

# Blood Flow Restriction Does Not Promote Additional Effects on Muscle Adaptations When Combined With High-Load Resistance Training Regardless of Blood Flow Restriction Protocol

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## Abstract

Teixeira, EL, Ugrinowitsch, C, de Salles Painelli, V, Silva-Batista, C, Aihara, AY, Cardoso, FN, Roschel, H, and Tricoli, V. Blood flow restriction does not promote additional effects on muscle adaptations when combined with high-load resistance training regardless of blood flow restriction protocol. *J Strength Cond Res* 35(5): 1194–1200, 2021—The aim of this study was to investigate, during high-load resistance training (HL-RT), the effect of blood flow restriction (BFR) applied during rest intervals (BFR-I) and muscle contractions (BFR-C) compared with HL-RT alone (no BFR), on maximum voluntary isometric contraction (MVIC), maximum dynamic strength (one repetition maximum [1RM]), quadriceps cross-sectional area (QCSA), blood lactate concentration ([La]), and root mean square of the surface electromyography (RMS-EMG) responses. Forty-nine healthy and untrained men ( $25 \pm 6.2$  years,  $178.1 \pm 5.3$  cm and  $78.8 \pm 11.6$  kg) trained twice per week, for 8 weeks. One leg of each subject performed HL-RT without BFR (HL-RT), whereas the contralateral leg was randomly allocated to 1 of 2 unilateral knee extension protocols: BFR-I or BFR-C (for all protocols,  $3 \times 8$  repetitions, 70% 1RM). Maximum voluntary isometric contraction, 1RM, QCSA, and acute changes in [La] and RMS-EMG were assessed before and after training. The measurement of [La] and RMS-EMG was performed during the control sessions with the same relative load obtained after the 1RM test, before and after training. Similar increases in MVIC, 1RM, and QCSA were demonstrated among all conditions, with no significant difference between them. [La] increased for all protocols in pre-training and post-training, but it was higher for BFR-I compared with the remaining protocols. Increases in RMS-EMG occurred for all protocols in pre-training and post-training, with no significant difference between them. In conclusion, despite of a greater metabolic stress, BFR inclusion to HL-RT during rest intervals or muscle contraction did not promote any additive effect on muscle strength and hypertrophy.

**Key Words:** low load, metabolites, muscle mass, strength

## Introduction

Resistance training (RT) has been commonly implemented in the routine of numerous populations such as the elderly and athletes, as well as exercise enthusiasts to promote muscle strength and mass accrual (23,32,33). Resistance training is traditionally prescribed using high loads (HLs) (i.e.,  $\geq 70\%$  one repetition maximum [1RM]), which may not be feasible/tolerable for clinical populations or for healthy individuals who might have their adherence/preference to RT programs negatively affected because of higher training intensities. As such, low-load resistance training (i.e.,  $\sim 20$ – $40\%$  1RM) associated with blood flow restriction (BFR) (LL-BFR) has been used as an alternative training method to high-load resistance training (HL-RT) because significant increases in muscle strength and mass also occur with LL-BFR, with the latter being observed at similar magnitudes than that of HL-RT (10,15,19–21,25).

Among the different mechanisms underpinning the benefits of HL-RT and LL-BFR, it seems consensual that LL-BFR-induced

elevated metabolic stress may trigger increased recruitment of fast-twitch muscle fibers (34–36), favoring both muscle strength (39) and mass (31), whereas it has been widely accepted that HL-RT-induced benefits occur through increased mechanical stress (26,27,31). Based on these concepts, some studies have combined BFR with HL-RT as an attempt of a potential additive effect from both training strategies (1,6,7,18,24); however, results are equivocal, and conclusions are limited by significant methodological differences.

