric; biceps brachii	iEMG during exercise (MVC)	LL-BFR: 4 sets to failure at 20% 1RM LL-RT: similar to LL-BFR	160 mm Hg; 3 cm	LL-BFR did not increase iEMG versus LL-RT
Cerqueira et al[71] (2017)	RCO	13 men; age = 21 ± 1.7 y; physically active or very active	Intermittent isometric; forearm flexors	EMGpeak and median frequency pre-exercise and postexercise (MVC)	LL-BFR: 1 set to failure at 45% MVC LL-RT: similar to LL-BFR	50% Arterial occlusion pressure; 14 cm	LL-BFR induced a greater increase in EMGpeak after failure versus LL-RT; no differences in median frequency
Jessee et al[54] (2018)	RCO	16 men; age range = 18–35 y; engaged in RT	Concentric and eccentric; triceps brachii	EMG amplitude during exercise (MVC)	LL-BFR: 4 sets to failure at 30% or 50% 1RM LL-RT: similar to LL-BFR	40% Arterial occlusion pressure; 5 cm	LL-BFR did not increase EMG amplitude versus LL-RT
Buckner et al[57] (2019)	RCO	20 men and women; age = 22 ± 2 y; engaged in RT	Concentric and eccentric; biceps brachii	EMG amplitude (MVC) during exercise	LL-BFR: 4 sets to failure at 15% 1RM LL-RT: similar to LL-BFR HL-RT: similar to LL-BFR at 70% 1RM	40% or 80% Arterial occlusion pressure; 5 cm	EMG amplitude was higher during HL-RT versus LL-BFR and LL-RT; increased EMG amplitude during LL-BFR versus LL-RT
Cerqueira et al[19] (2020)	RCO	12 men; age range = 19–25 y; physically active or very active	Intermittent isometric; forearm flexors	EMG amplitude and median frequency during exercise (first repetitions)	LL-BFR: 1 set to failure at 45% MVC LL-RT: similar to LL-BFR	50% Arterial occlusion pressure; 14 cm	LL-BFR did not increase EMG amplitude or reduce median frequency versus LL-RT

Table 1. Continued From Previous Page

Study	Design	Patient Characteristics and Training Status	Muscle Action Mode and Assessed Muscle	EMG Variables (Normalization Method)	Study Intervention: Exercise Measures[a]	BFR Pressure and Cuff Width[b]	Main Results
Long-term studies (lower limbs)							
Kubo et al[77] (2006)	RWP	9 men; age = 25 ± 2 y; NR	Concentric and eccentric; vastus lateralis, vastus medialis, and rectus femoris	iEMG (MVC) pretraining and posttraining	LL-BFR: 4 sets (25, 18, 15, 12 repetitions) at 20% 1RM (3 times/wk for 12 wk) HL-RT: 4 sets (10 repetitions/set) at 80% 1RM	Approximately 180–240 mm Hg; NR	No differences in iEMG between groups
Manimmanakorn et al[68] (2013)	RCT	20 females; age = 20.2 ± 3.3 y; netballers in preseason phase	Concentric; vastus lateralis and vastus medialis	RMS (MVC) pretraining and posttraining	LL-BFR: 4 sets to failure at 20% 1RM (3 times/wk for 5 wk) LL-RT: similar to LL-BFR	160–230 mm Hg; 5 cm	Increased RMS in LL-BFR versus LL-RT
Sousa et al[69] (2017)	RCT	29 men and women; age range = 18–30 y; untrained	Concentric and eccentric; vastus lateralis, vastus medialis, and rectus femoris	RMS and median frequency (MVC) pretraining and posttraining	LL-BFR: 4 sets to failure at 30% 1RM (2 times/wk for 6 wk) LL-RT: similar to LL-BFR HL-RT: similar to LL-BFR at 80% 1RM	80% Systolic blood pressure; 18 cm	No differences in RMS between groups; increased median frequency in HL-RT versus LL-BFR after 2 wk of training
Ramis et al[72] (2020)	RCT	28 men; age = 23.96 ± 2.67 y; physically active and not engaged in RT	Concentric; biceps brachii, rectus femoris, and vastus lateralis	RMS (MVC) pretraining and posttraining	LL-BFR: 4 sets of 21–23 repetitions at 30% 1RM (3 times/wk for 8 wk) HL-RT: 4 sets (8 repetitions/set) at 80% 1RM	20 mm Hg < Systolic blood pressure or 40 mm Hg > Arterial occlusion pressure; 14 or 16 cm	No differences in RMS between groups
Long-term studies (upper limbs)							
Moore et al[75] (2004)	RWP	8 men; age = 24.1 ± 3.5 y; not engaged in RT	Concentric and eccentric; biceps brachii	iEMG (NR) posttraining	LL-BFR: 3–5 sets to failure at 50% 1RM (3 times/wk for 8 wk) LL-RT: similar to LL-BFR	100 mm Hg; 7 cm	Increased iEMG in LL-BFR versus LL-RT
Neto et al[73] (2019)	RCT	17 men; age range = 18–36 y; engaged in RT	Concentric and eccentric; biceps brachii and triceps brachii	RMS (EMGpeak) pretraining and posttraining	LL-BFR: 4 sets (15 repetitions/set) at 20% 1RM (2 times/wk for 6 wk) LL-RT: similar to LL-BFR	80% Arterial occlusion pressure; 6 cm	No differences in RMS between groups

Abbreviations: BFR, blood-flow restriction; EMG, electromyography; EMGpeak, peak of the EMG signal; iEMG, integrated EMG; HL-RT, high-load resistance training with free blood flow; LL-BFR, low-load resistance training with blood flow restriction; LL-RT, low-load resistance training with free blood-flow; MPF, mean power frequency; MVC, maximal voluntary contraction; NR, not reported; RCO, randomized crossover; RCT, randomized clinical trial; RM, repetition maximum; RMS, root mean square; RT, resistance training; RWP, randomized within participants.

[a] Among EMG variables extracted at multiple points during exercise, only the latest time point was considered.

[b] Only for the LL-BFR group.

