

Effects of exercise intensity and occlusion pressure after 12 weeks of resistance training with blood-flow restriction

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Abstract

Purpose We compared the effects of different protocols of blood-flow restriction training (BFRT) with different occlusion pressures and/or exercise intensities on muscle mass and strength. We also compared BFRT protocols with conventional high-intensity resistance training (RT).

Methods Twenty-six subjects had each leg allocated to two of five protocols. BFRT protocols were performed at either 20 or 40 % 1-RM with either 40 or 80 % occlusion pressure: BFRT20/40, BFRT20/80, BFRT40/40, and BFRT40/80. Conventional RT was performed at 80 % 1-RM (RT80) without blood-flow restriction. Maximum dynamic strength (1-RM) and quadriceps cross-sectional area (CSA) were assessed at baseline and after 12 weeks.

Results Regarding muscle mass, increasing occlusion pressure was effective only at very low intensity (BFRT20/40 0.78 % vs. BFRT20/80 3.22 %). No additional increase was observed at higher intensities (BFRT40/40 4.45 % vs. BFRT40/80 5.30 %), with no difference between the latter protocols and RT80 (5.90 %). Exercise intensity played a role in CSA when comparing groups with similar occlusion pressure. Muscle strength was similarly

increased among BFRT groups (~12.10 %) but to a lesser extent than RT80 (21.60 %).

Conclusion In conclusion, BFRT protocols benefit from higher occlusion pressure (80 %) when exercising at very low intensities. Conversely, occlusion pressure seems secondary to exercise intensity in more intense (40 % 1-RM) BFRT protocols. Finally, when considering muscle strength, BFRT protocols seem less effective than high-intensity RT.

Keywords Occlusion training · Strength training · Muscle hypertrophy · Occlusion pressure · Exercise intensity · Muscle strength

Abbreviations

1-RM	One-repetition maximum dynamic strength
BFRT	Blood-flow restriction training
CSA	Cross-sectional area
ES	Effect size
ES _{CLdiff}	Confidence intervals of the effect size
MRI	Magnetic resonance imaging
RT	Resistance training

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Introduction

Chronic periods of low-intensity resistance training [i.e., 20 % of the one repetition maximum dynamic strength (1-RM) associated with partial blood-flow restriction (BFRT)] has been shown to promote increases in muscle size and strength comparable to those observed after conventional high-intensity resistance training (i.e., 80 % 1-RM) (Karabulut et al. 2010; Kubo et al. 2006; Laurentino et al. 2012; Lowery et al. 2014; Takarada et al. 2000).

Despite the alleged efficiency of BFRT, a multitude of training protocols is found in the literature, with great discrepancy in training volume and intensity as well as in occlusion pressure and cuff type between studies (Laurentino et al. 2012; Loenneke et al. 2012b; Takarada et al. 2000; Yasuda et al. 2011). Such differences hamper the comparison between studies and, consequently, little is known about the magnitude of the training-induced effects on neuromuscular adaptations when BFRT variables are manipulated (Loenneke et al. 2012b), especially when compared with conventional high-intensity RT.

In this regard, acute studies have suggested that increases in occlusion pressure may enhance the training-related response to BFRT (Loenneke et al. 2014a; Sugaya et al. 2011; Takarada et al. 2000; Yasuda et al. 2009). For instance, Loenneke et al. (2014a, b) observed a likely greater muscle activation after a BFRT protocol (20 or 30 % 1-RM) consisted by 50 % as compared to 40 % of the estimated arterial occlusion pressure. In support to this notion, increased occlusion pressure (i.e., 230 vs. 180-mmHg) has also been shown to induce greater phosphate inorganic accumulation (Sugaya et al. 2011), which has been considered as a well-known marker of muscle fatigue, leading, ultimately, to greater recruitment of fast-twitch fibers (Suga et al. 2009). Importantly, the latter has been associated with more pronounced training adaptations (e.g., muscle hypertrophy) (Takada et al. 2012).

In addition to the occlusion pressure, exercise intensity is also thought to mediate the acute responses to BFRT (Loenneke et al. 2014a; Suga et al. 2010). Loenneke et al. (2014a) observed greater muscle activation after BFRT with higher exercise intensity (i.e., 30 vs. 20 % 1-RM) while maintaining the occlusion pressure constant. Similarly, Suga et al. (2010) reported greater recruitment of fast-twitch fibers after a higher (40 % 1-RM) as compared to a lower intensity (20 % 1-RM) BFRT protocol. The authors also found that increases in exercise intensity were paralleled by increased metabolic stress.

Despite the previously demonstrated positive associations between metabolic stress and BFRT parameters, namely occlusion pressure and exercise intensity (Suga et al. 2009, 2010, 2012), the chronic effects of different BFRT exercise intensities and occlusion pressures on muscle mass and strength have not been tested, especially when comparing its effects against the standard RT recommendation (i.e., high-intensity conventional resistance training). In this respect, it seems plausible to suggest that greater occlusion pressure and/or exercise intensity may enhance the neuromuscular response to chronic periods of BFRT.