The major limitation is related to the heterogeneity between training protocols. Although some studies have applied BFR during muscle contractions and removed it during rest intervals (1,6,18), others have introduced it only at the end of the exercise session (7,24). It is known that high-load muscle contractions may induce partial BFR “per se” (9,28) and the removal of BFR during intervals may allow the clearance of intramuscular metabolites (36). In addition, BFR applied only after exercise does not augment muscle activation (7), and it has been suggested that metabolites alone do not have anabolic properties in the absence of mechanical stress (8,38). In light of the controversial results, Teixeira et al. (37) recently compared the acute effects of

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combining HL-RT with BFR during exercise alone or during rest intervals alone. Although similar decreases in muscle activation (i.e., electromyographic amplitude) were observed across conditions, the latter was demonstrated to result in higher metabolic stress (i.e., blood lactate concentration [La]), which could potentially support RT-related adaptations (26,27). However, the findings from Teixeira et al. (37) were only acutely examined. Because acute responses to RT are not necessarily translated into chronic changes (30,40), it remains unknown whether increasing metabolic stress by applying BFR in protocols of high mechanical stress would potentially reflect in additional chronic muscle adaptations.

Therefore, the aim of this study was to investigate the effects of 8 weeks of HL-RT combined with BFR during rest intervals (BFR-I) or during muscle contractions (BFR-C) and compare them to those of conventional HL-RT on muscle strength and mass. In addition, a secondary aim was to investigate the acute effects of these protocols on markers of metabolic stress and muscle activation pre-training and post-training. Our hypothesis was that, although the application of BFR during rest intervals (BFR-I) could result in a greater metabolic stress, BFR would not produce any additive effect on muscle adaptations when mechanical tension is already high, such as for BFR-I and BFR-C protocols.

## Methods

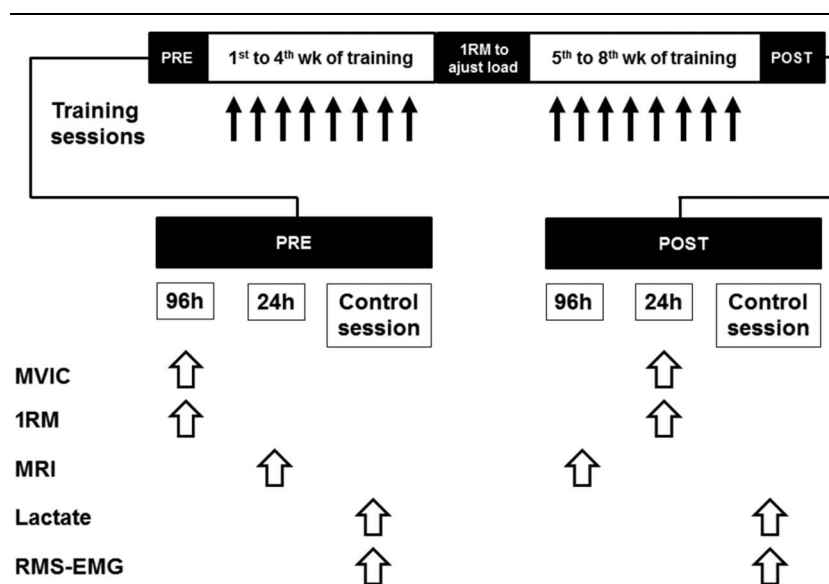
### Experimental Approach to the Problem

Before the experimental protocol (PRE), lower-body arterial occlusion pressure was measured. After that, all subjects were submitted to familiarization sessions to the maximum voluntary isometric contraction (MVIC) and dynamic (1RM) strength tests (in that order), every 72 hours, until variations in scores were  $\leq 5\%$ . Muscle strength values for all subjects were obtained within  $\leq 4$  visits. At least 72 hours after the last MVIC

and 1RM tests, quadriceps cross-sectional area (QCSA) was obtained through magnetic resonance imaging (MRI). After MRI, subjects completed 8 weeks of unilateral knee extension RT, twice a week, using HLs (70% 1RM) for all protocols. The HL-RT protocol was defined as a “positive” control; thus, one leg performed HL-RT while the contralateral leg was allocated, in a randomized and balanced fashion, according to 1RM, QCSA, and dominance to one of the 2 possible training protocols: BFR during between-set rest intervals and removed during muscle contractions (BFR-I) or BFR during muscle contractions and removed during between-set rest intervals (BFR-C). We decided not to apply BFR throughout HL-RT session because it may be very uncomfortable and painful (18 and pilot work data). In the first training session (control session 1), [La] and root mean square through surface electromyography (RMS-EMG) of vastus lateralis were also measured with subjects performing, in a randomized order, both the HL-RT and their respective training protocol for the contralateral leg, interspaced by 30 minutes. Training period was then initiated for all protocols for 8 weeks. After the fourth week, 1RM was reassessed 72 hours after the eighth training session to adjust the training load. Training continued for another 4 weeks with the adjusted load. Seventy-two hours after the last training session, QCSA was reassessed, with subsequent assessment of MVIC and 1RM 48 hours later. Using the same procedure of the first training session, final [La] and RMS-EMG assessments were performed 72 hours after the final QCSA measurement (control session 2). Experimental design is illustrated in Figure 1.