Table 2. **Risk of Bias Summary Showing Authors' Judgments About Each Risk of Bias Item for Each Included Study**

Authors (Year)	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	Group Similarity at Baseline
Barnes et al[55] (2018)	Low	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Buckner et al[57] (2019)	Unclear	Unclear	High	Unclear	High	Unclear	Unclear	Unclear
Cayot et al[51] (2016)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Cerqueira et al[71] (2017)	Low	Low	High	Low	High	Unclear	High	Low
Cerqueira et al[19] (2020)	Low	Low	High	Low	Unclear	Low	Unclear	Low
Cook et al[46] (2013)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Fahs et al[60] (2015)	Unclear	Unclear	High	Unclear	High	Unclear	Low	Unclear
Farup et al[61] (2015)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Fatela et al[53] (2018)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Low
Freitas et al[65] (2020)	Unclear	Unclear	High	Unclear	Unclear	Unclear	Low	Unclear
Hotta and Ito[76] (2011)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Husmann et al[52] (2018)	Unclear	Unclear	High	Unclear	Low	Unclear	High	Low
Ilett et al[16] (2019)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Low
Ishizaka et al[63] (2019)	Unclear	Unclear	High	Unclear	High	Unclear	High	Unclear
Jessee et al[54] (2018)	Unclear	Unclear	High	Unclear	High	Unclear	High	Unclear
Jessee et al[56] (2019)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Karabulut et al[70] (2006)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Karabulut et al[44] (2010)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Killinger et al[15] (2020)	Low	Unclear	High	Unclear	High	Unclear	Low	Unclear
Kinugasa et al[67] (2006)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Kjeldsen et al[62] (2019)	Unclear	Unclear	High	Unclear	Low	Unclear	High	Low
Kubo et al[77] (2006)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Low
Labarbera et al[59] (2013)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Lauver et al[66] (2017)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear
Loenneke et al[49] (2015)	Unclear	Unclear	High	Unclear	High	Unclear	High	Unclear
Manimmanakorn et al[68] (2013)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	High	Low
Moore et al[75] (2004)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Neto et al[73] (2019)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low
Ramis et al[72] (2020)	Unclear	Unclear	Unclear	Low	High	Unclear	Low	Low
Sousa et al[69] (2017)	Unclear	Unclear	Unclear	Unclear	High	Unclear	High	High
Thiebaud et al[64] (2014)	Unclear	Unclear	High	Unclear	Unclear	Unclear	Low	Unclear
Wernbom et al[18] (2009)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Wilson et al[45] (2013)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Low
Yasuda et al[58] (2006)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Yasuda et al[43] (2008)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Yasuda et al[74] (2009)	Unclear	Unclear	High	Unclear	Unclear	Unclear	Low	Low
Yasuda et al[47] (2013)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Yasuda et al[48] (2014)	Unclear	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
Yasuda et al[50] (2015)	Unclear	Unclear	High	Unclear	Unclear	Unclear	Low	Low

Study or Subgroup	LL-BFR Mean ± SD	LL-BFR Total	LL-RT Mean ± SD	LL-RT Total	Weight, %	Standardized Mean Difference, Inverse Variance, Random Effects, 95% CI	Standardized Mean Difference, Inverse Variance, Random Effects, 95% CI
Nonfailure							
Kinugasa et al[67] (2006)	48.51 ± 10.77	7	44.92 ± 18.94	7	4.6	0.22 (−0.83, 1.27)	
Yasuda et al[58] (2006)	65.61 ± 16.3	12	53.85 ± 13.58	12	6.1	0.76 (−0.08, 1.59)	
Yasuda et al[43] (2008)	1.91 ± 8.57	10	1.62 ± 0.34	10	5.8	0.05 (−0.83, 0.92)	
Karabulut et al[44] (2010)	88.37 ± 47.4218	14	80.13 ± 33.2371	14	6.9	0.20 (−0.55, 0.94)	
Wilson et al[45] (2013)	93.182 ± 6.818	12	84.848 ± 8.712	12	5.9	1.03 (0.17, 1.89)	
Yasuda et al[47] (2013)	2.45 ± 0.306	8	1.62 ± 0.156	8	2.4	3.23 (1.61, 4.85)	
Thiebaud et al[64] (2014)	2.195 ± 0.719	9	1.476 ± 0.331	9	4.7	1.22 (0.19, 2.25)	
Yasuda et al[48] (2014)	20.59 ± 8.79	9	19.06 ± 6.6	9	5.4	0.19 (−0.74, 1.11)	
Cayot et al[51] (2016)	29.53 ± 9.33	7	28.29 ± 8.08	7	4.6	0.13 (−0.92, 1.18)	
Lauver et al[66] (2017)	93.56 ± 34.92	8	64.07 ± 18.31	8	4.5	1.00 (−0.06, 2.06)	
Husmann et al[52] (2018)	185.48 ± 41.63	17	147.56 ± 32.3	17	7.2	0.99 (0.28, 1.71)	
Fatela et al[53] (2018)	87.2 ± 28.6	10	51.34 ± 19.07	10	4.9	1.41 (0.41, 2.42)	
Barnes et al[55] (2018)	0.1203 ± 0.0712	10	0.1551 ± 0.0981	10	5.7	−0.39 (−1.28, 0.50)	
Ilett et al[16] (2019)	36.456 ± 73.51	10	24.661 ± 30.848019	10	5.7	0.20 (−0.68, 1.08)	
Ishizaka et al[63] (2019)	25.2 ± 7.83836718	6	23.6 ± 7.83836718	6	4.1	0.19 (−0.95, 1.32)	
Kjeldsen et al[62] (2019)	155.04 ± 54.57	15	124.44 ± 35.71	17	7.2	0.66 (−0.06, 1.37)	
Freitas et al[65] (2020)	49.13 ± 14.35	14	42.21 ± 10.33	14	6.8	0.54 (−0.22, 1.29)	
Killinger et al[15] (2020)	45.7 ± 10	18	36.8 ± 11.3	18	7.6	0.82 (0.13, 1.50)	
Subtotal		196		198	100.0	0.61 (0.34, 0.88)	
Heterogeneity: $\tau^2 = 0.13$, $\chi^2_{17} = 28.07$, $P = .04$; $I^2 = 39\%$							
Test for overall effect: $Z = 4.41$, $P < .001$							
To failure							
Wernbom et al[18] (2009)	85 ± 24	11	93 ± 24	11	7.9	−0.32 (−1.16, 0.52)	
Cook et al[46] (2013)	65.882 ± 50.08	8	68.353 ± 46.587	8	5.8	−0.05 (−1.03, 0.93)	
Labarbera et al[59] (2013)	84.615 ± 40.133	20	75.321 ± 28.666	20	14.4	0.26 (−0.36, 0.88)	
Fahs et al[60] (2015)	55.33 ± 14.83	17	66.23 ± 18.18	17	11.7	−0.64 (−1.33, 0.05)	
Yasuda et al[50] (2015)	3.057 ± 1.353	10	3.617 ± 1.283	10	7.1	−0.41 (−1.29, 0.48)	
Farup et al[61] (2015)	49.34 ± 31.33	10	41.34 ± 26.9	10	7.2	0.26 (−0.62, 1.14)	
Jessee et al[54] (2018)	123 ± 60	9	100 ± 41	9	6.4	0.43 (−0.51, 1.36)	
Buckner et al[57] (2019)	54 ± 32	20	61 ± 22	20	14.4	−0.25 (−0.87, 0.37)	
Jessee et al[56] (2019)	76.8 ± 31.4	23	79 ± 22.9	23	16.7	−0.08 (−0.66, 0.50)	
Cerqueira et al[19] (2020)	64.9 ± 20.7	12	76.41 ± 22.22	12	8.4	−0.52 (−1.33, 0.30)	
Subtotal		140		140	100.0	−0.14 (−0.38, 0.10)	
Heterogeneity: $\tau^2 = 0.00$, $\chi^2_{9} = 7.36$, $P = .60$; $I^2 = 0\%$							
Test for overall effect: $Z = 1.17$, $P = .24$							

