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Blood Flow Restriction Attenuates Muscle Damage in Resistance Exercise Performed Until Concentric Muscle Failure

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ABSTRACT

International Journal of Exercise Science 16(2): 469-481, 2023. The present study aimed to evaluate whether blood flow restriction (BFR) can prevent exercise-induced muscle damage in resistance exercise (RE) performed until concentric muscle failure (CMF). Twenty healthy volunteers (25 ± 4 years, 80.4 ± 11.8 kg, 175 ± 8 cm) performed three sets of unilateral biceps curl exercise (40% of 1RM) with (RE + BFR) and without (RE) BFR until CMF. A third condition was to perform the same number of repetitions as RE + BFR without using BFR (matched). Performing fewer repetitions, RE + BFR caused muscle fatigue post-exercise as high as that caused by RE. In addition, the range of motion, upper arm circumference, pressure pain threshold, and maximal voluntary contraction were immediately affected by our exercise protocol with BFR, returning rapidly to basal values within 24 h, while in RE, muscle damage markers remained elevated until 48 h post-exercise. The same results were observed concerning serum creatine kinase and lactate dehydrogenase activity. Thus, BFR + RE performed until CMF attenuated muscle damage following similar metabolic stress to RE alone performed until CMF, with less work volume.

KEY WORDS: Eccentric contraction, muscle fatigue, injury, kaatsu, strength training

INTRODUCTION

The American College of Sports Medicine (1) recommends resistance exercise with an intensity similar to or higher than 70% of 1RM to induce muscle-skeletal strength and hypertrophy. One of the main acute responses observed following high-intensity resistance exercise (i.e., $\geq 80\%$ of 1RM) is exercise-induced muscle damage (EIMD) characterized by changes in muscle ultrastructure (e.g., Z-band streaming) (10) and alterations in maximum voluntary isometric contraction (MVC) and serum creatine kinase (CK) concentrations (18). Although EIMD

stimulates muscle adaptations to a subsequent bout of exercise, large EIMD is not favorable for high-frequency resistance-exercise training (18).

On the other hand, studies have shown that low-intensity resistance-exercise training (i.e., 20–50% of 1RM) combined with blood flow restriction (BFR) may stimulate muscle adaptations similar to those caused by high-intensity resistance-exercise training (14, 17). Studies have shown that a notably high training frequency with BFR (two BFR training sessions per day for up to six days per week, with a total of 12 training sessions per week) is successful over short periods (1–2 weeks), resulting in significant increases in muscle hypertrophy and strength, despite the very short recovery periods (23). It is thought that this high-frequency is possible since BFR may reduce or maintain the EIMD, returning to baseline values 24 h after the exercise session (18, 28). However, only two studies have applied BFR during high-intensity resistance exercise, but both used eccentric contractions. Sudo et al., (28) reported decreased muscle damage when BFR was applied in an animal model of electromotor-induced plantar flexion, and our group recently showed that BFR attenuates high-intensity EIMD in humans (9). It should be noted, however, that exercise was not performed until concentric muscle failure (CMF).

Studies evaluating the effect of BFR on EIMD have only used work-matched or high-intensity resistance exercise (24, 28). Furthermore, no studies have assessed whether BFR can prevent EIMD when resistance exercise is performed until CMF. Thus, the present study aimed to understand whether BFR can prevent EIMD even when low-intensity resistance exercise is performed until CMF.

METHODS

Participants

Twenty healthy volunteers (10 male and 10 female), who had been involved in regular resistance exercise at least three days per week for at least one year, were enrolled in the present study (Table 1). To calculate the sample size, $\alpha = 0.05$, $\beta (1 - \alpha) = 0.80$, and the large effect size (ES = 0.8) were adopted. A total of 15 volunteers were estimated for this study using G*Power software version 3.1.9.2. All procedures were performed following the ethical standards of the Institutional and National Research Committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all participants. The following exclusion criteria were adopted: a) use of drugs that could affect cardiorespiratory responses; b) bone-, joint-, or muscle-diagnosed problems that could limit the execution of elbow flexion; c) systemic hypertension ($\geq 140/90$ mmHg or the use of antihypertensive medication); d) metabolic disease; and e) use of exogenous anabolic-androgenic steroids, toxic drugs, or medication with potential effects on physical performance. Participants were instructed to refrain from strenuous activities for at least 72 h prior to the resistance exercise sessions, to avoid using pain-relieving medications (anti-inflammatory drugs), and to maintain their regular food intake and lifestyle habits throughout the study. This research was carried out entirely following the ethical standards of the International Journal of Exercise Science (20).