### Subjects

Sixty healthy, young and recreationally active (physical activity performed less than twice a week) men volunteered to participate in the study. Nine subjects dropped out before completion because of low adherence ( $<85\%$  of all sessions attended) and 2



**Figure 1.** Experimental design. Maximum voluntary isometric contraction (MVIC); one repetition maximum (1RM); quadriceps cross-sectional area (QCSA); root mean square through surface electromyography (RMS-EMG); BFR-I, in which BFR was applied during the rest intervals between sets and removed during the sets of muscle contractions; BFR-C, in which BFR was applied during the sets of muscle contractions and removed during the rest intervals between sets; and high-load resistance training without BFR (HL-RT).

subjects dropped out because of personal reasons; therefore, data from 49 subjects ( $25 \pm 6.2$  years,  $178.1 \pm 5.3$  cm and  $78.8 \pm 11.6$  kg; *SD*) were considered in the analysis. Subjects had not participated in any kind of regular resistance training within the previous 6 months before the experimental period. To meet inclusion criteria, subjects could not use any dietary supplements during the study and for at least 2 months before the study, as well as any previous administration of anabolic steroids. Subjects were instructed to maintain their habitual diets and were regularly questioned about any change in diet that could potentially influence study results, such as the use of dietary supplements or variances in protein or carbohydrate intake. All subjects were between 18 and 35 years old. All subjects were informed about the benefits, discomforts, and possible risks of the study before signing a free and written informed consent document. The study was conducted according to the Declaration of Helsinki, and the University of São Paulo Research Ethics Committee approved the experimental protocol (approval number: 9641715.0.0000.5391).

## Procedures

**Determination of Arterial Occlusion Pressure.** Arterial occlusion pressure was assessed at PRE to determine the pressure used for the BFR protocols. After 10 minutes of supine rest, a vascular Doppler probe (DV-600; Marted, Ribeirão Preto, SP, Brazil) was placed on the tibial artery to capture its auscultatory pulse. A nylon cuff ( $17.5 \times 90$  cm; JPJ, SP, Brazil) was placed at the top of the thigh and inflated to the lowest point at which an auscultatory pulse was no longer detected. This value was defined as the arterial occlusion pressure (13).

**Maximum Strength Testing Procedures.** The MVIC and 1RM tests in the unilateral knee extension exercise followed the guidelines of the American Society of Exercise Physiologists (2). Briefly, subjects ran for 5 minutes on a treadmill at  $9 \text{ km} \cdot \text{h}^{-1}$ , followed by 3 minutes of recovery. Then, subjects were positioned on the Biodex isokinetic dynamometer (Biodex System 4, Biomedical Systems, Newark, CA) seat, with safety belts fastened on the trunk, pelvis, and thigh to minimize extra body movements that could affect the peak torque values. The lateral epicondyle of the femur was used as a marker to align the knee rotation axis and the instrument rotation axis. A knee angle of  $60^\circ$  was used during the MVIC test, as it was previously shown that this angle is associated with the maximum force output (16). In this test, subjects performed 2 MVIC during 5 seconds, with a 60-second interval between trials. The highest recorded torque for each leg was determined as the MVIC.