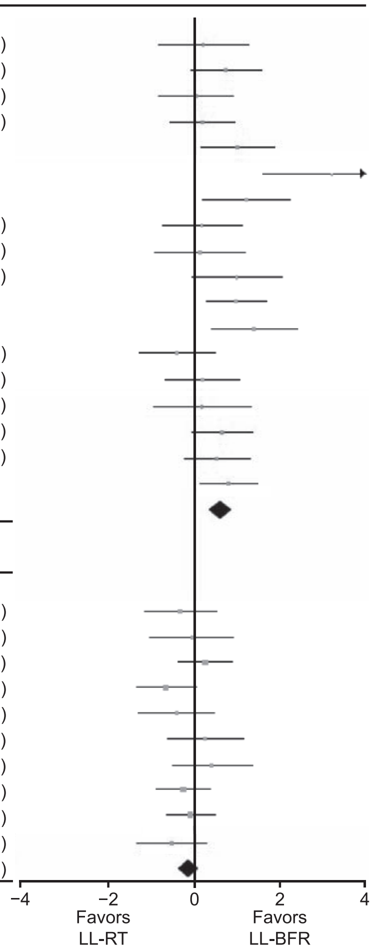

Figure 2. Forest plot illustrating the pooled short-term effects of low-load resistance training with blood-flow restriction (LL-BFR) versus low-load resistance training with free blood flow (LL-RT).

result (Figure 2). Regarding the frequency-domain values assessed during nonfailure protocols, in 2 studies[44,70] no differences in MPF were found, whereas in 2 studies, reduced CF[76] or MPF[74] was identified during LL-BFR compared with LL-RT. One study[19] was conducted using a failure protocol, and no differences in Fmed were observed between LL-BFR and LL-RT (Table 1).

Changes in muscle excitation pre-exercise and postexercise were evaluated in 9 studies. Among the studies conducted with nonfailure protocols, in 6 studies,[16,43,53,67,70,74] differences in muscle excitability were not observed, whereas in 1 study,[44] a reduced RMS post–LL-BFR compared with LL-RT was identified. One study[71] was conducted using a failure protocol, and a greater EMGpeak was observed post–LL-BFR compared with LL-RT. No postexercise differences were noted between LL-BFR and LL-RT regarding the frequency-domain measures, whether performed to failure[71] or not[44,53,70,74] (Table 1).

Comparison: LL-BFR and HL-RT. Based on 6 studies,[16,49,51,53,55,65] HL-RT had a large effect in increasing muscle excitability compared with LL-BFR during nonfailure protocols (SMD = –1.13; 95% CI = –1.94, –0.33; Z = 2.76; P = .006). Heterogeneity was considerably high for this meta-analysis (I^2 = 76%, $P < .001$). When a failure protocol was used (n = 3 studies[46,56,57]), HL-RT had a moderate effect on increasing muscle excitability compared with LL-BFR (SMD = –0.61; 95% CI = –1.01, –0.21; Z = 3.00; P = .003). The I^2 statistic of 0% (P = .98) represented very low heterogeneity (Figure 3). No authors evaluated frequency-domain values during LL-BFR compared with HL-RT.

In 2 studies[16,53] conducted using nonfailure protocols, no differences in muscle excitation post–LL-BFR compared with HL-RT were observed, and in 1 study,[53] no differences were seen in frequency-domain measures. We identified no studies that used a failure protocol and investigated either muscle excitability or the frequency-domain values post–LL-BFR compared with HL-RT (Table 1).

Long-Term Effects of LL-BFR on Myoelectric Activity

Comparison: LL-BFR and LL-RT. Based on 2 studies,[68,69] LL-BFR had a large effect in increasing muscle excitability compared with LL-RT during exercises (3–6 weeks) performed to failure (SMD = 1.09; 95% CI = 0.39, 1.79; Z = 3.07; P = .002). The I^2 statistic of 0% (P = .51)

Study or Subgroup	LL-BFR Mean ± SD	LL-BFR Total	HL-RT Mean ± SD	HL-RT Total	Weight, %	Standardized Mean Difference, Inverse Variance, Random Effects, 95% CI
Nonfailure						
Loenneke et al[49] (2015)	87 ± 27	14	97 ± 27	14	18.7	−0.36 (−1.11, 0.39)
Cayot et al[51] (2016)	48.8 ± 17.68	7	79.25 ± 17.91	7	14.4	−1.60 (−2.86, −0.34)
Barnes et al[55] (2018)	0.1203 ± 0.0712	10	0.1828 ± 0.1423	10	17.5	−0.53 (−1.43, 0.36)
Fatela et al[53] (2018)	87.2 ± 28.6	10	126.24 ± 42.67	10	17.0	−1.03 (−1.98, −0.08)
Ilett et al[16] (2019)	36.456 ± 73.50714	10	61.427 ± 41.34	10	17.5	−0.40 (−1.29, 0.49)
Freitas et al[65] (2020)	52.45 ± 15.09	14	111.84 ± 19.27	14	14.9	−3.33 (−4.53, −2.13)
Subtotal		65		65	100.0	−1.13 (−1.94, −0.33)
Heterogeneity: $\tau^2 = 0.76$, $\chi^2_5 = 20.94$, $P < .001$; $I^2 = 76\%$						
Test for overall effect: $Z = 2.76$, $P = .006$						
To failure						
Cook et al[46] (2013)	65.882 ± 50.08	8	95.941 ± 32.609	8	15.4	−0.67 (−1.69, 0.34)
Buckner et al[57] (2019)	54 ± 32	20	73 ± 27	20	39.2	−0.63 (−1.27, 0.01)
Jessee et al[56] (2019)	76.8 ± 31.4	23	104.7 ± 60.3	23	45.5	−0.57 (−1.16, 0.02)
Subtotal		51		51	100.0	−0.61 (−1.01, −0.21)
Heterogeneity: $\tau^2 = 0.00$, $\chi^2_2 = 0.04$, $P = .98$; $I^2 = 0\%$						
Test for overall effect: $Z = 3.00$, $P = .003$						

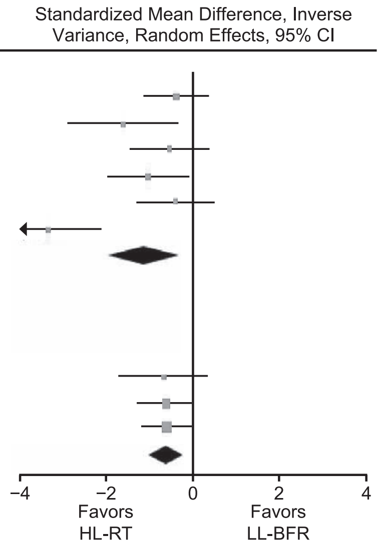

Figure 3. Forest plot illustrating the pooled short-term effects of low-load resistance training with blood-flow restriction (LL-BFR) versus high-load resistance training with free blood flow (HL-RT).

represented very low heterogeneity (Figure 4). Descriptively, in 1 study[75] using a failure protocol, high iEMG was demonstrated after 8 weeks of LL-BFR compared with LL-RT, and in 1 study[73] using a nonfailure protocol, similar RMS values occurred after 6 weeks of either LL-BFR or LL-RT training. In 1 study,[69] similar Fmed values were present after 6 weeks of LL-BFR or LL-RT performed to failure. No studies using nonfailure protocols and investigating long-term effects of LL-BFR compared with LL-RT on frequency-domain variables were identified (Table 1).