Table 1. Characteristics of the participants ($n = 20$).

Variable	Mean \pm SD	IC 95%
Experience of RE (moths)	29 \pm 18	21.4 - 37.5
Age (years)	25 \pm 3	23.4 - 26.3
Weight (kg)	72 \pm 12	66.2 - 77.5
Height (m)	1.70 \pm 0.1	1.66 - 1.74
BMI (kg/m ²)	25 \pm 0.1	23.4 - 25.8
SBP (mmHg)	118 \pm 13	111 - 127
DBP (mmHg)	70 \pm 8	66 - 75
rHR (bpm)	69 \pm 9	64 - 75

Data are the mean \pm and IC 95%. RE, resistance exercise; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; rHR heart rate; IC95%, interval confidence of 95.

Protocol

The protocol was a balanced, within-subjects, randomized crossover design. Each participant performed the unilateral biceps curl exercise using the dominant arm. Resistance exercise sessions were conducted under three conditions: 1) low-intensity resistance exercise with blood flow restriction until CMF (RE + BFR); 2) low-intensity resistance exercise without blood flow restriction, with the same number of repetitions as in the RE + BFR condition (matched); and 3) only low-intensity resistance exercise until CMF (RE), according to Ganesan et al., (13).

The subjects performed the three conditions with each session separated by at least four weeks to minimize the exposure of repeated-bout effects. The order of the conditions was randomly applied: order A, RE in the 1st session, RE + BFR in the 2nd session, and matched in the 3rd session; order B, RE + BFR in the 1st session, matched in the 2nd session, and RE in the 3rd session. Each experimental exercise session was performed in three sets, with a one-minute rest between sets.

All hemodynamic responses were evaluated according to the American Heart Association Guidelines (32). Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP) and resting heart rate (rHR) were measured using an automatic blood pressure monitor (model HEM-705CP; OMRON). The cuff was placed in the dominant arm, completely relaxed and extended. The measures were taken after 15 minutes of the subjects resting in a sitting position.

Perceptual responses during exercise sessions, acute concentrations of metabolic blood markers, and acute and delayed responses of indirect and blood markers of muscle damage were analyzed following each training session.

Participants were asked to lie down comfortably in the supine position to determine blood flow restriction pressure. A vascular doppler probe (DV-600, Martec, Ribeirao Preto, SP, Brazil) was placed over the radial artery to determine the BFR pressure (mmHg). A blood pressure cuff (width 6.5 cm, length 80 cm; Cardiomed, Curitiba, PR, Brazil) attached to the proximal portion of the arm was inflated to the point at which the auscultatory pulse of the radial artery was

interrupted. The cuff pressure used during the training protocol was determined to be 80% of the necessary pressure for complete blood flow restriction under resting conditions (9). The BFR pressure was maintained constant throughout the exercise session.