Therefore, the present study aimed to compare the effects of BFRT protocols with different occlusion pressures and/or exercise intensities on muscle mass and strength in response to a 12-week BFRT period. A secondary purpose was to compare the BFRT protocols with a standard high-intensity RT recommendation (i.e., conventional training at 80 % 1-RM).

Methods

Participants

Thirty-five male subjects volunteered to participate in the study. Subjects were not engaged in any kind of regular resistance training and/or aerobic training for at least 6 months prior to the experimental period and were free from any musculoskeletal disorders. Nine subjects withdrew from the study due to personal reasons, therefore, data from twenty-six subjects were considered for analysis. Subjects' main characteristics (at baseline) are presented in Table 1. All of the subjects gave their informed consent before the enrollment in the study. The study was conducted according to the Declaration of Helsinki and the University's Research Ethics Committee approved the experimental protocol.

Table 1 Subjects' main characteristics at baseline

Groups	<i>N</i>	Age (years)	Height (m)	BM (kg)	BMI (kg m ² ⁻¹)
BFRT20/40	11	26.1 ± 7.6	1.76 ± 0.1	80.6 ± 19.7	25.9 ± 5.6
BFRT20/80	14	28.9 ± 8.7	1.75 ± 0.1	75.3 ± 10.7	24.6 ± 3.3
BFRT40/40	8	26.1 ± 7.6	1.74 ± 0.1	74.7 ± 9.5	24.7 ± 2.1
BFRT40/80	10	28.9 ± 9.2	1.77 ± 0.1	78.9 ± 20.7	25.0 ± 5.8
RT80	9	29.2 ± 9.9	1.75 ± 0.1	74.9 ± 7.7	24.6 ± 2.7

Data are presented as means and standard deviations

BM body mass; *BMI* body mass index; *n* one subject leg; *RT* resistance training; *BFRT* blood-flow restriction training; *BFRT20/40* 20 % 1-RM, 40 % occlusion pressure; *BFRT20/80* 20 % 1-RM, 80 % occlusion pressure; *BFRT40/40* 40 % 1-RM, 40 % occlusion pressure; *BFRT40/80* 40 % 1-RM, 80 % occlusion pressure; *RT80* 80 % 1-RM without blood-flow restriction

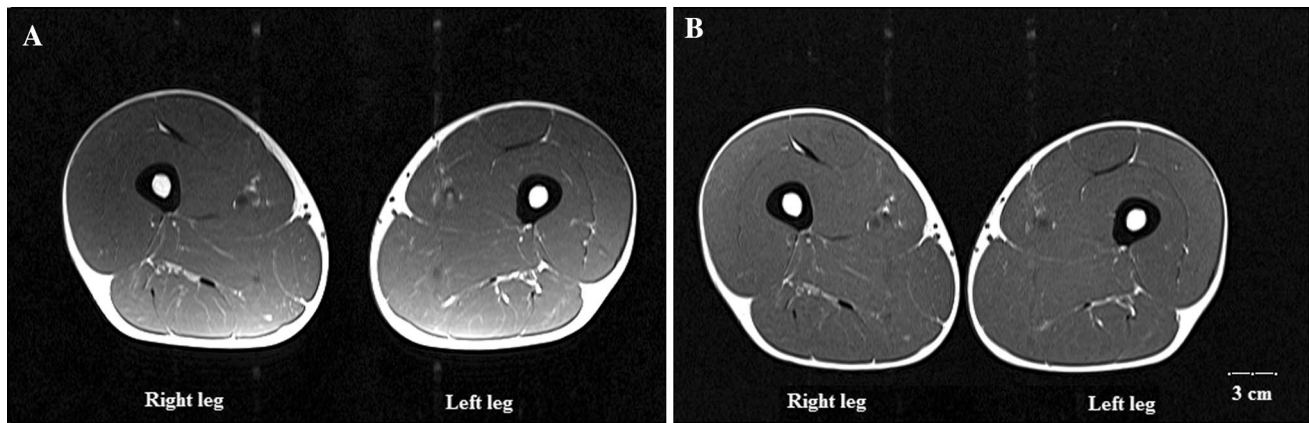


Fig. 1 Quadriceps muscle magnetic resonance imaging in the axial plane for the same subject; **a** pre and **b** post 12 weeks of training

