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ORIGINAL ARTICLE

Early phase adaptations in muscle strength and hypertrophy as a result of low-intensity blood flow restriction resistance training

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Abstract

Purpose Low-intensity venous blood flow restriction (vBFR) resistance training has been shown to promote increases in muscle strength and size. Eccentric-only muscle actions are typically a more potent stimulus to increase muscle strength and size than concentric-only muscle actions performed at the same relative intensities. Therefore, the purpose of this investigation was to examine the time-course of changes in muscle strength, hypertrophy, and neuromuscular adaptations following 4 weeks of unilateral forearm flexion low-intensity eccentric vBFR (Ecc-vBFR) vs. low-intensity concentric vBFR (Con-vBFR) resistance training performed at the same relative intensity.

Methods Thirty-six women were randomly assigned to either Ecc-vBFR ($n = 12$), Con-vBFR ($n = 12$) or control (no intervention, $n = 12$) group. Ecc-vBFR trained at 30% of eccentric peak torque and Con-vBFR trained at 30% of concentric peak torque. All training and testing procedures were performed at an isokinetic velocity of 120° s^{-1}.

Results Muscle strength increased similarly from 0 to 2 and 4 weeks of training as a result of Ecc-vBFR (13.9 and 35.0%) and Con-vBFR (13.4 and 31.2%), but there were no changes in muscle strength for the control group. Muscle thickness increased similarly from 0 to 2 and 4 weeks of training as a result of Ecc-vBFR (11.4 and 12.8%) and Con-vBFR (9.1 and 9.9%), but there were no changes for the control group. In addition, there were no changes in any of the neuromuscular responses.

Conclusions The Ecc-vBFR and Con-vBFR low-intensity training induced comparable increases in muscle strength and size. The increases in muscle strength, however, were not associated with neuromuscular adaptations.

Keywords Low load · Occlusion · Muscle damage · Blood flow · EMG

Abbreviations

Ecc-vBFR	Eccentric venous blood flow restriction
Con-vBFR	Concentric venous blood flow restriction
vBFR	Venous blood flow restriction
EMG	Electromyography
1RM	One-repetition maximum
MVIC	Maximal voluntary isometric contraction
SE	Standard error
ICC	Intraclass correlation coefficient
MD	Minimal difference
SEM	Standard error of measurement

Introduction

Recent studies (Abe et al. 2006; Fujita et al. 2008; Laurentino et al. 2012) have examined the effects of venous blood flow restriction (vBFR) vs. non-vBFR resistance training on muscle strength and hypertrophy. For example, 1 week of low-intensity [20% of one-repetition maximum (1RM)] vBFR leg extension resistance training increased 1RM and muscle cross-sectional area by 6.7 and 3.5%, respectively (Fujita et al. 2008). Low-intensity non-vBFR resistance training at the same intensity, however, had no effects on 1RM or muscle cross-sectional area (Fujita et al. 2008). In addition, 8 weeks of low-intensity (20% of 1RM) vBFR leg extension resistance training increased 1RM and muscle cross-sectional area by 40.1 and 6.3%, respectively, while low-intensity non-vBFR resistance training at the same intensity resulted in smaller increases of 20.7% for 1RM and no significant changes in muscle cross-sectional area (Laurentino et al. 2012).

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Previous investigations (Karabulut et al. 2010; Takarada et al. 2000; Ellefsen et al. 2015) have also demonstrated that low-intensity (≤ 50% of 1RM) vBFR resistance training elicited comparable increases in muscle strength and hypertrophy as high-intensity (≥ 50% of 1RM) non-vBFR resistance training. For example, Takarada et al. (2000) reported no differences for training-induced increases in muscle strength (18.4–22.6%) and muscle cross-sectional area (18.4–20.3%) following 16 weeks of low-intensity (30–50% of 1RM) vBFR vs. high-intensity (50–80% of 1RM) non-vBFR forearm flexion resistance training. In addition, Ellefsen et al. (2015) found no differences between 12 weeks of low-intensity (30% of 1RM) vBFR leg extension resistance training and high-intensity (60–80% of 1RM) non-vBFR resistance training for increases in 1RM (10–12%) or muscle cross-sectional area (6–7%).