For the 1RM test, a leg extension machine was used (SL 1030, Righetto, Campinas, SP, Brazil). After a 30-minute interval from the MVIC test, subjects performed a specific warm-up composed of 8 repetitions at approximately 50% 1RM, and after a 2-minute rest, 3 repetitions at approximately 70% 1RM. Both loads were estimated based on the subjects' familiarization sessions. Three minutes after the specific warm-up, 1RM was determined as the maximum possible weight lifted in a single and complete repetition. Knee joint amplitude was set at  $90^\circ$  using a goniometer. Rest periods of 3 minutes between attempts were used, with a maximum of 5 attempts allowed. Coefficients of variation for MVIC and 1RM between 2 measures (last familiarization session and 1RM test) performed in different days, 72 hours apart, were 3.5 and 3.9%, respectively.

**Quadriceps Cross-Sectional Area Assessment.** The QCSA measurement was performed by magnetic resonance imaging (1.5T Signa LX 9.1; Healthcare, Milwaukee, WI). A T1-weighted, spin-echo, axial plane sequence was obtained using the following parameters: pulse sequence with a field of view between 400 and 420 mm, repetition time of 350 ms, echo time from 9 to 11 ms, slice thickness of 0.8 cm, 2 signal acquisitions, and matrix of reconstruction  $256 \times 256$  mm. Subjects initially rested quietly in the supine position with knees extended and legs straight for 15 minutes to allow fluid distribution before the assessments (4). Velcro straps were used to restrain legs movements during image acquisition, and the exact positioning of the individual's legs on the stretcher was demarcated with tape for subsequent similar reproduction of this measurement. An initial reference image was obtained to determine the perpendicular distance between the inferior border of the lateral epicondyle of the femur and the greater trochanter of the femur, which was defined as the segment length. Cross-sectional area for all 4 muscles of the quadriceps was measured at 50% of the segment length with 0.8-cm slices for 3 seconds. The segment slice was divided into skeletal muscle, subcutaneous fat, bone, and residual tissue. Quadriceps cross-sectional area measures were then determined by subtracting the bone and subcutaneous fat area. All images were transferred to a computer (Mac OS X, version 10.5.4; Apple, Cupertino, CA), manually outlined, and analyzed using open-source software (OsiriX, version 3.2.1; OsiriX Imaging Software, Geneva, Switzerland). Care was taken to exclude intramuscular fat and blood vessels from MRI analyses. The QCSA images were traced in triplicates by a specialized researcher, and their mean values were used for all further analysis. All QCSA analyses were conducted by the same trained blinded researcher. The coefficient of variation values between 2 measures performed 72 hours apart for the QCSA was 0.87%.

**Resistance Training Program.** Subjects performed the unilateral knee extension exercise in a leg extension machine (SL 1030, Righetto, Campinas, SP, Brazil) twice a week for 8 weeks. Each training session subjects started with a 5-minute general warm-up at  $9 \text{ km} \cdot \text{h}^{-1}$  on a treadmill. Subsequently, they executed a specific warm-up composed of 5 repetitions at 50% 1RM. One minute later, training protocols were started. HL-RT, BFR-I, and BFR-C protocols consisted of 3 sets of 8 repetitions at 70% 1RM. All protocols were performed with a 60-second rest period between sets, and cadence of repetitions was performed with a controlled concentric and eccentric cycle of approximately 2 second each (controlled by a metronome). The initial protocol performed was alternated in each session. For the BFR protocols, a pressure cuff ( $17.5 \times 90$  cm) was placed proximally on the thigh (at the inguinal fold) and inflated to 80% of their resting arterial occlusion pressure (19,37). The average pressure throughout the training protocols was  $98.3 \pm 8.7$  mm Hg. For BFR-I, the cuff was inflated to the target occlusion pressure immediately after each exercise set and remained inflated during the whole resting period and deflated immediately before the next set. For BFR-C, the cuff was inflated immediately before each set and remained inflated during muscle contractions, and it was deflated immediately after the set ending.

**Blood Lactate Concentration.** To determine [La], blood samples were collected during the control sessions 1 and 2 from the earlobe at rest, after the first (post-set 1), second (post-set 2), and third sets (post-set 3) and at 3, 5, and 10 minutes after the session. After aseptics, 25- $\mu\text{L}$  samples were immediately stored in 1% sodium fluoride solution at  $4^\circ \text{C}$  for posterior

electrochemical analysis in an automated device (1,500 Sport; Yellow Springs, OH).