Comparison: LL-BFR and HL-RT. Given missing quantitative data, we compared LL-BFR and HL-RT via a descriptive and qualitative approach. Based on 3 studies, no differences in muscle excitability were observed after 6 to 12 weeks of LL-BFR or HL-RT performed to failure[69] or not.[72,77] In 1 study[69] conducted using a failure protocol, a higher Fmed in HL-RT than in LL-BFR was shown after 2 weeks of training. No studies conducted using a nonfailure protocol and investigating the long-term effects of LL-BFR compared with HL-RT on frequency domains were identified (Table 1).

DISCUSSION

In this systematic review, we aimed to examine the short- and long-term effects of LL-BFR on myoelectric activity and compare them with those of LL- and HL-RT. As previous researchers[18,19] found that exercising to failure might mediate the effects of LL-BFR and LL-RT on muscle excitability, we also intended to provide strong evidence regarding the true effects of fatiguing or nonfatiguing exercise protocols. Our findings indicated that LL-BFR acutely increased muscle excitability compared with LL-RT only during a nonfailure protocol, whereas muscle excitability was greater with HL-RT than LL-BFR during either a failure or nonfailure protocol. In addition, long-term LL-BFR may lead to higher muscle excitation compared with LL-RT. From a qualitative viewpoint, the studies were limited in number and had conflicting results; thus, the evidence is inconclusive about the short-term effects of LL-BFR versus LL- and HL-RT on muscle excitability pre-exercise and postexercise and the short- and long-term effects on EMG frequency-domain measures.

Study or Subgroup	LL-BFR Mean ± SD	LL-BFR Total	LL-RT Mean ± SD	LL-RT Total	Weight, %	Standardized Mean Difference, Inverse Variance, Random Effects, 95% CI
Nonfailure						
Manimmanakorn et al[68] (2013)	0.24 ± 0.13	10	0.1 ± 0.06	10	49.7	1.32 (0.34, 2.31)
Sousa et al[69] (2017)	1.23 ± 0.35	10	0.68 ± 0.83	8	50.3	0.86 (−0.12, 1.84)
Subtotal		20		18	100.0	1.09 (0.39, 1.79)
Heterogeneity: $\tau^2 = 0.00$, $\chi^2_1 = 0.42$, $P = .51$; $I^2 = 0\%$						
Test for overall effect: $Z = 3.07$, $P = .002$						

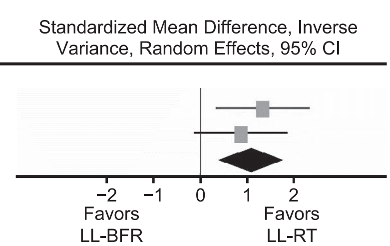

Figure 4. Forest plot illustrating the pooled long-term effects of low-load resistance training with blood-flow restriction (LL-BFR) versus low-load resistance training with free blood flow (LL-RT).

Short-Term Effects of LL-BFR on Myoelectric Activity

Comparison: LL-BFR and LL-RT. Our results demonstrated a higher level of muscle excitation favoring LL-BFR compared with LL-RT exercises using a matched number of repetitions but not when exercise was performed to failure. It has been hypothesized[7] that the hypoxic muscular environment generated during LL-BFR can cause high metabolic stress levels and activate mechanisms for muscle growth induction. One of the hypothetical mechanisms is the increased fast-twitch fiber recruitment,[14,75] because these fibers may be more susceptible to exercise-induced cross-sectional area gains compared with slow-twitch fibers.[78] Although limitations exist regarding the inference of fiber-type recruitment using surface EMG, researchers[37] using high-density EMG and decomposition techniques have shown that LL-BFR facilitates the early recruitment of higher-threshold motor units compared with LL-RT.

Indeed, LL-BFR produces greater muscle strength and growth than does LL-RT if applied with repetition-matched protocols[79]; however, this may be mitigated during exercises performed to volitional failure.[60,61] In this sense, and considering the reduced perceived exertion, discomfort, and soreness reported during a nonfailure protocol using LL-BFR,[80] our findings support prescribing a nonfailure protocol with LL-BFR as an effective approach to increase muscle excitability. The BFR can be useful in reducing the time to volitional failure during training performed to failure.[81] This can save time and minimize overload because of the large number of repetitions performed during LL-RT.[61]

Frequency-domain values are generally used as indirect markers of muscle fatigue.[19] Our qualitative analysis revealed that MPF and CF may or may not be reduced during nonfailure protocols using LL-BFR compared with LL-RT. This conflicting result may be due to methodologic differences, especially owing to the different muscles being studied. For example, frequency-domain measures may be reduced in the biceps brachii[74,76] but not in the vastus lateralis.[44,70] Differences in Fmed during LL-BFR compared with LL-RT were not observed in 1 study using a failure protocol,[19] suggesting similar fatigue in both conditions during submaximal (45% MVC) efforts performed to task failure.

No differences in muscle excitability postexercise with matched repetitions were found in most included studies, whereas greater muscle excitability was noted immediately after LL-BFR in 1 study[71] using a failure protocol. Furthermore, no differences were identified in frequency-domain values postexercise, regardless of muscle failure. To summarize, these results indicate similar muscle fatigue levels after LL-BFR and LL-RT.

Comparison: LL-BFR and HL-RT. Greater muscle excitability was observed during HL-RT compared with LL-BFR regardless of muscle failure, probably because higher loads demand greater motor-unit recruitment at exercise onset to produce higher force.[10] It has been suggested that muscle excitability during LL-BFR with loads of 40% to 50% of 1RM can reach levels comparable with those demonstrated during HL-RT, whereas it can be lower during LL-BFR with reduced loads (approximately 20% of 1RM).[12,53,75] In fact, most included studies (8 studies[16,46,49,51,53,55–57] of 9 studies[16,46,49,51,53,55–57,65]; Table 1) used loads between 15% and 30% of 1RM; thus, it remains unclear whether LL-BFR performed with loads of approximately 50% of MVC can result in muscle-excitation levels similar to those of HL-RT.

Given the previous knowledge regarding the indirect repercussions of high muscle-excitation levels on muscle-strength gains induced by resistance training,[12,13] our findings are in line with those of previous systematic reviews[1,7] in which researchers observed higher strength gains after HL-RT compared with LL-BFR. We did not locate any study comparing frequency-domain measures between LL-BFR and HL-RT. In this sense, it is unclear whether fatigue is different when these 2 conditions are performed or not performed to failure.