The procedures adopted for the 1RM test of unilateral elbow flexor muscles followed the recommendations described by Brown & Weir (3). In short, participants ran for 5 min on a treadmill at 9 km/h, followed by upper-limb light stretching exercises and two warm-up sets of unilateral elbow flexor exercises (unilateral biceps curls). In the first set, eight repetitions were performed with a load corresponding to 50% of their estimated 1RM obtained during the familiarization sessions. In the second set, three repetitions were performed with a load corresponding to 70% of their estimated 1RM. An interval of 2 min was allowed between warm-up sets. Following completion of the second set, participants rested for 3 min and then had up to five attempts to achieve their 1RM, with 3-min intervals between attempts. Since previous studies have shown that submaximal eccentric contractions can confer a protective effect against EIMD inflicted by high-intensity eccentric exercise performed within the following weeks (4), both warm-up sets and 1RM trials were conducted with the subject lifting the load using only concentric contractions (elbow flexion phase), similar to that reported by Sieljacks et al. (24). An investigator lowered the weight to liberate the subject from performing the eccentric part of the movement. The 1RM strength of the elbow flexor muscles was recorded and reproduced throughout the study. An experienced physical education professional conducted tests, and strong verbal encouragement was provided during the attempts.

The exercise volume was evaluated by the maximum number of repetitions performed after each set (Set 1, Set 2, and Set 3). The work volume was defined as the total maximum number of repetitions multiplied by the external load (21).

Immediately after each set, the subjects were asked to report their rating of perceived exertion (RPE) and pain (RPP) using Borg's scale (1 to 10), similar to previous studies (9), where 0 corresponds to "no exertion or pain" and 10 corresponds to "extreme/maximal exertion or pain". Participants received standardized instructions for each measure using this scale prior to the exercise session. They were asked first to report their RPE followed by their RPP.

Metabolic responses were evaluated before (Pre), immediately after (Post-0), and 10 min after (Post-10 min) exercise. The analyzed metabolic parameters were blood glucose and lactate concentrations. Following local cleansing of the index finger, the side of the participant's finger was lanced and a blood sample (5 μ L) was collected. An experienced professional performed capillary blood glucose measurements using a validated glucometer (Accu-Chek, Roche Diagnostics). All measurements were performed following the manufacturer's instructions. The blood lactate concentration was analyzed in capillary blood (25 μ L) collected from the middle finger into heparinized capillary tubes. Blood samples were placed in tubes containing 50 μ L NaF (1%) and stored on ice for approximately 30 min. The blood lactate concentration was determined using an electrochemical device (YSI 1500; Yellow Springs, USA).

Indirect markers of muscle damage were measured before (Pre), immediately after (Post), and 24 h and 48 h after each exercise session. The analyzed indirect markers of muscle damage were: range of motion (ROM); upper arm circumference (CIR); pressure pain threshold (PPT); and maximum voluntary isometric contraction (MVC).

For the ROM analyses, the elbow joint angles for the fully extended and flexed positions were measured using a fleximeter (Sanny, Brazil) positioned on the distal forearm, while participants were asked to extend and flex the elbow as much as possible. The ROM was defined as the difference between the extended and flexed elbow joint angles (29).

Relaxed CIR was assessed at 66% of the distance from the acromion process of the scapula to the cubit fossa using a standard tape measure (Sanny, Brazil) (9, 27). The measurement point on the subjects' arm was marked to ensure consistent placement of the tape measure. The mean value of three measurements was used for the analysis. The PPT was assessed at the mid-point on the biceps brachii muscle with the participants in the supine position. The points were marked using a permanent marker to replicate the exact recording sites during the entire study period. During the PPT test, an algometer with a 1-cm² hard rubber tip (Wagner FDN, USA) was used, and great care was taken to apply pressure directly in the perpendicular plane at a gradually increasing rate (~3 kg/cm²/s). The subjects were instructed to indicate to the investigator the moment that the pressure generated "slightly uncomfortable pain", and the force at this point was recorded. Each recording was repeated three times randomly between the stimulation sites. The same investigator similarly performed all measurements for all participants, and the mean value of the three measures was used as the PPT value.

The MVC (N.m) of the elbow flexors was measured at 90° elbow flexion using an isokinetic dynamometer (Biodex System Dynamometer, USA). Participants performed three 5-s maximal isometric contractions with a 60-s rest between trials, and strong verbal encouragement was provided during the measurements. The highest value of the three MVC trials was used for further analysis (29).