It has been hypothesized that the increases in muscle strength and hypertrophy associated with low-intensity vBFR resistance training are related to cell swelling (Loenneke et al. 2012a) and/or metabolite accumulation (Loenneke et al. 2011) that stimulate the mTOR pathway via an intrinsic volume sensor (Haussinger 1996). Hoffmann et al. (2009) suggested that the changes in intracellular pH associated with cell hydration and/or swelling likely affect the anabolic responses by enhancing the activity of ion exchange pumps. In addition, unlike high-intensity non-vBFR resistance training (Phillips 2000; Moritani and deVries 1979; Staron et al. 1994), the early phase increases in muscle strength as a result of low-intensity vBFR resistance training appear to be driven primarily by hypertrophy and to a lesser extent, neuromuscular adaptations (Loenneke et al. 2012b).

Yasuda et al. (2013) reported that 6 weeks of low-intensity (30% of 1RM) concentric-only vBFR (Con-vBFR) resistance training resulted in greater increases in muscle strength (8.6 vs. 3.8%) and hypertrophy (11.7 vs. 3.9%) than eccentric-only vBFR (Ecc-vBFR) resistance training. These findings (Yasuda et al. 2013) were contrary to high-intensity non-vBFR resistance training where the increases in muscle strength and hypertrophy are typically greater during eccentric-only than concentric-only resistance training performed at a similar relative intensity (i.e., maximal eccentric vs. maximal concentric training) (Roig et al. 2009). The differences in training adaptions reported by Yasuda et al. (2013), however, may have been due to the relative training intensity that was lower during Ecc-vBFR (approximately 10% of eccentric 1RM) than Con-vBFR (30% of concentric 1RM). In addition, Yasuda et al. (2013) examined low-intensity Ecc-vBFR vs. Con-vBFR isotonic resistance training. During isotonic resistance training, the time under tension that the external load is resisted changes due to acceleration and deceleration phases and based on the trajectory of the external load relative to gravitational pull. These changes in the time duration that the external load is resisted may affect training-induced adaptations as a result of Ecc-vBFR vs. Con-vBFR. For example, Burd et al. (2012) demonstrated that muscle protein synthesis (a precursor to hypertrophy and strength adaptations) was enhanced when time under tension was increased (slow vs. fast repetitions) during work-matched leg extension muscle actions performed at 30% of 1RM. In addition, Popov et al. (2006) reported that increasing the time that the external load was maintained throughout a range of motion during leg press resistance training elicited greater increases in blood lactate, growth hormone, insulin-like growth factor, and cortisol. Together, these findings (Burd et al. 2012; Popov et al. 2006) indicated that time under tension affects the training response. During isotonic resistance training, however, it is difficult to maintain time under tension or consistent force against the external load throughout a range of motion. Thus, the present study examined the effects of low-intensity Ecc-vBFR vs. Con-vBFR isokinetic resistance training where the resistance of the external load was consistent throughout the range of motion.

Therefore, the purpose of this investigation was to examine the time-course of changes in muscle strength, hypertrophy, and neuromuscular adaptations following 4 weeks of unilateral forearm flexion low-intensity Ecc-vBFR vs. low-intensity Con-vBFR resistance training performed at the same relative intensity. Based on previous investigations (Roig et al. 2009; Loenneke et al. 2012b; Yasuda et al. 2013), we hypothesized that Ecc-vBFR would result in greater increases in muscle strength and hypertrophy than Con-vBFR, but there would be no changes in the neuromuscular responses for either mode of training.