When the EMG signal was evaluated immediately postexercise, no differences were present in muscle excitation and frequency-domain values between LL-BFR and HL-RT performed with a matched number of repetitions, indicating similar fatigue levels. No studies evaluating muscle excitation and frequency-domain measures after LL-BFR and HL-RT performed to failure were identified.

Long-Term Effects of BFR on Myoelectric Activity

Comparison: LL-BFR and LL-RT. In a recent meta-analysis, Centner and Lauber[82] determined that long-term LL-BFR training increased muscle excitability compared with LL-RT. We built on existing evidence[19] that exercising to failure might be a potential influencing factor and examined subgroups of studies using failure and nonfailure protocols. Although studies using nonfailure protocols are scarce, our meta-analysis indicated that when LL-BFR was performed to failure, it increased muscle excitability compared with LL-RT. Long-term adaptations in muscle excitability also occurred after LL-BFR with a matched number of repetitions[75]; however, evidence is still scarce and contradictory. In terms of underlying mechanisms, researchers[8,62] have suggested that increased muscle excitability after long-term LL-BFR training may be due to increased motor-unit recruitment or firing frequency.

Comparison: LL-BFR and HL-RT. Long-term adaptation of muscle excitability did not differ between LL-BFR and HL-RT performed or not performed to failure. This is intriguing because HL-RT immediately induces higher muscle excitability than does LL-BFR. In this sense, similar results would also be expected after a long training period, but this notion was not confirmed. Further investigation is necessary to explore differences between the immediate responses and long-term adaptations to resistance training using BFR.

Regarding frequency-domain values, limited data suggested a greater Fmed after 2 weeks of HL-RT compared with LL-BFR performed to failure. In addition, no studies were conducted using a matched number of repetitions.

Limitations

Our study had several limitations. For example, proposing EMG variables as surrogate endpoints for both strength and hypertrophy may lead to misinterpretations because whether increased muscle excitability assessed using surface EMG predicts long-term adaptations is still unknown.[13,83] Also, we included studies that applied either individualized or arbitrary BFR pressures. This might have influenced the results because high occlusion pressures may be related to greater muscle activation.[49] Moreover, most of the included studies had a high or moderate risk of bias, and I^2 was very high in the comparison of LL-BFR versus HL-RT not performed to failure. This high risk of bias might partly have reflected the fact that participant blinding is often impossible in this research field. Given the high heterogeneity of studies and exercise protocols, further research is needed to allow better comparisons among studies and draw more solid conclusions. Finally, as several populations were mixed, future authors should address differences in muscle excitability between specific populations (eg, younger versus older populations, healthy versus patient populations). Therefore, our results must be interpreted while taking this context into account.

Clinical Implications

The topic of this present systematic review and meta-analysis is of high importance for sport practitioners and rehabilitation settings. Especially in orthopaedic rehabilitation, arthrogenic muscle inhibition and neural-drive alterations are frequent phenomena after anterior cruciate ligament reconstruction[84] and chronic ankle instability.[85] Hence, investigating potential rehabilitation and training strategies is vitally relevant. Although blood-flow restriction training has been shown to be effective in musculoskeletal rehabilitation,[5,86] data regarding underlying mechanisms are scarce. Here, we demonstrated that adding BFR to low-load exercise regimens increased EMG amplitudes during nonfailure protocols. However, HL-RT regimens seemed to be superior to LL-BFR. Enhancements in neural drive and muscle excitability might be beneficial for sports in which ballistic and reactive contractions are necessary and for populations with an increased risk of falling to improve postural control.[87]

CONCLUSIONS

Our results provide evidence of greater muscle excitability during acute LL-BFR compared with LL-RT using nonfailure protocols. Muscle excitability appeared to be greater during HL-RT than during LL-BFR, regardless of muscle failure. Given the scarce and conflicting evidence regarding long-term adaptations, future longitudinal studies should be done to consider volitional failure as a prescription variable that interferes directly with myoelectric activation and indirectly with strength and muscle-mass gains after LL-BFR training.

ACKNOWLEDGMENTS

Mikhail Santos Cerqueira, MSc, PT, and Daniel Germano Maciel, MSc, PT, thank Coordination for the Improvement of High Level (CAPES, Brazil), finance code 001, for the scholarship concession.

REFERENCES

1. Centner C, Wiegel P, Gollhofer A, König D. Effects of blood flow restriction training on muscular strength and hypertrophy in older individuals: a systematic review and meta-analysis. *Sports Med*. 2019;49(1):95–108. doi:10.1007/s40279-018-0994-1
2. Grnfeldt BM, Lindberg Nielsen J, Mieritz RM, Lund H, Aagaard P. Effect of blood-flow restricted versus heavy-load strength training on muscle strength: systematic review and meta-analysis. *Scand J Med Sci Sports*. 2020;30(5):837–848. doi:10.1111/sms.13632
3. Patterson SD, Hughes L, Warmington S, et al. Blood flow restriction exercise: considerations of methodology, application, and safety. *Front Physiol*. 2019;10:533. doi:10.3389/fphys.2019.00533
4. Cerqueira MS, de Brito Vieira WH. Effects of blood flow restriction exercise with very low load and low volume in patients with knee osteoarthritis: protocol for a randomized trial. *Trials*. 2019;20(1):135. doi:10.1186/s13063-019-3238-2
5. Hughes L, Rosenblatt B, Haddad F, et al. Comparing the effectiveness of blood flow restriction and traditional heavy load resistance training in the post-surgery rehabilitation of anterior cruciate ligament reconstruction patients: a UK National Health Service randomised controlled trial. *Sports Med*. 2019;49(11):1787–1805. doi:10.1007/s40279-019-01137-2
6. Scott BR, Loenneke JP, Slattery KM, Dascombe BJ. Blood flow restricted exercise for athletes: a review of available evidence. *J Sci Med Sport*. 2016;19(5):360–367. doi:10.1016/j.jsams.2015.04.014
7. Hughes L, Paton B, Rosenblatt B, Gissane C, Patterson SD. Blood flow restriction training in clinical musculoskeletal rehabilitation: a systematic review and meta-analysis. *Br J Sports Med*. 2017;51(13):1003–1011. doi:10.1136/bjsports-2016-097071
8. De Castro FMP, Aquino R, Berti JA II, Gonçalves LGC, Puggina EF. Strength training with vascular occlusion: a review of possible adaptive mechanisms. *Hum Mov*. 2017;18(2):3–14. doi:10.1515/humo-2017-0010
9. Takada S, Okita K, Suga T, et al. Low-intensity exercise can increase muscle mass and strength proportionally to enhanced metabolic stress under ischemic conditions. *J Appl Physiol (1985)*. 2012;113(2):199–205. doi:10.1152/japplphysiol.00149.2012
10. Dankel SJ, Mattocks KT, Jessee MB, Buckner SL, Mouser JG, Loenneke JP. Do metabolites that are produced during resistance exercise enhance muscle hypertrophy? *Eur J Appl Physiol*. 2017;117(11):2125–2135. doi:10.1007/s00421-017-3690-1
11. Centner C, Ritzmann R, Schur S, Gollhofer A, König D. Blood flow restriction increases myoelectric activity and metabolic accumulation during whole-body vibration. *Eur J Appl Physiol*. 2019;119(6):1439–1449. doi:10.1007/s00421-019-04134-5
12. Wernbom M, Aagaard P. Muscle fibre activation and fatigue with low-load blood flow restricted resistance exercise—an integrative physiology review. *Acta Physiol (Oxf)*. 2020;228(1):e13302. doi:10.1111/apha.13302
13. Vigotsky AD, Halperin I, Lehman GJ, Trajano GS, Vieira TM. Interpreting signal amplitudes in surface electromyography studies in sport and rehabilitation sciences. *Front Physiol*. 2018;8:985. doi:10.3389/fphys.2017.00985
14. Pearson SJ, Hussain SR. A review on the mechanisms of blood-flow restriction resistance training-induced muscle hypertrophy. *Sports Med*. 2015;45(2):187–200. doi:10.1007/s40279-014-0264-9
15. Killinger B, Lauver JD, Donovan L, Goetschius J. The effects of blood flow restriction on muscle activation and hypoxia in individuals with chronic ankle instability. *J Sport Rehabil*. 2020;29(5):633–639. doi:10.1123/jsr.2018-0416
16. Ilett MJ, Rantalainen T, Keske MA, May AK, Warmington SA. The effects of restriction pressures on the acute responses to blood flow restriction exercise. *Front Physiol*. 2019;10:1018. doi:10.3389/fphys.2019.01018
17. Scott BR, Slattery KM, Sculley DV, Dascombe BJ. Hypoxia and resistance exercise: a comparison of localized and systemic methods. *Sports Med*. 2014;44(8):1037–1054. doi:10.3389/fphys.2019.01018
18. Wernbom M, Järrebring R, Andreasson MA, Augustsson J. Acute effects of blood flow restriction on muscle activity and endurance