Blood markers of muscle damage were measured before the 1st exercise session (Pre), 24 h and 48 h after each exercise session. Blood samples of approximately 5 mL were collected from the antecubital vein into vacutainer tubes. The blood samples were kept at room temperature for 10–15 min to allow clotting of the serum. Then, samples were centrifuged at 3000 rpm for 20 min at 4°C. The serum was transferred to sample tubes and immediately stored at -80°C until further analysis. Creatine kinase (CK) and lactate-dehydrogenase (LDH) activities were analyzed spectrophotometrically using a Cobas Mira Plus analyzer (Roche, Germany) and commercially available kits (BioTécnica, Brazil).

Statistical Analysis

Values are expressed as the mean ± standard deviation (mean ± SD) for all variables. Physical characteristics were compared using an unpaired t-test and 95% confidence intervals (95% CI). Statistical analyses were performed using a two-way ANOVA with repeated measures (trials ×

time). Tukey's post-hoc test was used to elucidate differences between conditions when the ANOVA showed a significant interaction. In addition, the effect size (ES) was used to verify the magnitudes of changes between assessments of the protocols as trivial (0–0.19), small (0.20–0.49), medium (0.50–0.79), and large (0.80 and greater) (7). Statistical analyses were performed using the Prism software (Prism 5, GraphPad Software, USA). A value of $p \leq 0.05$ was regarded as statistically significant.

RESULTS

Exercise Volume: The work volume was significantly lower in the BFR condition (RE: $6,768 \pm 4,013$ kg vs. RE + BFR: $2,628 \pm 1,358$ kg, $p < 0.0001$, ES: 1.11), once the maximum number of repetitions was significantly reduced ($p < 0.05$, Table 2). The matched condition performed the same number of repetitions as observed in the RE + BFR condition.

Table 2. Comparison of the number of repetitions in each set.

Variable	Protocol	Set 1	Set 2	Set 3
Number of Repetitions	RE + BFR	39 ± 10^a	13 ± 6^{ab}	7 ± 4^{ab}
	Matched	39 ± 10	13 ± 6^b	7 ± 4^b
	RE	94 ± 28	35 ± 16^b	24 ± 7^b

Data are the mean \pm SD. RE, resistance exercise condition; RE + BFR, resistance exercise with blood flow restriction condition; Matched, resistance exercise work-matched to RE + BFR. ^a $p < 0.05$ vs. RE, ^b $p < 0.05$ vs. Set 1

Rating of Perceived Exertion and Pain: Both conditions that performed the exercise sessions until CMF (RE and RE + BFR) demonstrated high scores for RPE (Table 3); however, the RPP score was significantly higher in the RE + BFR condition as compared with both the RE ($p < 0.05$, ES: 1.61) and matched conditions ($p < 0.001$, ES: 2.57).

Table 3. Comparison of RPE and RPP after each set.

Variable	Protocol	Set 1	Set 2	Set 3
RPE	RE + BFR	7 ± 1^a	8 ± 1^{ab}	8 ± 1^{ab}
	Matched	3 ± 1	2 ± 1	2 ± 1
	RE	7 ± 1^a	8 ± 1^{ab}	8 ± 1^{ab}
RPP	RE + BFR	7 ± 1^{ac}	8 ± 1^{abc}	9 ± 1^{abc}
	Matched	2 ± 2	1 ± 2	1 ± 1
	RE	5 ± 2^a	6 ± 2^{ab}	6 ± 2^{ab}

Data are the mean \pm SD. RPE, rating of perceived exertion; RPP, rating of perceived pain; RE, resistance exercise condition; RE + BFR, resistance exercise with blood flow restriction condition; Matched, resistance exercise work-matched to RE + BFR. ^a $p < 0.05$ vs. Matched, ^b $p < 0.05$ vs. Set 1, ^c $p < 0.05$ vs. RE and Matched.

Metabolic Responses: Table 4 shows the absolute values of blood glucose and lactate concentrations. Again, there were no significant differences in these concentrations among all conditions prior to exercise sessions.