Experimental procedures

Before the 12-week experimental period, quadriceps muscle cross-sectional area (CSA) was assessed by magnetic resonance imaging (MRI). After that, subjects performed two familiarization sessions to both, the unilateral knee-extension 1-RM test and training protocols. Familiarization sessions were interspaced by 48 h. Seventy-two hours after the last familiarization session, 1-RM test was performed to assess quadriceps muscle strength. To reduce inter-subjects variability, each subject's leg was allocated—in a randomized and balanced way, according to quadriceps muscle CSA and dominance—to one of the five exercise protocols [this procedure has been reported elsewhere (Mitchell et al. 2012)]. In short, subjects' legs were divided into quartiles according to quadriceps muscle CSA; afterwards, legs within each quartile were allocated by dominance into the five experimental groups in a balanced way: (1) BFRT20/40: 20 % 1-RM with 40 % occlusion pressure; (2) BFRT20/80: 20 % 1-RM with 80 % occlusion pressure; (3) BFRT40/40: 40 % 1-RM with 40 % occlusion pressure; (4) BFRT40/80: 40 % 1-RM with 80 % occlusion pressure; and (5) RT80: 80 % 1-RM without blood-flow restriction. Participants completed 12 weeks of unilateral knee-extension resistance training. After the sixth week (12th session), 1-RM was re-assessed to adjust training load. Seventy-two hours after the last training session (24th session), quadriceps muscle CSA and 1-RM were re-assessed.

Quadriceps muscle cross-sectional area

Quadriceps muscle CSA was obtained through MRI (Signa LX 9.1, GE Healthcare, Milwaukee, WI, USA). Subjects lay on the device in a supine position with the knees extended for approximately 20 min to allow fluid shift (Berg et al. 1993). Velcro straps were used to restrain

knee movements during image acquisition. An initial image was captured to determine the perpendicular distance from the greater trochanter to the inferior border of the lateral epicondyle of the femur, which was defined as quadriceps length. Quadriceps muscle CSA image was acquired at 50 % of the segment length in 8-mm slices for 3 s. The pulse sequence was performed with a view field between 400 and 420 mm, time repetition of 350 ms, echo time from 9 to 11 ms, two signal acquisitions, and matrix of reconstruction of 256×256 . Images were transferred to a workstation (Advantage Workstation 4.3, GE Healthcare, Milwaukee, WI, USA) for quadriceps muscle CSA determination. In short, segment slice was divided into the following components: skeletal muscle, subcutaneous fat tissue, bone and residual tissue (Fig. 1 depicts a representative pre- and post-image for quadriceps CSA determination). Finally, quadriceps muscle CSA was measured by computerized planimetry (i.e., CSA was contoured following the muscle fascia using an 800 dpi mouse) in two different days, 72 h apart (intra-researcher reliability). The coefficient of variation between measurements was less than 1 %. MRI files had a dicom extension (i.e., Digital Imaging and Communications in Medicine), which ensured that all of the machine's settings (i.e., conversion factors) were recorded in the files.

Maximum dynamic strength

Unilateral quadriceps maximum dynamic strength was assessed using the 1-RM test on a leg-extension machine (Movement technology®, Brudden, Sao Paulo, Brazil) following previous recommendations (Brown and Weir 2001). Briefly, the protocol consisted of a 5-min general warm-up on a treadmill (Movement technology®, Brudden, São Paulo, Brazil) at 9 km h^{-1} . This was followed by a specific warm-up consisted of one set of eight repetitions at 50 %

Table 2 Training protocols

Protocols	1-RM (%)	Blood-flow pressure (%)	Interval (s)	Blood-flow pressure (mmHg)	Weeks 1–12	
					Sets	Repetitions
BFRT20/40	20	40	60	55.5 ± 7.6	2–3	15
BFRT20/80	20	80	60	109.6 ± 9.4	2–3	15
BFRT40/40	40	40	60	54.5 ± 4.6	2–3	15
BFRT40/80	40	80	60	105.0 ± 18.5	2–3	15
RT80	80	0	60	0	2–3	10

Data are presented as means and standard deviations

RT resistance training; BFRT blood-flow restriction training; 1-RM one repetition maximum dynamic strength; blood-flow pressure (%) delta percentage of total occlusion pressure

of the estimated 1-RM, followed by one set of three repetitions at 70 % of the estimated 1-RM with a 1-min rest between sets. After a 3-min resting period, subjects had up to five attempts to achieve their 1-RM. The smallest incremental load for the next attempt was approximately one kilogram. A 3-min rest interval was allotted between attempts and the higher load achieved (full eccentric–concentric movement with 90° range of motion) was considered as 1-RM.

Determination of the blood-flow restriction pressure

Before the commencement of the training protocol, blood-flow restriction pressure was determined. Subjects were asked to comfortably lie supine—for approximately 10 min—while a vascular Doppler probe (DV-600, Marted, Ribeirão Preto, SP, Brazil) was placed over the tibial artery to capture its auscultatory pulse. Cuff pressure (mmHg) necessary for complete blood-flow restriction (pulse elimination pressure) was determined by attaching a standard blood pressure cuff (175 × 92 mm; JPJ Industria Comercio Assistencia tecnica Mat Hospitalar Ltda Me, Sao Paulo, Brazil) to the participant's thigh (inguinal fold region) and then inflating it up to the point in which the auscultatory pulse was interrupted (Gualano et al. 2010). For visual details on the procedures for the determination of blood-flow restriction pressure and administration of BFRT, please refer to previous detailed description from our group (Gualano et al. 2010).