Methods

Subjects

Thirty-six women volunteered to participate in this investigation and were randomly assigned to one of three groups: Ecc-vBFR ($n = 12$; mean age ± SD = 21.7 ± 1.0 years; body mass = 56.0 ± 6.6 kg; height = 166.4 ± 6.7 cm), Con-vBFR ($n = 12$; mean age ± SD = 22.1 ± 1.7 years; body mass = 55.4 ± 5.0 kg; height = 165.9 ± 5.2 cm), or control ($n = 12$; mean age ± SD = 23.3 ± 2.0 years; body mass = 55.7 ± 5.1 kg; height = 165.7 ± 5.5 cm). The subjects had no known cardiovascular, pulmonary, metabolic, muscular, and/or coronary heart disease, or regularly used prescription medication. All subjects were recreationally active at the time of testing, but no subjects had been actively participating in resistance training for at least the past six months. The subjects visited the laboratory on 15 occasions (familiarization, baseline, 13 testing/training visits) within a 5-week period and performed the testing procedures at the same time of day. The study was

approved by the University Institutional Review Board for Human Subjects and all subjects completed a health history questionnaire and signed a written informed consent prior to testing.

Experimental design

A randomized, repeated measures, between-group, parallel design was used for this study. Thirty-six women were randomly assigned to one of three groups: (1) low-intensity Ecc-vBFR; (2) low-intensity Con-vBFR; or (3) a control group that received no intervention. Currently, women are an understudied population in the resistance training literature and less is known regarding the effects of vBFR on muscle strength and muscle hypertrophy (Counts et al. 2016b). Venous BFR was applied using a KAATSU resistance band and vBFR was determined for each subject as 40% of the lowest amount of pressure needed to completely occlude the brachial artery as indicated by ultrasound. Subjects assigned to Ecc-vBFR trained at 30% of eccentric peak torque and Con-vBFR trained at 30% of concentric peak torque and training was performed three times per week for 4 weeks. Training consisted of 75 eccentric (Ecc-vBFR) or concentric (Con-vBFR) isokinetic muscle actions of the forearm flexors performed over four sets (1 × 30, 3 × 15) and each set was separated by 30 s of rest. The subjects in the control group did not perform resistance training or receive vBFR. All subjects performed testing procedures that were completed at the baseline, 0, 2, and 4 weeks testing visits and all testing and training procedures were performed using an isokinetic dynamometer performed at a velocity of 120° s^{-1} and were performed at the same time of day (± 2 h). During each testing session, ultrasound, muscle strength, and electromyography (EMG) were measured.

Procedures

Familiarization

The first laboratory visit consisted of an orientation session to familiarize the subjects with the testing protocols. During the orientation, subjects performed submaximal and maximal isometric muscle actions as well as submaximal and maximal concentric and eccentric isokinetic muscle actions of the forearm flexors at 120° s^{-1} on a Cybex 6000 isokinetic dynamometer. To familiarize the subjects with the training protocols, the subjects also practiced performing concentric or eccentric isokinetic muscle actions at 30% of their concentric or eccentric peak torque, respectively. Torque was visually tracked using real-time torque displayed on a computer monitor.

Determination of eccentric peak torque, concentric peak torque, and maximal voluntary isometric contraction

During the baseline, 0, 2, and 4 weeks testing visits, the subjects performed a warm-up consisting of 10 submaximal (approximately 50% effort), concentric and eccentric muscle actions of the forearm flexors performed at 120° s^{-1}. Following the warmup, the subjects rested for five minutes and then performed two randomly ordered maximal eccentric, concentric, and isometric muscle actions of the forearm flexors at 120° s^{-1} to determine the pretest eccentric peak torque, concentric peak torque, and maximal voluntary isometric contraction (MVIC) values, respectively. The highest peak torque and MVIC force produced during each of the two attempts was used for further analyses. The eccentric and concentric muscle actions were performed through a 120° range of motion (0°–120° of elbow flexion, where 0° corresponds to full extension at the elbow) and the MVIC muscle actions were performed at 45° sustained for a period of 3-s.