during fatiguing dynamic knee extensions at low load. *J Strength Cond Res*. 2009;23(8):2389–2395. doi:10.1519/JSC.0b013e3181bc1c2a
19. Cerqueira MS, Pereira R, Nunes de Mesquita G, Rocha T, Galvao de Moura Filho A. Influence of blood flow restriction level on muscle fatigue during an intermittent isometric exercise taken to failure. *Muscles Ligaments Tendons J*. 2020;10(3):408–415. doi:10.32098/mltj.03.2020.08
20. Manini TM, Clark BC. Blood flow restricted exercise and skeletal muscle health. *Exerc Sport Sci Rev*. 2009;37(2):78–85. doi:10.1097/JES.0b013e31819c2e5c
21. Morton RW, Sonne MW, Farias Zuniga A, et al. Muscle fibre activation is unaffected by load and repetition duration when resistance exercise is performed to task failure. *J Physiol*. 2019;597(17):4601–4613. doi:10.1113/JP278056
22. Muller K. Statistical power analysis for the behavioral sciences. *Technometrics*. 1989;31(4):499–500.
23. Sullivan GM, Feinn R. Using effect size—or why the *P* value is not enough. *J Grad Med Educ*. 2012;4(3):279–282. doi:10.4300/JGME-D-12-00156.1
24. Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0. The Cochrane Collaboration. Updated 2011. Accessed June 16, 2019. https://training.cochrane.org/handbook/archive/v5.1/
25. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. *Introduction to Meta-Analysis*. John Wiley & Sons; 2009.
26. Hagger MS. Meta-analysis in sport and exercise research: review, recent developments, and recommendations. *Eur J Sport Sci*. 2006;6(2):103–115. doi:10.1080/17461390500528527
27. Tennent DJ, Hylden CM, Johnson AE, Burns TC, Wilken JM, Owens JG. Blood flow restriction training after knee arthroscopy. *Clin J Sport Med*. 2017;27(3):245–252. doi:10.1097/JSM.0000000000000377
28. Pope ZK, Willardson JM, Schoenfeld BJ, Emmett JD, Owen JD. Hypertrophic and strength responses to eccentric resistance training with blood flow restriction: a pilot study. *Int J Sports Sci Coaching*. 2015;10(5):919–931. doi:10.1260/1747-9541.10.5.919
29. Silva J, Neto GR, Freitas E, et al. Chronic effect of strength training with blood flow restriction on muscular strength among women with osteoporosis. *J Exerc Physiol*. 2015;18(4):33–41.
30. Barros NA, Aidar FJ, de Matos DG, et al. Comparison of traditional strength training and Kaatsu strength training on thermal asymmetry, fatigue rate, and peak torque. *J Exerc Physiol*. 2017;20(1):1–12.
31. Rodrigues Neto G, da Silva JCG, Freitas L, et al. Effects of strength training with continuous or intermittent blood flow restriction on the hypertrophy, muscular strength and endurance of men. *Acta Sci Health Sci*. 2019;41(1):42273. doi:10.4025/actascihealthsci.v41i1.42273
32. Thiebaud RS, Yasuda T, Loenneke JP, Abe T. Effects of low-intensity concentric and eccentric exercise combined with blood flow restriction on indices of exercise-induced muscle damage. *Interv Med Appl Sci*. 2013;5(2):53–59. doi:10.1556/IMAS.5.2013.2.1
33. Karabulut M, Perez G. Neuromuscular response to varying pressures created by tightness of restriction cuff. *J Electromyogr Kinesiol*. 2013;23(6):1494–1498. doi:10.1016/j.jelekin.2013.07.010
34. Dankel SJ, Buckner SL, Jessee MB, et al. Can blood flow restriction augment muscle activation during high-load training? *Clin Physiol Funct Imaging*. 2018;38(2):291–295. doi:10.1111/cpf.12414
35. Amani-Shalamzari S, Farhani F, Rajabi H, et al. Blood flow restriction during futsal training increases muscle activation and strength. *Front Physiol*. 2019;10:614. doi:10.3389/fphys.2019.00614
36. Mahoney SJ, Dicks ND, Lyman KJ, Christensen BK, Hackney KJ. Acute cardiovascular, metabolic, and muscular responses to blood flow restricted rowing exercise. *Aerosp Med Hum Perform*. 2019;90(5):440–446. doi:10.3357/AMHP.5258.2019
37. Fatela P, Mendonca GV, Veloso AP, Avela J, Mil-Homens P. Blood flow restriction alters motor unit behavior during resistance exercise. *Int J Sports Med*. 2019;40(9):555–562. doi:10.1055/a-0888-8816
38. Biazon TMPC, Ugrinowitsch C, Soligon SD, et al. The association between muscle deoxygenation and muscle hypertrophy to blood flow restricted training performed at high and low loads. *Front Physiol*. 2019;10:446. doi:10.3389/fphys.2019.00446
39. Jessee MB, Mattocks KT, Buckner SL, et al. The acute muscular response to blood flow-restricted exercise with very low relative pressure. *Clin Physiol Funct Imaging*. 2018;38(2):304–311. doi:10.1111/cpf.12416
40. Hill EC, Housh TJ, Keller JL, et al. Low-load blood flow restriction elicits greater concentric strength than non-blood flow restriction resistance training but similar isometric strength and muscle size. *Eur J Appl Physiol*. 2020;120(2):425–441. doi:10.1007/s00421-019-04287-3
41. Yasuda T, Ogasawara R, Sakamaki M, Ozaki H, Sato Y, Abe T. Combined effects of low-intensity blood flow restriction training and high-intensity resistance training on muscle strength and size. *Eur J Appl Physiol*. 2011;111(10):2525–2533. doi:10.1007/s00421-011-1873-8
42. Copithorne DB, Rice CL. The effect of blood flow occlusion during acute low-intensity isometric elbow flexion exercise. *Eur J Appl Physiol*. 2019;119(3):587–595. doi:10.1007/s00421-019-04088-8
43. Yasuda T, Brechue WF, Fujita T, Sato Y, Abe T. Muscle activation during low-intensity muscle contractions with varying levels of external limb compression. *J Sports Sci Med*. 2008;7(4):467–474.
44. Karabulut M, Cramer JT, Abe T, Sato Y, Bemben MG. Neuromuscular fatigue following low-intensity dynamic exercise with externally applied vascular restriction. *J Electromyogr Kinesiol*. 2010;20(3):440–447. doi:10.1016/j.jelekin.2009.06.005
45. Wilson JM, Lowery RP, Joy JM, Loenneke JP, Naimo MA. Practical blood flow restriction training increases acute determinants of hypertrophy without increasing indices of muscle damage. *J Strength Cond Res*. 2013;27(11):3068–3075. doi:10.1519/JSC.0b013e31828a1ffa
46. Cook SB, Murphy BG, Labarbera KE. Neuromuscular function after a bout of low-load blood flow-restricted exercise. *Med Sci Sports Exerc*. 2013;45(1):67–74. doi:10.1249/MSS.0b013e31826c6fa8
47. Yasuda T, Loenneke J, Ogasawara R, Abe T. Influence of continuous or intermittent blood flow restriction on muscle activation during low-intensity multiple sets of resistance exercise. *Acta Physiol Hung*. 2013;100(4):419–426. doi:10.1556/APhysiol.100.2013.4.6
48. Yasuda T, Fukumura K, Fukuda T, et al. Effects of low-intensity, elastic band resistance exercise combined with blood flow restriction on muscle activation. *Scand J Med Sci Sports*. 2014;24(1):55–61. doi:10.1111/j.1600-0838.2012.01489.x
49. Loenneke JP, Kim D, Fahs CA, et al. Effects of exercise with and without different degrees of blood flow restriction on torque and muscle activation. *Muscle Nerve*. 2015;51(5):713–721. doi:10.1002/mus.24448
50. Yasuda T, Fukumura K, Iida H, Nakajima T. Effect of low-load resistance exercise with and without blood flow restriction to volitional fatigue on muscle swelling. *Eur J Appl Physiol*. 2015;115(5):919–926. doi:10.1007/s00421-014-3073-9
51. Cayot TE, Lauver JD, Silette CR, Scheuermann BW. Effects of blood flow restriction duration on muscle activation and microvascular oxygenation during low-volume isometric exercise. *Clin Physiol Funct Imaging*. 2016;36(4):298–305. doi:10.1111/cpf.12228
52. Husmann F, Mittlmeier T, Bruhn S, Zschorlich V, Behrens M. Impact of blood flow restriction exercise on muscle fatigue development and recovery. *Med Sci Sports Exerc*. 2018;50(3):436–446. doi:10.1249/MSS.0000000000001475
53. Fatela P, Reis JF, Mendonca GV, et al. Acute neuromuscular adaptations in response to low-intensity blood-flow restricted