**Root Mean Square Through Surface Electromyography Measurement.** Muscle electrical activity was recorded with an 8-channel EMG system (EMG System, São José dos Campos, Brazil) with an acquisition frequency of 1,000 HZ and band-pass filter of 20–500 HZ. After trichotomy and asepsis, a single differential electrode was used in which two 36-mm diameter electrodes (Ag-Ag/Cl; Kendal, SP, Brazil) were placed over the belly of the vastus lateralis muscle and aligned in parallel with the expected muscle fiber orientation. Moreover, a ground electrode was placed on the medial portion of the patella. The EMG was recorded during each set of unilateral knee extensions. Raw electromyographic signals were digitally filtered (fourth order Butterworth, band-pass 20–500 HZ) and converted to RMS for each concentric phase. Electromyography signal obtained during the concentric muscle action of the last 3 repetitions of each set was averaged and normalized as a percentage of the average of the first 5 repetitions from the specific warm-up. To identify the concentric phase of movement during exercise, an electrogoniometer (EMG system) was fixed on the side of the subject's knee, and the electrogoniometer signal was synchronized with the EMG.

### Statistical Analysis

Data are presented as mean  $\pm$  SD, effect sizes (ESs), and 95% confidence interval (CI). Data normality was tested by the Shapiro-Wilk test and visually inspected (box plots) for the presence of “outliers” (no outliers were detected). A mixed model analysis was performed for dependent variables (MVIC, 1RM, and QCSA), using “protocol” (HL-RT, BFR-I, and BFR-C) and “time” (PRE and POST) as fixed factors and “subjects” as a random factor. For dependent variables [La] and RMS-EMG, analysis assumed “protocol” (HL-RT, BFR-I, and BFR-C), “time” (PRE and POST), and “moment” (Rest, post-set 1, post-set 2, post-set 3, 3 minutes post-set 3, 5 minutes post-set 3, and 10 minutes post-set 3 for [La]; and Warm-up, set 1, set 2, and set 3 for RMS-EMG) as fixed factors and “subjects” as a random factor. A Tukey's adjustment was used for multiple comparisons. Effect sizes were calculated using Cohen's  $d$  and were interpreted as follows:  $<0.2$ , negligible effect;  $0.2$ – $0.39$ , small effect;  $0.40$ – $0.75$ , moderate effect; and  $>0.75$ , large effect (5). A significance level was set at  $p \leq 0.05$ . Between-group differences at PRE on dependent variables were tested by one-way analysis of variance, and no significant differences (all  $p > 0.05$ ) were detected. Data were analyzed using statistical package SAS 9.3 (SAS Institute Inc., Cary, NC).

## Results

### Quadriceps Cross-Sectional Area

Significant PRE to POST changes in QCSA were detected (Figure 2A) for all training protocols (main time effect,  $p < 0.0001$ ; HL-RT: 6.7%; ES = 0.43; 95% CI =  $-0.10$  to  $0.96$ ; BFR-I: 7.7%; ES = 0.45; 95% CI =  $-0.25$  to  $1.16$ ; and BFR-C: 7.0%; ES = 0.38; 95% CI =  $-0.34$  to  $1.10$ ). No significant between-protocol differences were detected ( $p = 0.96$ ).

### Maximum Dynamic Strength (One Repetition Maximum)

One repetition maximum significantly increased from PRE to POST training (Figure 2B) for all training protocols (main time effect,  $p < 0.0001$ ; HL-RT: 12.0%; ES = 0.60; 95% CI =  $0.07$  to  $1.14$ ; BFR-I: 13.7%; ES = 0.71; 95% CI =  $0.00$  to  $1.43$ ; and BFR-C: 11.5%; ES = 0.58; 95% CI =  $-0.15$  to  $1.31$ ). No significant between-protocol differences were detected ( $p = 0.86$ ).