Eccentric and concentric training interventions

The subjects in the Ecc-vBFR and Con-vBFR groups completed 4 weeks of training at a frequency of three training sessions per week (separated by 48-h) for a total of 12 training sessions. Each training session consisted of 75 eccentric or concentric muscle actions of the forearm flexors performed over four sets (1 × 30, 3 × 15) and each set was separated by 30 s of rest (Thiebaud et al. 2013; Loenneke et al. 2016; Counts et al. 2016a; Yasuda et al. 2013). The training intervention was randomly assigned to either the dominant or non-dominant arm. All muscle actions were performed at a velocity of 120° s^{-1} and all eccentric or concentric muscle actions were followed by a passive concentric or eccentric muscle action, respectively, that was assisted by the investigator (E.C.H). The Ecc-vBFR and Con-vBFR training interventions were performed at the same relative intensity. Specifically, the Ecc-vBFR training group performed 75 eccentric muscle actions of the forearm flexors at 30% of eccentric peak torque and the Con-vBFR training group performed 75 concentric forearm flexion muscle actions at 30% of concentric peak torque. Thus, the relative training intensity, velocity and tempo, number of repetitions performed, and rest between sets were identical between the Ecc-vBFR and Con-vBFR interventions. The relative training intensity, repetitions, rest between sets, and frequency of training were consistent with previous investigations (Thiebaud et al. 2013; Loenneke et al. 2016; Counts et al. 2016a; Yasuda et al. 2013) that have examined low-intensity vBFR and were selected to optimize the training-induced adaptations on muscle strength and hypertrophy. Furthermore, a recent meta-analysis (Loenneke et al. 2012b) reported that effects sizes for increasing muscle strength and hypertrophy

as a result of vBFR resistance training were greatest using training loads of 15–30% of 1RM, performing 60–70 repetitions with 30 s between sets, performed 2–3 days per week. In addition, there were no differences in muscle thickness, whole body lactate, or muscle activation using vBFR arterial occlusion pressures of 40–90% when combined with a training load of 30% of 1RM (Loenneke et al. 2016; Counts et al. 2016a).

Venous blood flow restriction

Venous blood flow restriction was applied using a 30 mm wide cuff (KAATSU Master, Sato Sports Plaza, Tokyo, Japan) placed on the most proximal portion of the upper arm (Fig. 1). The cuff pressure was initially applied at 30 mmHg and progressively inflated and deflated over a 60-s period until the target pressure was reached. Target pressure was calculated during the baseline, 0, and 2 weeks testing visits as 40% of the lowest amount of pressure needed to completely occlude the brachial artery as indicated by ultrasound (Counts et al. 2016a; Loenneke et al. 2016, 2013). Previous investigations (Counts et al. 2016a; Loenneke et al. 2016, 2013) have indicated that 40% of vBFR induces similar training-induced responses as 90% of vBFR when combined with low-intensity training (30% 1RM). The cuff remained inflated during the duration of the training bout and was deflated immediately after completing the 75 repetitions. The total duration of vBFR was approximately five minutes.

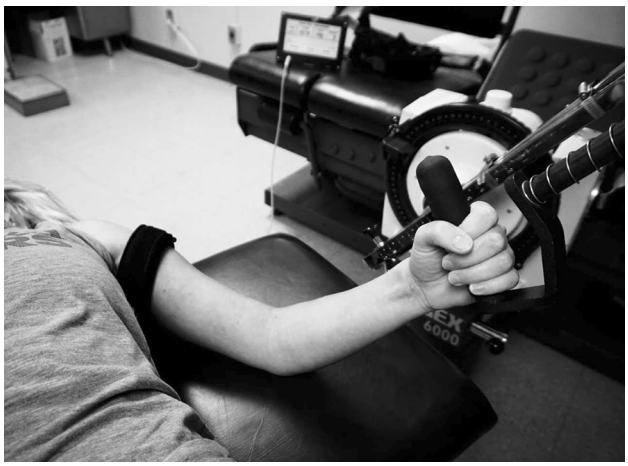

Fig. 1 Venous blood flow restriction (vBFR) was applied using a 30-mm wide cuff (KAATSU Master, Sato Sports Plaza, Tokyo, Japan) placed on the most proximal portion of the upper arm. The cuff pressure was initially applied at 30 mmHg and progressively inflated and deflated over a 60-s period until the target pressure was reached. Target pressure was calculated during the baseline, 0, and 2 weeks testing visits as 40% of the lowest amount of pressure needed to completely occlude the brachial artery as indicated by ultrasound (Counts et al. 2016a; Loenneke et al. 2016, 2013). The cuff remained inflated during the duration of the training bout and was deflated immediately after completing the 75 repetitions. The total duration of vBFR was approximately five minutes