exercise and high-intensity resistance exercise. *J Strength Cond Res*. 2018;32(4):902–910. doi:10.1519/JSC.0000000000002022
54. Jessee MB, Mouser JG, Buckner SL, et al. Effects of load on the acute response of muscles proximal and distal to blood flow restriction. *J Physiol Sci*. 2018;68(6):769–779. doi:10.1007/s12576-018-0593-9
55. Barnes MJ, Fraser J, Coley K, Perry BG. Is postexercise blood flow restriction a viable alternative to other resistance exercise protocols? *Res Q Exerc Sport*. 2018;89(4):504–510. doi:10.1080/02701367.2018.1510170
56. Jessee MB, Buckner SL, Mattocks KT, et al. Blood flow restriction augments the skeletal muscle response during very low-load resistance exercise to volitional failure. *Physiol Int*. 2019;106(2):180–193. doi:10.1556/2060.106.2019.15
57. Buckner SL, Jessee MB, Dankel SJ, et al. Acute skeletal muscle responses to very low-load resistance exercise with and without the application of blood flow restriction in the upper body. *Clin Physiol Funct Imaging*. 2019;39(3):201–208. doi:10.1111/cpf.12557
58. Yasuda T, Fujita T, Miyagi Y, et al. Electromyographic responses of arm and chest muscle during bench press exercise with and without KAATSU. *Int J KAATSU Train Res*. 2006;2(1):15–18. doi:10.3806/ijktr.2.15
59. Labarbera KE, Murphy BG, Laroche DP, Cook SB. Sex differences in blood flow restricted isotonic knee extensions to fatigue. *J Sports Med Phys Fitness*. 2013;53(4):444–452.
60. Fahs CA, Loenneke JP, Thiebaud RS, et al. Muscular adaptations to fatiguing exercise with and without blood flow restriction. *Clin Physiol Funct Imaging*. 2015;35(3):167–176. doi:10.1111/cpf.12141
61. Farup J, de Paoli F, Bjerg K, Riis S, Ringgard S, Vissing K. Blood flow restricted and traditional resistance training performed to fatigue produce equal muscle hypertrophy. *Scand J Med Sci Sports*. 2015;25(6):754–763. doi:10.1111/sms.12396
62. Kjeldsen SS, Næss-Schmidt ET, Hansen GM, Nielsen JF, Stubbs PW. Neuromuscular effects of dorsiflexor training with and without blood flow restriction. *Heliyon*. 2019;5(8):e02341. doi:10.1016/j.heliyon.2019.e02341
63. Ishizaka H, Uematsu A, Mizushima Y, et al. Blood flow restriction increases the neural activation of the knee extensors during very low-intensity leg extension exercise in cardiovascular patients: a pilot study. *J Clin Med*. 2019;8(8):1252. doi:10.3390/jcm8081252
64. Thiebaud RS, Loenneke JP, Fahs CA, et al. Muscle damage after low-intensity eccentric contractions with blood flow restriction. *Acta Physiol Hung*. 2014;101(2):150–157. doi:10.1556/APhysiol.101.2014.2.3
65. Freitas EDS, Miller RM, Heishman AD, Ferreira-Júnior JB, Araújo JP, Bemben MG. Acute physiological responses to resistance exercise with continuous versus intermittent blood flow restriction: a randomized controlled trial. *Front Physiol*. 2020; 17(11):132. doi:10.3389/fphys.2020.00132
66. Lauver JD, Cayot TE, Rotarius T, Scheuermann BW. The effect of eccentric exercise with blood flow restriction on neuromuscular activation, microvascular oxygenation, and the repeated bout effect. *Eur J Appl Physiol*. 2017;117(5):1005–1015. doi:10.1007/s00421-017-3589-x
67. Kinugasa R, Watanabe T, Ijima H, et al. Effects of vascular occlusion on maximal force, exercise-induced T2 changes, and EMG activities of quadriceps femoris muscles. *Int J Sports Med*. 2006;27(7):511–516. doi:10.1055/s-2005-865780
68. Manimmanakorn A, Manimmanakorn N, Taylor R, et al. Effects of resistance training combined with vascular occlusion or hypoxia on neuromuscular function in athletes. *Eur J Appl Physiol*. 2013;113(7):1767–1774. doi:10.1007/s00421-013-2605-z
69. Sousa J, Neto GR, Santos HH, Araújo JP, Silva HG, Cirilo-Sousa MS. Effects of strength training with blood flow restriction on torque, muscle activation and local muscular endurance in healthy subjects. *Biol Sport*. 2017;34(1):83–90. doi:10.5114/biolsport.2017.63738
70. Karabulut M, Cramer JT, Ryan ED, et al. Effects of KAATSU on muscular function during isometric exercise. *Int J KAATSU Train Res*. 2006;2(2):19–28. doi:10.3806/ijktr.2.19
71. Cerqueira MS, Pereira R, Rocha T, et al. Time to failure and neuromuscular response to intermittent isometric exercise at different levels of vascular occlusion: a randomized crossover study. *Int J Applied Exerc Physiol*. 2017;6(1):55–70. doi:10.22631/ijaep.v6i1.108
72. Ramis TR, Muller CHL, Boeno FP, et al. Effects of traditional and vascular restricted strength training program with equalized volume on isometric and dynamic strength, muscle thickness, electromyographic activity, and endothelial function adaptations in young adults. *J Strength Cond Res*. 2020;34(3):689–698. doi:10.1519/JSC.0000000000002717
73. Neto GR, Santos HH, Neto EAP, et al. Are there differences in the activation of the agonist and antagonist muscles during strength training sessions with continuous or intermittent blood flow restriction? *Rev Bras Ciênc Mov*. 2019;27(3):139–149. doi:10.31501/rbcm.v27i3.9877
74. Yasuda T, Brechue WF, Fujita T, Shirakawa J, Sato Y, Abe T. Muscle activation during low-intensity muscle contractions with restricted blood flow. *J Sports Sci*. 2009;27(5):479–489. doi:10.1080/02640410802626567
75. Moore DR, Burgomaster KA, Schofield LM, Gibala MJ, Sale DG, Phillips SM. Neuromuscular adaptations in human muscle following low intensity resistance training with vascular occlusion. *Eur J Appl Physiol*. 2004;92(4–5):399–406. doi:10.1007/s00421-004-1072-y
76. Hotta Y, Ito K. EMG-based detection of muscle fatigue during low-level isometric contraction: effects of electrode configuration and blood flow restriction. *Annu Int Conf IEEE Eng Med Biol Soc*. 2011;2011:3877–3879. doi:10.1109/IEMBS.2011.6090963
77. Kubo K, Komuro T, Ishiguro N, et al. Effects of low-load resistance training with vascular occlusion on the mechanical properties of muscle and tendon. *J Appl Biomech*. 2006;22(2):112–119. doi:10.1123/jab.22.2.112
78. Suetta C, Andersen JL, Dalgas U, et al. Resistance training induces qualitative changes in muscle morphology, muscle architecture, and muscle function in elderly postoperative patients. *J Appl Physiol (1985)*. 2008;105(1):180–186. doi:10.1152/japplphysiol.01354.2007
79. Laurentino GC, Ugrinowitsch C, Roschel H, et al. Strength training with blood flow restriction diminishes myostatin gene expression. *Med Sci Sports Exerc*. 2012;44(3):406–412. doi:10.1249/MSS.0b013e318233b4bc
80. Sieljacks P, Degn R, Hollaender K, Wernbom M, Vissing K. Non-failure blood flow restricted exercise induces similar muscle adaptations and less discomfort than failure protocols. *Scand J Med Sci Sports*. 2019;29(3):336–347. doi:10.1111/sms.13346
81. Cerqueira MS, Pereira R, Mesquita GN, Rocha T, Moura Filho AG. Rate of force development to evaluate the neuromuscular fatigue and recovery after an intermittent isometric handgrip task with different blood flow restriction conditions. *Motriz Rev Educ Fís*. 2019;25(1):1–6. doi:10.1590/S1980-6574201900010009
82. Centner C, Lauber B. A systematic review and meta-analysis on neural adaptations following blood flow restriction training: what we know and what we don't know. *Front Physiol*. 2020;11:887. doi:10.3389/fphys.2020.00887
83. Halperin I, Vigotsky AD, Foster C, Pyne DB. Strengthening the practice of exercise and sport-science research. *Int J Sports Physiol Perform*. 2018;13(2):127–134. doi:10.1123/ijspp.2017-0322
84. Pietrosimone BG, Lepley AS, Ericksen HM, Clements A, Sohn DH, Gribble PA. Neural excitability alterations after anterior cruciate ligament reconstruction. *J Athl Train*. 2015;50(6):665–674. doi:10.4085/1062-6050-50.1.11