Resistance training protocols

Resistance training protocols were performed unilaterally using a conventional leg-extension machine (Movement technology®, Brudden, São Paulo, Brazil), twice a week for 12 weeks (a total of 24 sessions). At the beginning of the training session subjects performed a general warm-up on a treadmill (Movement technology®, Brudden, São Paulo, Brazil) at 9 km h⁻¹ for 5 min. After that, the cuff

(175 × 92 mm) was placed proximately upon the thigh (inguinal fold region) and inflated according to each experimental group training protocol. For all the BFRT protocols the occlusion pressure was maintained throughout the exercise session. During the first 2 weeks of training, all groups performed two sets of exercise. From week 3 onwards (until the completion of the trial), exercise volume was increased to three sets of exercise for all subjects. Table 2 summarizes the five training protocols.

Statistical analysis

Data are presented as means and standard deviations. Data were analyzed with a magnitude-based inference using effect sizes (ES). The estimated mean and standard deviation delta changes from each group were used to calculate effect sizes and confidence interval (CI) for between-groups comparisons. Additionally, the effect size and confidence interval for each group was calculated for within-group comparison (pre vs. post). Several authors have suggested the use of effect sizes for between-groups comparisons, as they do not give a dichotomic answer (i.e., significant or not significant) allowing for the determination of the magnitude of the treatment effect and the interpretation of its practical significance (Nakagawa and Cuthill 2007). Thus, confidence intervals of ES of the differences between delta scores (ES_{CI_{diff}}) were calculated using a non-central *t* distribution to perform two between-groups analyses. In the first between-groups analysis, the BFR groups were used (compared) to identify possible intensity and occlusion pressure effects on muscle strength and mass. In the second between-groups comparisons, the RT80 group was used as a control condition. Thus, all BFR groups were compared against RT80 to test if the BFR protocols produced similar muscle strength and mass gains than RT80. Positive and negative confidence intervals [i.e., not crossing zero (0)] were considered as significant. In addition, the absolute delta changes for each dependent variable (CSA and 1-RM) were analyzed by a one-way ANOVA. Significance level

Table 3 Changes in quadriceps muscle cross-sectional area (CSA) and one repetition maximum dynamic strength (1-RM) before (week 0), after 6 weeks (week 6) and after 12 weeks of intervention (week 12)

Groups	CSA (cm ²)		1-RM (kg)		
	Week 0	Week 12	Week 0	Week 6	Week 12
BFRT20/40	87.9 ± 16.0	88.6 ± 15.3	88.2 ± 20.9	90.8 ± 21.4	97.3 ± 22.4
BFRT20/80	86.2 ± 10.9	89.0 ± 11.0	87.1 ± 15.0	91.1 ± 17.7	98.6 ± 18.3
BFRT40/40	81.8 ± 12.1	85.4 ± 12.5	86.9 ± 19.3	90.3 ± 20.8	97.5 ± 20.9
BFRT40/80	87.9 ± 13.0	92.5 ± 12.8	89.5 ± 19.8	92.4 ± 18.7	100.8 ± 20.1
RT80	83.5 ± 10.9	88.5 ± 11.5	86.1 ± 13.6	96.0 ± 15.7	104.7 ± 18.8

Data are presented as means and standard deviations

RT resistance training; BFRT blood-flow restriction training; BFRT20/40: 20 % 1-RM, 40 % occlusion pressure; BFRT20/80 20 % 1-RM, 80 % occlusion pressure; BFRT40/40 40 % 1-RM, 40 % occlusion pressure; BFRT40/80 40 % 1-RM, 80 % occlusion pressure; RT80 80 % 1-RM without blood-flow restriction

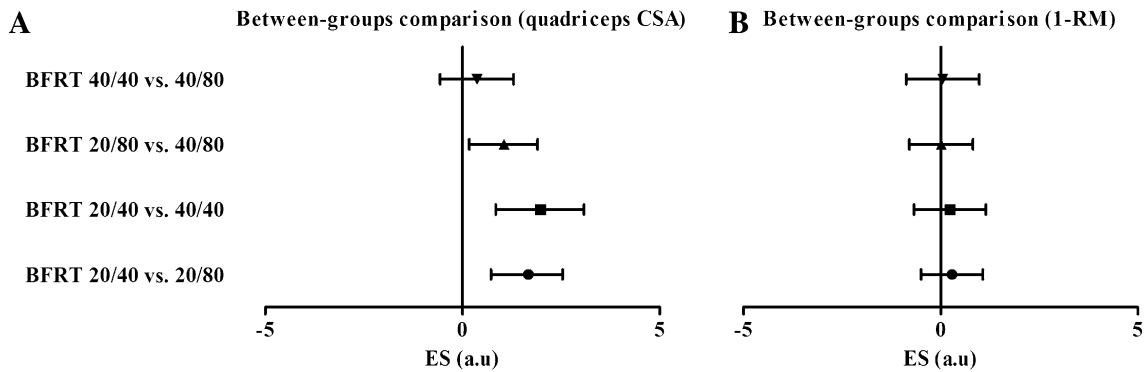


Fig. 2 Effect size (ES) and confidence interval comparisons between BFRT protocols. **a** Quadriceps muscle cross-sectional area (CSA) and **b** maximum dynamic strength (1-RM). Positive and negative confidence intervals [i.e., not crossing zero (0)] were considered as significant. BFRT: blood-flow restriction training; BFRT20/40: 20 %