Neuromuscular

During baseline, 0, 2, and 4 weeks testing visits, pre-gelled surface electrodes (Ag/AgCl, AccuSensor, Lynn Medical, Wixom, MI, USA) were placed in a bipolar arrangement (30 mm center-to-center) on the biceps brachii muscle of the trained arm according to the recommendations of Barbero et al. (2012). The reference electrode was placed over the acromion process and prior to each electrode placement, the skin was shaved, carefully abraded, and cleaned with alcohol. The raw EMG signals were digitized at 2000 Hz with a 32-bit analog-to-digital converter (Model MP150, Biopac Systems, Inc.) and stored in a personal computer (ATIV Book 9 Intel Core i7 Samsung Inc., Dallas, TX, USA) for subsequent analyses. The EMG signals were amplified (gain: $\times 1000$) using differential amplifiers (EMG 100, Biopac Systems, Inc., Santa Barbara, CA, USA) with a common mode rejection ratio of 110 dB min and an impedance of 2M Ω. The signals were digitally bandpass filtered (fourth-order Butterworth, zero-phase shift) at 10–500 Hz and all signal processing was performed in LabVIEW (National Instruments, Austin, TX, USA) using custom written programs. The amplitude of the EMG (μV root-mean-square, μVrms) signals were calculated from 40° to 80° of flexion at the elbow (0° corresponds to full extension of the elbow). Thus, signal epochs of 0.33 s (667 data points) were used to calculate the EMG values associated with the eccentric and concentric muscle actions. Similarly, the EMG values during the MVIC muscle actions were calculated for a time period that corresponds to 0.33 s (667 data points) over the middle one-ninth of the muscle action.

To examine potential trained-induced neural adaptations, electrical efficiency was determined during the baseline, 0, 2, and 4 weeks testing visits. Electrical efficiency was calculated as the ratio of EMG amplitude to torque production (i.e., μV_{RMS} per Nm), whereby a decrease in electrical efficiency reflected improved efficiency (Pasquet et al. 2000; Lenman 1959; deVries 1968).

Ultrasound measurements

Muscle thickness and echo intensity were assessed via ultrasound prior to each testing and training visit. Ultrasound images of the trained arm (biceps brachii) were obtained using a portable brightness mode (B-mode) ultrasound-imaging device (GE Logiqe, USA) and a multi-frequency linear-array probe (12L-Rs; 5–13 MHz; 38.4 mm field-of-view). All ultrasound measurements were performed at a sampling rate of 10 MHz and at a gain of 58 dB. Ultrasound images were analyzed using ImageJ software (Version

1.47v., National Institutes of Health, Bethesda, MD, USA) and prior to all analyses, images were scaled from pixels to centimeters using the straight line function in ImageJ. Muscle thickness and echo intensity were assessed at 66% of the distance from the medial acromion of the scapula to the fossa cubit. Muscle thickness was determined as the distance from the adipose tissue–muscle interface to the muscle–bone interface. Echo intensity, as assessed by gray-scale analysis (0 arbitrary units (AU) corresponds to black image, 255 AU corresponds to white image) was performed using the histogram function and was determined from the same region of interest as muscle thickness. Great care was taken to ensure that consistent, minimal pressure was applied with the probe to limit compression of the tissue. To enhance acoustic coupling and reduce near field artifacts, a generous amount of water-soluble transmission gel was applied to the skin prior to each measurement.

Blood flow measurements were assessed at an insonation angle of 60° to the brachial artery. All measurements were taken while the subjects were lying in the supine position on the isokinetic dynamometer with both arms and legs supported. Blood flow was assessed from the brachial artery proximal to the antecubital fossa using Pulsed Wave Doppler. Blood flow was used to determine the vBFR pressure needed to completely occlude the brachial artery (assessed at baseline, 0, and 2 weeks).