85. McLeod MM, Gribble PA, Pietrosimone BG. Chronic ankle instability and neural excitability of the lower extremity. *J Athl Train*. 2015;50(8):847–853. doi:10.4085/1062-6050-50.4.06
86. Centner C, Mauch M, Paul J, Ritzmann R. Evidence-based effects of blood flow restriction training in the rehabilitation of knee osteoarthritis and anterior cruciate ligament reconstruction: a systematic review. *Sports Orthop Traumatol*. 2020;36(2):131–142. doi:10.1016/j.orthtr.2020.04.009
87. Aagaard P, Simonsen EB, Andersen JL, Magnusson P, Dyhre-Poulsen P. Increased rate of force development and neural drive of human skeletal muscle following resistance training. *J Appl Physiol (1985)*. 2002;93(4):1318–1326. doi:10.1152/japplphysiol.00283.2002

Address correspondence to Wouber Hérickson De Brito Vieira, PhD, PT, Neuromuscular Performance Analysis Laboratory, Department of Physical Therapy, Federal University of Rio Grande do Norte (UFRN), Natal, RN, Brazil Av Senador Salgado Filho, 3000 - Campus Universitário, Lagoa Nova, Natal, Rio Grande do Norte 59072-970, Brazil. Address email to hericksonfisio@yahoo.com.br.