1-RM, 40 % occlusion pressure; BFRT20/80: 20 % 1-RM, 80 % occlusion pressure; BFRT40/40: 40 % 1-RM, 40 % occlusion pressure; BFRT40/80: 40 % 1-RM, 80 % occlusion pressure. Values are presented as the difference in ES between BFRT protocols

was set at $p < 0.05$. Statistical analyses were performed using SAS 9.3 Software (SAS Institute Inc., Cary, NC).

Results

Quadriceps muscle CSA

Quadriceps muscle CSA increased significantly from pre- to post-test (within-group comparison) in all groups except BFRT20/40 (BFRT20/40 0.78 %, ES 0.04, CI -0.01 to 0.08; BFRT20/80 3.22 %, ES 0.25, CI 0.14–0.36; BFRT40/40 4.45 %, ES 0.29, CI 0.11–0.47; BFRT40/80 5.30 %, ES 0.36, CI 0.17–0.55, RT80 5.90 %, ES 0.42, CI 0.19–0.65) (Table 3).

The comparison between the BFRT groups demonstrated that increasing occlusion pressure was effective on augmenting muscle mass only when training at lower intensities (i.e., BFRT20/80 vs. BFRT20/40: ES_{Cl_{diff}} 0.74–2.54). Accordingly, occlusion pressure did not have a significant effect when comparing higher intensity BFRT

groups (40/80 vs. 40/40: ES_{Cl_{diff}} -0.57 to 1.29). Training intensity had a significant effect in increasing quadriceps CSA when comparing BFRT groups with the same occlusion pressure. The BFRT 40/40 and 40/80 presented greater increases in muscle CSA than their respective counterparts with the same occlusion pressure (BFRT 20/40 and 20/80; ES_{Cl_{diff}} 0.84–3.08 and 0.17–1.90, respectively) (Fig. 2a). The comparison of the BFRT groups having the RT80 as a control condition unraveled an intensity effect (Fig. 3a). The BFRT 20/40 and 20/80 groups showed a lower hypertrophy response of the quadriceps CSA as compared with RT80 (ES_{Cl_{diff}} -4.04 to -1.55 and -2.49 to -0.58, respectively). The BFRT 40/40 and 40/80 groups had similar hypertrophy to RT80 as the respective confidence intervals of the effect sizes did cross zero (ES_{Cl_{diff}} -1.63 to 0.31 and -1.11 to 0.68, respectively).

Overall, the inferential analyses points in the same direction as BFRT20/40 had significantly smaller increase in muscle CSA as compared with BFRT20/80 ($p = 0.014$), evidencing the positive effect of occlusion pressure when training at lower exercise intensities. Similar to our magnitude-based

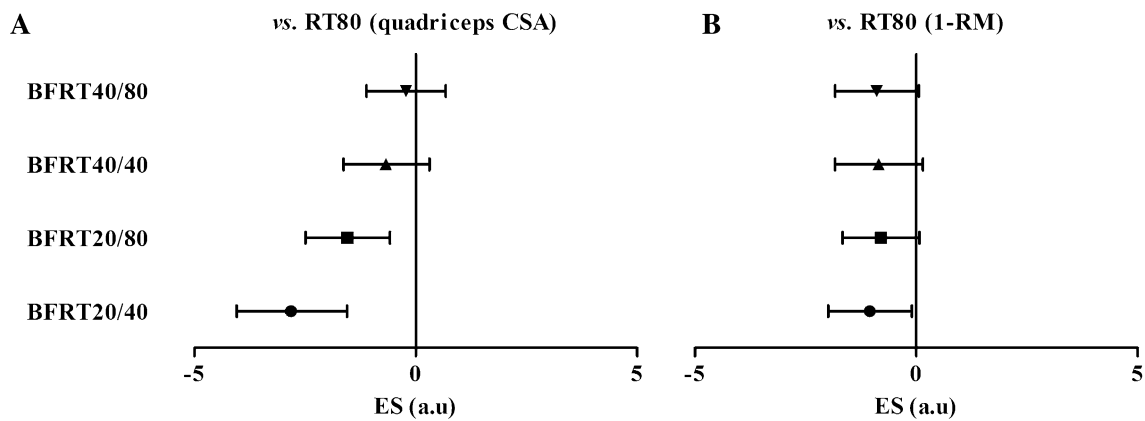


Fig. 3 Effect size (ES) and confidence intervals comparisons between BFRT protocols vs. RT80. **a** quadriceps muscle cross-sectional area (CSA) and **b** maximum dynamic strength (1-RM). Positive and negative confidence intervals [i.e., not crossing zero (0)]; were considered as significant. BFRT: blood-flow restriction training; RT: resistance training; BFRT20/40: 20 % 1-RM, 40 % occlusion pres-

sure; BFRT20/80: 20 % 1-RM, 80 % occlusion pressure; BFRT40/40: 40 % 1-RM, 40 % occlusion pressure; BFRT40/80: 40 % 1-RM, 80 % occlusion pressure; and RT80: 80 % 1-RM without blood-flow restriction. Values are presented as the difference in ES between BFRT protocols and RT80