Data analysis

Reliability

Test–retest reliability for eccentric peak torque, concentric peak torque, MVIC, muscle thickness, echo intensity, and neuromuscular responses (EMG amplitude and electrical efficiency assessed during the eccentric peak, concentric peak torque, and MVIC muscle actions) were assessed from the baseline and 0-week testing visits. Repeated measures ANOVAs were used to assess systematic error, and model 2,k (26) was used to calculate intraclass correlation coefficients (ICCs), standard errors of measurement (SEM), and minimal difference (MD) needed to consider a change as real (29). The 95% confidence intervals for the means of the dependent variables were calculated with the Student's *t* distribution.

Normalization

The absolute EMG amplitude values at the baseline, 0, 2, and 4 weeks testing visits during the eccentric peak torque, concentric peak torque, and MVIC muscle actions were normalized to the EMG amplitude values obtained during the baseline MVIC muscle actions. Thus, all EMG amplitude values for each group (Ecc-vBFR, Con-vBFR, and control) and for each mode (eccentric peak torque, concentric peak, and MVIC) were expressed as percent changes from the EMG amplitude values obtained during the baseline MVIC muscle actions (Fig. 6).

Statistical analyses

Torque, EMG amplitude, and electrical efficiency were examined using separate 3 [Group (Ecc-vBFR, Con-vBFR, control)] × 4 [Time (baseline, 0 week, 2 weeks, 4 weeks)] × 3 [Mode (eccentric peak torque, concentric peak torque, and MVIC)] mixed factorial ANOVAs. Muscle thickness and echo intensity were examined using separate 3 [Group (Ecc-vBFR, Con-vBFR, control)] × 4 [Time (baseline, 0 week, 2 weeks, 4 weeks)] mixed factorial ANOVAs. In addition, a 2 [Group (Ecc-vBFR, Con-vBFR)] × 2 [Time (2 weeks, 4 weeks)] mixed factorial ANOVA was used to compare exercise volume performed during the first 2 weeks (2-week) and the second 2 weeks (4-week) of the training interventions. Significant interactions were decomposed with follow-up mixed factorial or repeated measures ANOVAs and Bonferonni-corrected independent or dependent samples *t* tests. Greenhouse–Geisser corrections were applied when sphericity was not met according to Mauchly's Test of Sphericity and partial eta squared effect sizes (η_p^2) were calculated for each ANOVA. All statistical analyses were performed using IBM SPSS v. 25 (Armonk, NY, USA) and an alpha of $p \leq 0.05$ considered statistically significant for all comparisons.

Results

Reliability

Table 1 includes the test–retest reliability and MD values from the baseline and 0-week measurements of muscle thickness, echo intensity, eccentric peak torque, concentric peak torque, MVIC, EMG amplitude, and electrical efficiency determined during each of the eccentric peak torque, concentric peak torque, and MVIC muscle actions. There were no mean differences for baseline vs. 0-week testing visits ($p > 0.05$) for any of the variables. The ICC values for all measured variables ranged from 0.719 to 0.971 and the SEM values ranged from 2.2 to 22.2% of the grand mean. For each measurement, the ICC and SEM are provided in Table 1.

Torque responses

There was no significant three-way interaction (Group × Time × Mode), but there was a significant two-way interaction (Group × Time) and a significant main effect for

Table 1 Test–retest reliability assessed from the baseline and 0-week testing visits for all subjects ($n = 36$)