### Maximum Voluntary Isometric Contraction

All training protocols showed a significant increase in MVIC from PRE to POST training (Figure 2C) (main time effect,  $p < 0.0001$ ; HL-RT: 8.0%; ES = 0.40; 95% CI =  $-0.13$  to  $0.93$ ; BFR-I: 7.8%; ES = 0.40; 95% CI =  $-0.30$  to  $1.10$ ; and BFR-C: 6.9%; ES = 0.40; 95% CI =  $-0.32$  to  $1.13$ ), but the between-protocol increases were similar ( $p = 0.87$ ).

### Blood Lactate Concentration and Root Mean Square Through Surface Electromyography

No differences between training protocols were shown for [La] at Rest (all  $p > 0.05$ ) in PRE and POST training. PRE and POST training [La] levels increased in all moments when compared with Rest, for all training protocols (all  $p < 0.05$ ). However, [La] was significantly higher for BFR-I at “post-set 3,” “3 minutes post-set 3,” and “5 minutes post-set 3” compared with the other protocols (all  $p < 0.05$ ) (Table 1).

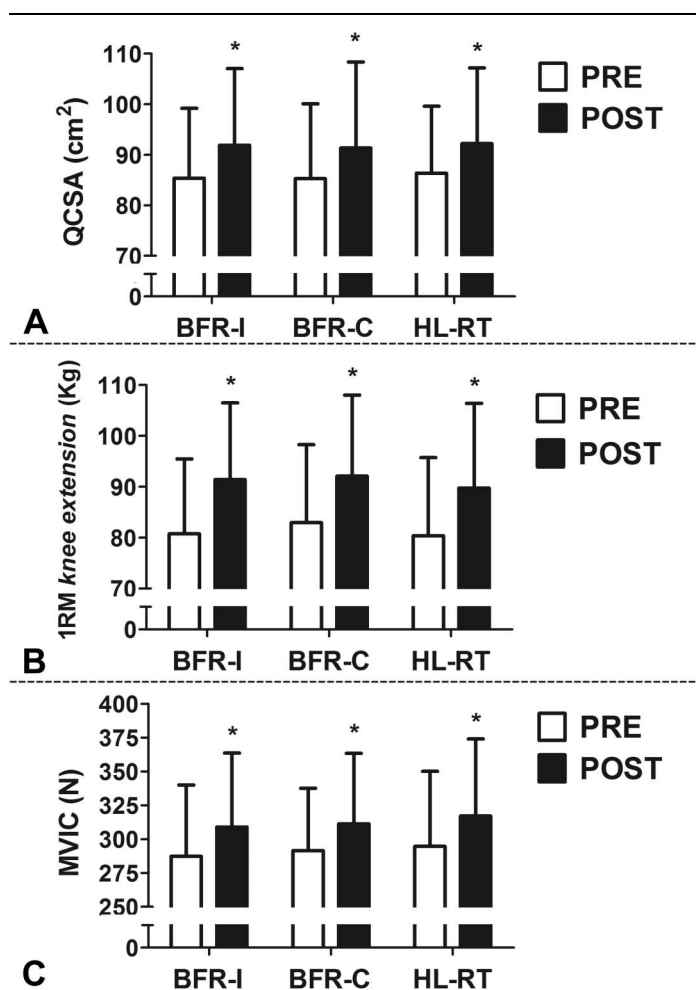
Compared with “Warm-up,” RMS-EMG significantly increased after “set 1” and “set 2” for HL-RT, BFR-I, and BFR-C (all  $p < 0.05$ ; Table 1) in PRE and POST training. However, at PRE training, RMS-EMG remained elevated in “set 3” only for HL-RT and BFR-C ( $p < 0.05$ ).

## Discussion

In this study, combining BFR with HL-RT, irrespective of protocol, resulted in similar gains in muscle mass and strength compared with HL-RT alone. Furthermore, although BFR application during rest intervals (BFR-I) resulted in a greater metabolic stress, it did not translate into additive effects on muscle activation.