Both conditions that performed the exercise until CMF (RE and RE + BFR) showed similar metabolic stress after exercise sessions ($p < 0.05$), with significant decreases in the blood glucose concentration immediately after (RE: $\Delta -14.7 \pm 11$ mg/dL, and RE + BFR: $\Delta -9.0 \pm 9.8$ mg/dL) and 10 min after exercise (RE: $\Delta -13.1 \pm 12.8$ mg/dL, and RE + BFR: $\Delta -6.1 \pm 10.1$ mg/dL), and increases in blood lactate concentration immediately after (RE: $\Delta 2.3 \pm 1.1$ mmol/L, and RE + BFR: $\Delta 2.5 \pm 1.1$ mmol/L) and 10 min after exercise (RE: $\Delta 1.6 \pm 0.7$ mmol/L, and RE + BFR: $\Delta 1.1 \pm 1.2$ mmol/L). Thus, although BFR reduced the total work volume, this condition showed similar metabolic stress to the RE condition. No significant differences were observed for blood glucose and blood lactate in the matched condition.

Table 4. Blood glucose and lactate concentrations prior to and following exercise.

Variable	Protocol	Pre	Post - 0min	Post - 10min
Glucose (mg/dL)	RE + BRF	94 ± 12	85 ± 9 ^b	88 ± 9 ^b
	Matched	96 ± 13	91 ± 15 ^a	92 ± 12 ^a
	RE	96 ± 10	82 ± 8 ^b	83 ± 11 ^b
Lactate (mmol/L)	RE + BRF	1.8 ± 0.5	4.2 ± 1.1 ^a	3.1 ± 0.8 ^a
	Matched	1.4 ± 0.2	2.4 ± 0.2	2.0 ± 0.3
	RE	1.5 ± 0.5	3.9 ± 1.4 ^a	3.2 ± 0.8 ^b

Data are the mean ± SD. RE, resistance exercise condition; RE + BFR, resistance exercise with blood flow restriction condition; Matched, resistance exercise work-matched to RE + BFR. ^a $p < 0.05$ vs. Pre, ^b $p < 0.05$ vs. Matched.

Muscle Damage: Figure 1A shows the elbow ROM. The RE + BFR condition caused a significant reduction ($p < 0.05$) in the ROM immediately after exercise ($\Delta -12.2 \pm 12.6^\circ$); however, this returned to basal values 24 h post-exercise. On the other hand, the RE condition reduced the ROM values immediately after exercise ($\Delta -13.3 \pm 11.6^\circ$), which remained reduced even after 24 h ($\Delta -8.8 \pm 12.2^\circ$) and 48 h ($\Delta -5.7 \pm 9.1^\circ$).

For CIR (Fig. 1B), both the RE and RE + BFR conditions caused significant increases ($p < 0.05$) immediately after exercise. However, for the RE + BFR condition, the CIR returned to the pre-exercise values 24 h post-exercise, while in the RE condition, the CIR remained elevated 24 h after the exercise session ($\Delta 0.7 \pm 0.8$ cm, $p < 0.05$).

The RE + BFR and matched conditions did not change the PPT values at any time point (Fig. 1C). In contrast, the RE condition caused a significant reduction in PPT ($p \leq 0.05$) immediately after exercise ($\Delta -3.8 \pm 5.6$ kg/cm²), which remained reduced 24 h ($\Delta -5.2 \pm 5.6$ kg/cm²) and 48 h post-exercise ($\Delta -3.4 \pm 4.1$ kg/cm²).

For MVC (Fig. 1D), all conditions showed a significant reduction after exercise (post-0 h, post-24 h and post-48 h). However, the reduction in MVC immediately after exercise was significantly smaller in the RE + BFR condition ($\Delta -18.8 \pm 10.9\%$, $p < 0.05$, ES: 0.78) and the matched condition ($\Delta -10.7 \pm 8.6\%$, $p < 0.01$, ES: 1.51) as compared with the RE condition ($\Delta -26.4 \pm 14.2\%$). No changes in MVC were observed among conditions 48 h post-exercise.