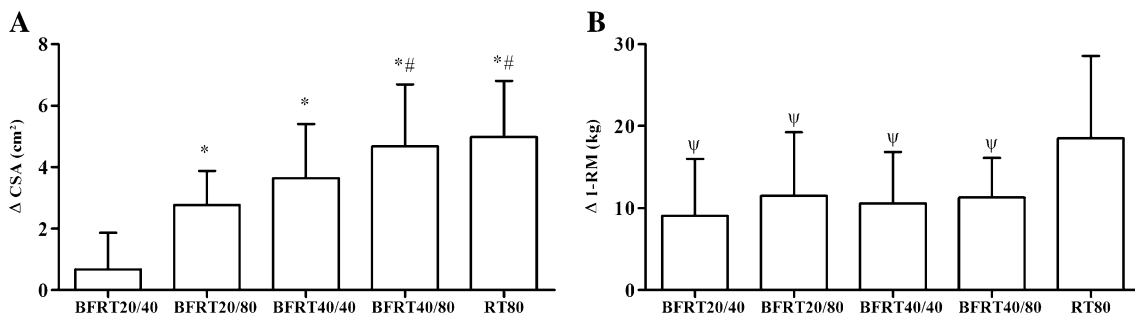


Fig. 4 Absolute delta changes (Δ) from pre to post the 12-week training period. **a** quadriceps muscle cross-section area (CSA) and **b** maximum dynamic strength (1-RM). RT: resistance training; BFRT: blood-flow resistance training; BFRT20/40: 20 % 1-RM, 40 % occlusion pressure; BFRT20/80: 20 % 1-RM, 80 % occlusion pressure; BFRT40/40: 40 % 1-RM, 40 % occlusion pressure; BFRT40/80:

40 % 1-RM, 80 % occlusion pressure; RT80: 80 % 1-RM without blood-flow restriction. Asterisk $p < 0.05$ when compared with BFRT20/40 and hash $p < 0.05$ when compared with BFRT20/80 (**a**); Greek capital letter psi $p < 0.05$ when compared with RT80 (**b**). Data are presented as means and standard deviations

inference analyses, occlusion pressure manipulation did not alter the hypertrophic response when exercising at higher intensities (i.e., BFRT40/40 vs. BFRT40/80, $p = 0.655$). Furthermore, delta change analyses confirmed that increased exercise intensity had a positive effect on muscle growth when comparing BFRT protocols with similar occlusion pressures (i.e., BFRT20/40 vs. BFRT40/40, $p = 0.001$ and BFRT20/80 vs. BFRT40/80, $p = 0.043$). Finally, BFRT-induced increase in quadriceps CSA was similar to that of RT80 only when training at higher intensities (i.e., BFRT40/40 and BFRT40/80 vs. RT80, $p = 0.409$ and $p = 0.999$, respectively). Conversely, lower intensity BFRT resulted in a lesser muscle mass accrual when compared with RT80 (i.e., BFRT20/40 and BFRT20/80 vs. RT80, $p < 0.0001$ and $p = 0.015$, respectively) (Fig. 4a).

Maximum dynamic strength

All tested protocols promoted increases in maximum dynamic strength when compared to baseline (within-group comparison; BFRT20/40 10.30 %, ES 0.41, CI 0.15–0.66; BFRT20/80 13.20 %, ES 0.63, CI 0.30–0.96; BFRT40/40 12.20 %, ES 0.50, CI 0.17–0.85; BFRT40/80 12.70 %, ES 0.56, CI 0.26–0.86, RT80 21.60 %, ES 0.99, CI 0.39–1.59) (Table 3).

The comparisons between the BFRT groups showed similar increases in maximum dynamic strength, as all of the confidence intervals crossed zero (ES_{CI diff}: 20/40 vs. 20/80 -0.5 to 1.07 ; 20/40 vs. 40/40 -0.68 to 1.14 ; 20/80 vs. 40/80 -0.79 to 0.82 ; and 40/40 vs. 40/80 -0.87 to 0.98), (Fig. 2b).

Figure 3b displays a likely lower training effect on maximum dynamic strength for all of the BFRT groups when compared with RT80 as the upper limits of the confidence intervals of these groups were all very close to zero (ES_{Cliff} : BFRT20/40 -1.98 to -0.09 ; BFRT20/80 -0.80 to 0.07 ; BFRT40/40 -0.85 to 0.15 ; and BFRT40/80 -0.89 to 0.06).