Current evidence suggest that both metabolic and mechanical stress may contribute to an increased recruitment of fast-twitch muscle fibers (26,34–36), contributing to muscle hypertrophy. However, no significant additive effects have been shown from BFR incorporation into HL-RT, neither at the end of the exercise sets (7,24) nor during muscle contractions (1,18). Our data corroborate these previous studies. It has been suggested that metabolites alone do not have anabolic properties in the absence of mechanical stress (8,38), invalidating the application of BFR alone after the end of exercise. Furthermore, high-load muscle contractions may induce partial BFR “per se” (9,28), whereas releasing BFR during rest intervals allows for the removal of intramuscular metabolites (36). Taken together, these might explain the lack of additional effect in the BFR-C protocol in our study. Considering that blood flow is partially restricted by muscle contraction during HL-RT, and that the rest interval between the sets allows the removal of intramuscular metabolites, we tested the application of BFR alone during the rest interval between sets (BFR-I); however, no additional effects on muscle hypertrophy or strength were observed.





**Figure 2.** A) Quadriceps cross-sectional area (QCSA, in cm<sup>2</sup>), (B) maximum dynamic strength (1RM, in kg), and (C) maximum voluntary isometric contraction (MVIC, in N·m<sup>-1</sup>·s<sup>-1</sup>) before (PRE) and after 8 weeks for BFR-I, BFR-C, and HL-RT protocols. \*Refers to a significant within-protocol effect ( $p < 0.001$ ).

**Table 1**

**Acute changes for lactate concentration (mmol·L<sup>-1</sup>) and root mean square of surface electromyography (RMS-EMG; % average of the repetitions warm-up) during each training protocol in the preintervention and postintervention.\*†**

	BFR-I		BFR-C		HL-RT	
	PRE	POST	PRE	POST	PRE	POST
<b>Lactate</b>						
Rest	1.04 ± 0.33	1.15 ± 0.85	0.80 ± 0.36	0.80 ± 0.36	0.97 ± 0.40	1.13 ± 0.46
Post-set 1	2.57 ± 0.56‡	2.80 ± 1.32‡	1.62 ± 0.88‡	1.62 ± 0.88‡	2.10 ± 0.65‡	2.22 ± 0.61‡
Post-set 2	2.99 ± 1.40‡	3.49 ± 1.69‡	2.27 ± 0.98‡	2.27 ± 0.98‡	2.77 ± 0.97‡	2.89 ± 0.93‡
Post-set 3	4.10 ± 1.54‡§	4.70 ± 1.47‡§	2.43 ± 0.66‡	2.43 ± 0.66‡	2.98 ± 0.85‡	3.10 ± 0.76‡
3 min post-set 3	4.86 ± 0.95‡§	5.19 ± 1.32‡§	2.76 ± 0.83‡	2.76 ± 0.83‡	3.14 ± 1.04‡	3.06 ± 0.98‡
5 min post-set 3	4.87 ± 1.29‡§	4.75 ± 1.29‡§	2.57 ± 1.07‡	2.57 ± 1.07‡	2.53 ± 0.95‡	2.25 ± 0.94‡
10 min post-set 3	2.71 ± 1.23‡	3.24 ± 1.14‡	1.91 ± 0.84‡	1.91 ± 0.84‡	2.31 ± 0.80‡	2.17 ± 0.57‡
<b>RMS-EMG</b>						
Warm-up	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Set 1	1.55 ± 0.24‡	1.56 ± 0.21‡	1.52 ± 0.21‡	1.57 ± 0.23‡	1.53 ± 0.48‡	1.55 ± 0.41‡
Set 2	1.46 ± 0.34‡	1.59 ± 0.21‡	1.55 ± 0.35‡	1.56 ± 0.18‡	1.56 ± 0.45‡	1.56 ± 0.41‡
Set 3	1.25 ± 0.27	1.55 ± 0.18‡	1.48 ± 0.50‡	1.51 ± 0.16‡	1.51 ± 0.41‡	1.53 ± 0.42‡

\*BFR-I = blood flow restriction applied during rest intervals; BFR-C = blood flow restriction applied during muscle contractions; HL-RT = high-load resistance training.

†Data are presented as mean ± SD.

‡Significant difference compared with Rest (for lactate) and Warm-up (for RMS-EMG).

§Significant difference compared with HL-RT and BFR-C in the same moment.

||Significant difference compared with post-set 1, post-set 2, and 10 minute post-set 3.