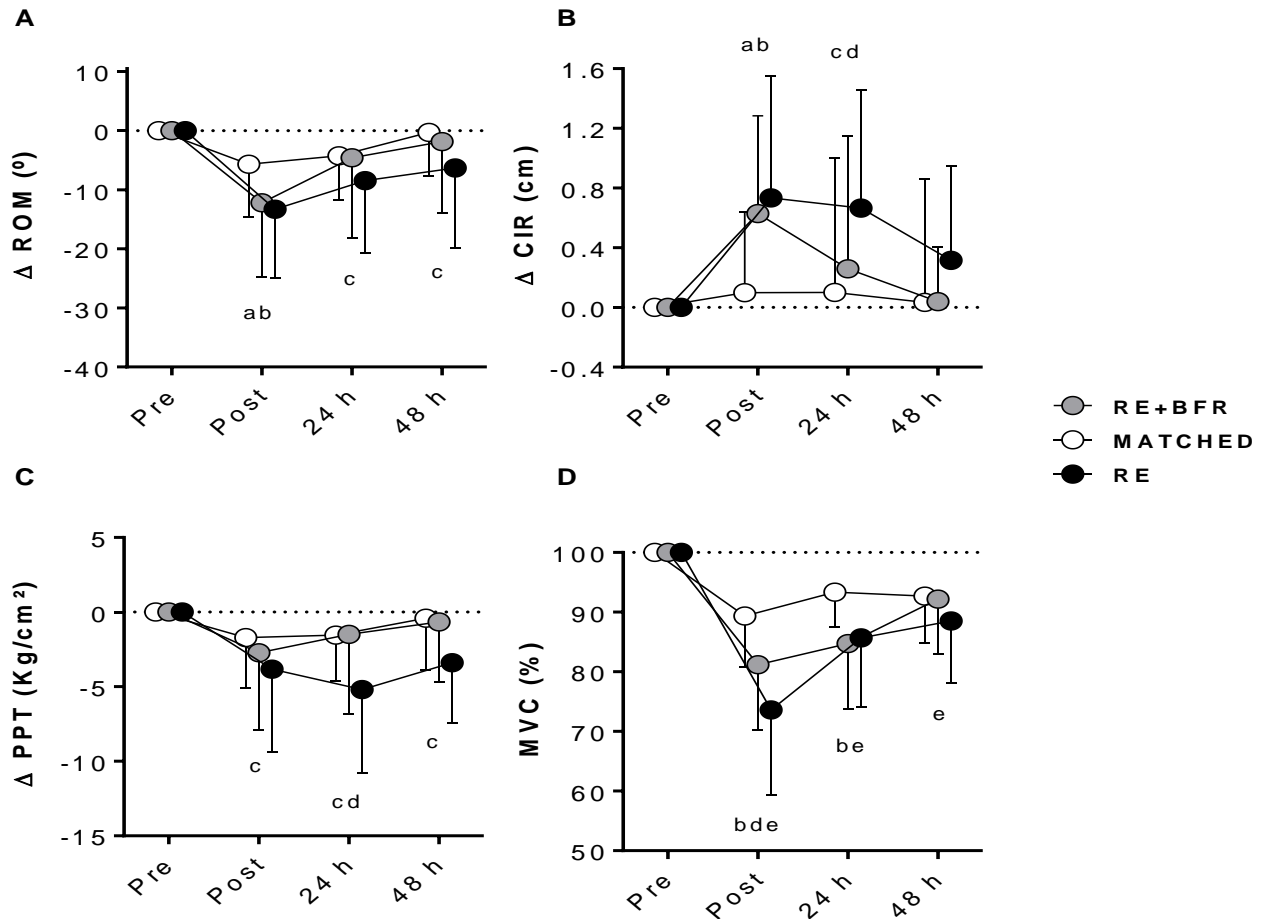


Figure 1. Indirect muscle damage analysis. Data are the mean \pm SD. ROM, range of motion; CIR, upper arm circumference; PPT, pressure pain threshold; MVC, maximum voluntary isometric contraction; RE, resistance exercise condition; RE + BFR, resistance exercise with blood flow restriction condition; Matched, resistance exercise work-matched to RE + BFR. ^a $p < 0.05$, RE and RE + BFR vs. Pre, ^b $p < 0.05$, RE and RE + BFR vs. Matched, ^c $p < 0.05$, RE vs. Pre, ^d $p < 0.05$, RE vs. RE + BFR and Matched, and ^e $p < 0.05$, all conditions vs. Pre.