Inferential analysis confirmed our findings above, as neither manipulating occlusion pressure nor exercise intensity resulted in significantly different increases in muscle strength when comparing BFRT protocols (all $p > 0.05$ for between-BFRT comparisons). Additionally, as suggested by magnitude-based inference, all BFRT groups showed significant or at least a trend towards significant smaller increases in maximum dynamic strength when compared with RT80 (i.e., BFRT20/40, BFRT20/80, BFRT40/40, and BFRT40/80 vs. RT80, $p = 0.006$, $p = 0.029$, $p = 0.031$, $p = 0.036$, respectively) (Fig. 4b).

Discussion

The aims of the present study were to compare: (a) the effects of different BFRT protocols; and (b) the effects of different BFRT protocols with conventional high-intensity training at 80 % 1-RM on muscle mass and strength in response to a 12-week training period. Based on previous findings of acute studies, we hypothesized that the combination of higher exercise intensity and occlusion pressure would result in greater gains in muscle mass and strength. The main findings of the present study are: (a) occlusion pressure affected the muscle hypertrophy response only at lower training intensities; (b) exercise intensity significantly modulated the muscle mass response when comparing groups with similar occlusion pressures; (c) only higher BFRT intensities produced similar muscle hypertrophy responses to that of RT80; and (d) occlusion pressure and/or exercise intensity modulation did not affect the muscle strength response between BFRT protocols and produced likely lower muscle strength gains than RT80.

It has been speculated that higher occlusion pressure and/or higher exercise intensity protocols may be able to enhance the anabolic response to BFRT (Abe et al. 2012; Loenneke et al. 2014a, b; Suga et al. 2010; Sugaya et al. 2011; Takarada et al. 2000; Yasuda et al. 2008). This assumption is based on acute findings that increases in occlusion pressure and/or exercise intensity are capable of enhancing metabolic stress and, consequently, motor-unit recruitment (Loenneke et al. 2014a; Suga et al. 2010; Sugaya et al. 2011; Yasuda et al. 2008).

In our long-term (i.e., 12 weeks) design, we found that, in BFRT, lower exercise intensities (i.e., 20 % 1-RM) may benefit from higher occlusion pressures (i.e., 80 %) when

considering muscle mass accrual as the outcome. Unpublished data from our laboratory indicate that increased occlusion pressure seems to reduce blood flow to the muscle, which may lead to increases in phosphate inorganic accumulation (an index of muscle fatigue) (Sugaya et al. 2011). Consequently, additional motor units (mainly fast-twitch muscle fibers) are recruited to maintain force production (Pincivero et al. 2006). Provided that recruitment of fast-twitch fibers is considered as an important factor in exercise-induced muscle hypertrophy (Loenneke et al. 2011; McCall et al. 1996; Takada et al. 2012), increases in motor-unit recruitment, as those likely observed in higher occlusion-pressure BFRT protocols (Loenneke et al. 2014a), may partially explain our findings. However, despite the suggestion of a positive effect of occlusion pressure (BFRT 20/40 vs. 20/80), the gains in quadriceps CSA observed at lower BFRT intensities showed to be smaller when compared with conventional high-intensity RT, regardless of the occlusion pressure utilized. In this respect, even though acute data suggest that increasing occlusion pressure may result in additional motor-unit recruitment (Loenneke et al. 2014a), this strategy has been demonstrated to be less effective than conventional high-intensity RT (Manini and Clark 2009), supporting the current findings of a lesser effect of BFRT20/80 than RT80 on muscle mass.

Importantly, there was no additional benefit of increasing occlusion pressure in the more intense BFRT protocols (i.e., BFRT 40/40 vs. 40/80), as similar increases in muscle mass were observed between the two groups and the conventional high-intensity RT. This seems in line with a recent paper from Counts et al. (2015). Similar to our data, the authors found that increasing occlusion pressure (i.e.; from 40 to 90 %) did not promote greater muscle mass accrual in young individuals submitted to an 8-week BFRT protocol (30 % 1-RM). Collectively, this partially refutes our initial hypothesis, as we expected that combining higher intensity with higher occlusion pressure (i.e., BFRT40/80) would result in a greater hypertrophic response. It is plausible to assume that the increased exercise intensity per se resulted in significant blood-flow restriction, hindering any effect of occlusion pressure manipulation. In fact, it was previously demonstrated that moderate exercise intensities (~ 50 – 65 % maximum voluntary contraction) are sufficient to significantly reduce muscle blood flow (Sadamoto et al. 1983). Moreover, there seems to be no additive benefit of adding intermittent blood-flow restriction (i.e., 80 % occlusion pressure during exercise with released pressure during rest intervals) to moderate-intensity RT (i.e., 60 % 1-RM) on muscle mass, when compared with RT alone (Laurentino et al. 2008). Therefore, although speculative, it is possible that combining a lower than previously tested load (i.e., 40 % 1-RM) with low occlusion pressure (i.e., 40 %)

may have been sufficient to induce significant blood-flow restriction, mitigating the effect of further occlusion pressure manipulation.