Regarding muscle activation, Dankel et al. (8) applied BFR for 3 minutes immediately after one set of HL-RT, followed by a further set of HL-RT while maintaining BFR, whereas a parallel condition performed the same protocol without any BFR. The authors did not observe additional effects on muscle activation when BFR was added to HL-RT. In addition, Teixeira et al. (37) compared 3 sets of HL-RT without BFR vs. the same protocol combined with BFR applied either during the exercise or during rest intervals. Despite the higher metabolic stress (i.e., [La]) during BFR application in the rest intervals, RMS-EMG showed a reduced muscle activation from the first to second and third sets, suggesting no further effect from BFR addition to HL-RT during rest intervals. Similarly, although a greater increase in [La] occurred with BFR-I in the current study, RMS-EMG values were similar between the high-load protocols, regardless of BFR. Therefore, because the high mechanical stress promoted by HLs already induces greater levels of muscle activation (15,22), BFR addition to HL-RT does not seem to potentiate muscle activation, suggesting that muscle activation is more impacted by mechanical than metabolic stress. On the other hand, RMS-EMG is not a direct reflection of motor units' recruitment and may also be influenced by firing frequency, synchronization and disruption of motor units, and the use of different training protocols (11,40). Thus, other mechanisms beyond the scope of this study and independent of muscle activation may also be related to increased muscle mass, such as the activation and proliferation of myogenic stem cells, reduced expression of genes related to muscle protein breakdown, and increased muscle protein synthesis (14,27).

Importantly, muscle strength gains were similar across conditions regardless of test specificity (i.e., dynamic or isometric strength testing). Three studies have examined whether the BFR application during muscle contractions can augment muscle strength using HL-RT (1,6,18). Although one study (6) reported marginal advantage (3 kg, 2%), 2 other studies reported no added benefit on muscle strength (1,18), which was also confirmed by our study, regardless of BFR protocol. It has been suggested that gains in muscle strength during RT are maximized by the use of heavier loads (17,29). These results are theorized to occur through alterations in neuromuscular factors including greater recruitment and firing rate of motor units and greater changes in the agonist-antagonist co-activation rate compared with lower loads (12). Thus, irrespective of BFR protocol, when a high relative load is used, similar strength gains should be expected. Despite the similar muscle strength gains between protocols, a relative change was markedly lower for the isometric compared with the dynamic test. A possible explanation may lay on the principle of specificity (3), which states that strength gains would be strongly attributed to the training protocol that most closely resembles the testing protocol (i.e., 1RM test was the same exercise used for all protocols). Collectively, this reinforces testing specificity as an important factor to accurately conclude on muscle strength gains promoted by different protocols.

Our study has limitations. First, our results are specifically applied to young, untrained men, and it is uncertain whether the observed changes in muscle strength and mass would be similar for other populations, such as women, elderly, or trained individuals. Second, the [La] was estimated from ear-lobe blood samples. Although this allowed us to quantify systemic lactate accumulation, it did not allow us to detect

differences in lactate accumulation within or around the active muscle tissue. Third, surface EMG is not a direct measure of muscle activation and may be impacted by several mechanisms related to muscle recruitment. Finally, we cannot rule out the possibility of a cross-education effect given the within-subject design. However, if in fact this phenomenon occurred, it is very unlikely it had any effect on the results considering the use of similar loads between all training protocols.

In conclusion, our data suggest that despite resulting in greater increases in metabolic stress, irrespective of the restrictive stimulus application strategy, the combination of BFR with HL-RT does not induce any additional effect on muscle activation and, to a greater extent, on strength and muscle hypertrophy gains.

### Practical Applications

From an applied standpoint, our results indicate that the addition of BFR to HL-RT does not contribute to a greater extent on neuromuscular adaptations. Considering that our findings are limited to young, untrained individuals, it remains to be clarified whether the current results would be replicated with longer periods of training or in other populations, such as elderly or resistance-trained individuals. Moreover, when the goal is to maximize strength and hypertrophy gains, practitioners can perform HL-RT without BFR or, as an alternative in which high-load resistance exercise may not be tolerable, low-load resistance training in combination with BFR.

### Acknowledgments

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