The CK activity showed a significant increase ($p < 0.05$) 24 h post-exercise in all conditions (Table 5). However, in the RE + BFR condition, the CK increase was lower than in the RE condition (RE + BFR: $\Delta 215.8 \pm 227.7$ U/L vs. RE: $\Delta 405.1 \pm 461.7$ U/L, $p < 0.05$, ES: 0.61). Furthermore, CK returned to the basal values 48 h post-exercise in the RE + BFR condition, while in the RE condition, the CK remained significantly high ($p < 0.05$).

Serum LDH (Table 5) activity also showed a significant increase 24 h post-exercise in all conditions. However, in the RE + BFR condition, the LDH increases were lower than in the RE condition (RE + BFR: $\Delta 34.5 \pm 27.8$ U/L vs. RE: $\Delta 57.4 \pm 39.5$ U/L, $p < 0.05$, ES: 0.36). LDH activity returned to basal values in all conditions 48 h after exercise.

Table 5. Serum activity of CK and LDH at different time points (Basal, 24 h and 48 h after exercise sessions).

Variable	Protocol	Basal	24 h	48 h
CK (U/L)	RE + BFR	205 ± 134	448 ± 307 ^a	279 ± 295
	Matched	“	334 ± 295 ^a	193 ± 109
	RE	“	647 ± 528 ^{ab}	369 ± 373 ^{ac}
LDH (U/L)	RE + BFR	143 ± 27	183 ± 40 ^a	157 ± 32
	Matched	“	163 ± 24 ^a	147 ± 26
	RE	“	192 ± 53 ^{ab}	157 ± 45

Data are the mean ± SD. CK, creatine kinase; LDH, lactate dehydrogenase; RE, resistance exercise condition; RE + BFR, resistance exercise with blood flow restriction condition; Matched, resistance exercise work-matched to RE + BFR. ^a*p* < 0.05 vs. Basal, ^b*p* < 0.05 vs. RE + BFR and Matched, ^c*p* < 0.05 vs. Matched.

DISCUSSION

This study aimed to evaluate the effects of BFR on exercise-induced muscle damage (EIMD) during low-intensity exercise performed until CMF. As expected, it was observed a drastic drop in the number of repetitions during the BFR condition until the CMF, however, metabolic responses were similar when compared to the condition without BFR. Even with similar metabolic responses, the present study highlights for the first time that BFR can prevent exercise-induced muscle damage (EIMD) when exercise is performed until CMF.

Our first hypothesis for less exercise-induced muscle damage under BFR conditions is the relationship between metabolic stress and reduced work volume. Classically, high-intensity exercise induces muscle damage by mechanical stress, which is considered the primary factor in muscle adaptive response (25). However, high-volume resistance exercise also induces muscle damage similar to that seen with high-intensity resistance exercise (2). Furthermore, studies have shown that BFR decreases the capacity to perform exercise volume, inducing an early CMF (12, 13), which has been associated with increased metabolic stress (39). Therefore, considering that our results show that the BFR caused a significant decrease in the maximal work volume with similar metabolic responses, the lower muscle damage observed in the BFR condition may be associated with the lower maximal workload performed.

Another possible hypothesis why BFR attenuated muscle damage caused by resistance exercise may be attributed to the following mechanisms: an increase in [Ca²⁺] (33), accumulation of intramuscular metabolites (21), and higher fiber recruitment (18). Moreover, it has been shown that circulating neutrophils are involved in muscle damage by migrating into the muscle tissue and inducing inflammation (15), and BFR may reduce this infiltration of neutrophils and subsequent muscle inflammation. Therefore, this hypothesis may be considered a possible mechanism to explain the results reported by Sudo et al., (28) and Curty et al., (9), in which BFR attenuated muscle damage induced by high-intensity eccentric resistance exercise.