The comparison between groups under the same occlusion pressure revealed an important role of exercise intensity (i.e., BFRT 20/40 vs. 40/40 and BFRT 20/80 vs. 40/80). This is in accordance with our hypothesis, as it has been previously demonstrated that increases in exercise intensity are paralleled by higher metabolic stress and motor-unit recruitment (Loenneke et al. 2014a; Suga et al. 2010), which could ultimately positively affect hypertrophy. On the other hand, recent work has demonstrated otherwise (Barcelos et al. 2015). The authors observed no between-group differences in muscle CSA between low- and moderate-intensity protocols with or without blood-flow restriction. These dissonant findings are hard to reconcile; however, one may speculate that differences in occlusion pressure protocols between the study by Barcelos et al. (2015) and ours may have influenced the results. Contrary to Barcelos et al. (2015), occlusion pressure was individualized in the present study, (see “Methods”). Importantly, it has been suggested that individualized occlusion pressure determination may be a more robust approach in BFRT studies, as it avoids under- or overestimation of occlusion pressure (Loenneke et al. 2012a), thus allowing a more accurate exercise prescription. Additionally, Barcelos et al. (2015) used failure or near-failure protocols, which has been shown to elicit similar muscle mass accrual, despite the exercise intensity utilized (Mitchell et al. 2012).

Leg-extension 1-RM data demonstrated that all BFRT groups displayed a trend towards lower muscle strength adaptations when compared with conventional high-intensity RT. One possible explanation to the discrepant response in 1-RM gains between BFRTs and high-intensity conventional RT protocols may be related to the different degree of muscle activation induced by each protocol. In fact, it has been demonstrated that high-intensity RT produces greater muscle activation as compared to low-intensity BFRT (Kubo et al. 2006; Manini and Clark 2009). However, these findings are not consensual, as others have found otherwise (Suga et al. 2012; Takarada et al. 2000); importantly, significant differences between RT protocols can be identified between these studies, which could explain the dissonant results. Kubo et al. (2006), for example, provided the high-intensity RT group—but not the BFRT group—with progressive loads throughout the intervention, limiting the conclusions of their study. Exercise total volume is also dramatically different among studies. In particular, previous works showing similar gains in muscle strength between BFRT and conventional high-intensity RT have employed either (a) repetitions-to-failure or, (b) more exercise sets and repetitions, which could have greatly affected total volume when compared with

ours (Laurentino et al. 2012; Takarada et al. 2000). Thus, additional studies should investigate the neuronal response between high- and low-intensity protocols with and without blood-flow restriction and with different exercise volumes in a submaximal or in a repetition-to-failure mode of execution. Another possible explanation for the trend towards lower muscle strength gains in the BFRT protocols as compared to high-intensity RT may be related to the specificity of the 1-RM test. In the present study, muscle strength was measured with a maximum dynamic strength test; thus, as the high-intensity group (RT80) routinely trained with higher loads, they may have had additional benefits compared to the BFRT groups using lighter loads (Mitchell et al. 2012). In fact, Mitchell et al. (2012) demonstrated lower muscle strength gains for 30 % 1-RM vs. 80 % 1-RM in a dynamic test similar to ours; however, comparable increases in muscle strength were observed between the two different intensities in a non-specific isometric strength test.

This study is not without limitations. The absence of direct measures of metabolic stress and motor-unit recruitment does not allow us to assure the alleged differences in these parameters between the tested protocols. However, results from previous studies provide strong support for our contention, as increases in blood-flow restriction pressure and/or exercise intensity have been consistently shown to enhance both metabolic stress and muscle fiber recruitment (Loenneke et al. 2014a; Sugaya et al. 2011; Yasuda et al. 2008). Finally, it is worth noting that the present results should not be extrapolated to different exercise (e.g., different combinations of occlusion pressure and exercise intensity) and pressure cuff (e.g., differences in width) conditions, as occlusion pressure is highly dependent on the type of pressure cuff utilized (Loenneke et al. 2012a).

Conclusion

The results of the present study demonstrate that BFRT protocols performed with very low exercise intensity (i.e., 20 % 1-RM) may benefit from higher levels of occlusion pressure (i.e., 80 % occlusion pressure) when attempting to improve muscle mass; although, the hypertrophic responses seem to be lower as compared to conventional RT (80 % 1-RM). Conversely, occlusion pressures seem secondary to exercise intensity in BFRT protocols using higher intensities (e.g., ~40 % 1-RM), as there seems not to be any additional benefit of combining higher exercise intensities with higher occlusion pressures to muscle hypertrophy. Additionally, training intensity had a significant effect in increasing quadriceps CSA when comparing BFRT groups with the same occlusion pressure. Regarding muscle strength, all BFRT protocols tested seem to be less effective as compared to conventional high intensity, despite the

different combinations of occlusion pressure and exercise intensities. Based on the results from the present study it is possible to suggest that exercises intensities above 20 % 1-RM should be utilized in BFRT, as this leads to significant muscle hypertrophic response despite the occlusion pressure utilized.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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