Since BFR induces a lower work volume and muscle damage, it is noteworthy that this is a sufficient condition to cause chronic musculoskeletal adaptations similar to those seen following

low (12) and high-intensity resistance exercises (26). In addition, it has already been shown that muscle damage does not necessarily need to occur to result in muscle hypertrophy (10, 27), and that the symptoms of severe muscle damage can last days after the exercise session, consequently requiring longer rest periods than that following BFR training (9). Thus, low-intensity resistance exercise combined with BFR may be an alternative method of resistance training resulting in less damage to muscle tissue.

The present study sought to understand whether BFR can prevent muscle damage induced by low-intensity resistance exercise performed until CMF. Recently, it has been shown that to use high-intensity resistance exercise to induce an additional gain in strength, it is not necessary to exercise until CMF (19). These data suggest that a submaximal repetition regimen is sufficient to promote strength gains. However, on the other hand, when resistance exercise is performed with low-intensity, repetitions until CMF appear to be essential for an increase in muscle strength and hypertrophy (22). Furthermore, using BFR combined with low-intensity resistance exercise performed until CMF can also induce muscle hypertrophy independent of differences in the final work volume (12). Thus, low-intensity resistance exercise combined with BFR is an alternative since it consumes much less time per exercise session, requires a low external load, which may be beneficial for individuals with recent injury and surgery, and does not require long periods of rest between exercise sessions, once the muscle damage is lower than that caused by the RE condition.

Optimal applied pressure is an important factor when studying RE under BFR conditions. However, the devices restricting blood flow have also evolved between studies. In our study, we set applied pressure based on the measurement of arterial occlusion pressure since it considers the characteristics of the cuff and the individual, which account for significant influences in the occlusion stimulus. For example, larger limb sizes require greater pressure and wider cuffs require lower pressure. Several studies have addressed the differences in BFR protocols and devices. These differences may result in inconsistencies between studies and should be considered when interpreting new findings (5, 8, 11).

In conclusion, blood flow restriction attenuates the muscle damage caused by low-intensity resistance exercise performed until concentric muscle failure in trained subjects. In addition, our exercise protocol with BFR caused metabolic stress as high as that seen by exercising until concentric muscle failure, although with less work volume performance.

Our data have practical applications both in sports and clinical settings. From the athlete's point of view, we believe that BFR may be helpful during periods of high training volume, promoting improved recovery between training sessions and competitions. On the clinical application, we see the BFR as an effective option to boost muscle mass and strength gains, imposing less overload on the joints and promoting faster recovery in muscle function between training sessions. It can, therefore, be an exciting strategy in the clinical environment for patients with functional limitations.

Some limitations of the study should be raised. First, the isokinetic was used only for the evaluation of the MVC but other isometric assessments could also have been obtained that would add the interpretation of the loss of muscle performance by the RE protocols. However, it is well accepted that the MVC is the best marker to identify muscle damage in human beings, as it is directly related to the magnitude and change in the temporal course that occurs after EIMD (6, 31). Second, the CR-10 scale was used, while, as it was a study using RE, the OMNI-RES scale could also have been used. However, Lagally et al. in 2006 (32) demonstrated that the OMNI-RES presents a positive linear correlation of $R = 0.94-0.97$ with the CR-10 scale, indicating that both scales measure the same property of effort in resistance exercise.

From future study perspectives, we intend to understand the molecular differences in blood circulation when exercise is practiced with the BFR. We and others have already shown that BFR can prevent EIMD when associated with RE, but few studies are available on the body's biochemical responses in these situations. Since we have already proposed cfdDNA as a marker for EIMD and BFR decreases EIMD, we now seek to study the response of cfdDNA in different conditions of BFR.

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