Variables	Baseline	0-week	*p* value	ICC	$ICC_{95\%}$	SEM	MD	Grand mean
Muscle thickness (cm)	2.21 ± 0.24	2.23 ± 0.24	0.220	0.971	0.943–0.985	0.05	0.14	2.20
Echo intensity (Au)	108.2 ± 12.8	109.1 ± 11.1	0.633	0.719	0.448–0.857	9.0	25.8	108.6
Eccentric peak torque (Nm)	31.8 ± 6.7	34.1 ± 7.4	0.268	0.881	0.677–0.952	2.8	8.1	32.9
Concentric peak torque (Nm)	18.7 ± 4.1	17.3 ± 3.6	0.354	0.888	0.654–0.957	1.5	4.3	18.0
MVIC (Nm)	20.8 ± 5.5	18.9 ± 5.1	0.661	0.917	0.630–0.972	1.8	5.1	19.9
Eccentric EMG amplitude (μV)	785.9 ± 336.9	725.8 ± 305.6	0.139	0.836	0.681–0.916	142.1	407.9	755.9
Eccentric electrical efficiency (μV/Nm)	24.7 ± 9.8	22.6 ± 9.0	0.118	0.772	0.558–0.883	4.4	12.7	23.7
Concentric EMG amplitude (μV)	785.6 ± 312.2	791.8 ± 285.6	0.877	0.811	0.627–0.904	132.8	381.3	788.7
Concentric electrical efficiency (μV/Nm)	44.1 ± 16.6	46.1 ± 20.7	0.437	0.810	0.629–0.903	4.7	13.4	45.1
MVIC EMG amplitude (μV)	807.3 ± 308.0	796.6 ± 357.2	0.827	0.769	0.545–0.883	177.8	510.4	802.0
MVIC electrical efficiency (μV/Nm)	38.8 ± 15.7	38.8 ± 18.6	0.994	0.805	0.615–0.901	4.1	11.7	38.8

p value (ANOVA for systematic error)

ICC intraclass correlation coefficient, $ICC_{95\%}$ ICC 95% confidence interval, *SEM* standard error of the measurement, *MD* minimal difference, *MVIC* maximal voluntary isometric contraction, *EMG* electromyography

Mode (Table 2). As a result of Ecc-vBFR, torque increased from baseline and 0 week to 2 weeks (9.1 and 13.9%) and 4 weeks (29.4 and 35.0%), respectively, and increased 18.6% from 2 to 4 weeks (collapsed across Mode) (Figs. 2, 3). For Con-vBFR, torque increased from baseline and 0 week to 2 weeks (14.9 and 13.4%) and 4 weeks (32.9 and 31.2%) and increased 15.7% from 2 to 4 weeks (collapsed across Mode). There were no changes in torque across Time for the control group.

There were no Group differences in torque at baseline or at 0 week. At 2 weeks, torque was greater as a result of Ecc-vBFR (27.4 Nm) compared to the control groups (25.7 Nm), and at 4 weeks torque was greater as a result of Ecc-vBFR (32.5 Nm) and Con-vBFR (30.9 Nm) compared to the control group (25.5 Nm) (collapsed across Mode).

The main effect for Mode indicated that MVIC torque (23.5 Nm) was greater than concentric peak torque (20.1 Nm), and eccentric peak torque (36.1 Nm) was greater than both MVIC and concentric peak torque (collapsed across Group and Time).

Muscle thickness

There was a significant two-way interaction (Group × Time) for muscle thickness (Table 2). Follow-up analyses indicated that muscle thickness increased from baseline and 0 week to 2 weeks (13.3 and 11.4%) and 4 weeks (14.6 and 12.8%) as a result of Ecc-vBFR, but there were no differences between 2 and 4 weeks (Fig. 4a). Similarly, muscle thickness increased from baseline and 0 week to 2 weeks (9.9 and 9.1%) and 4 weeks (10.7 and 9.9%), but there were no differences between 2 and 4 weeks (Figs. 4a, 5). In addition, at 2 weeks of training muscle thickness was greater as a result of Ecc-vBFR (2.41 cm) compared to control (2.15 cm) and at 4 weeks of training muscle thickness was greater as a result of Ecc-vBFR (2.44 cm) and Con-vBFR (2.35 cm) compared to control (2.15 cm).

Echo intensity

There was no significant two-way interaction (Group × Time) or significant main effects for Group or Time (Table 2). In addition, there were no changes in echo intensity at any of the time points (Fig. 4b). Thus, echo intensity was not affected by either Ecc-vBFR or Con-vBFR training. These findings suggested that neither Ecc-vBFR or Con-vBFR resulted in exercise-induced edema.

EMG amplitude

There was no significant three-way interaction (Group × Time × Mode), but there was a significant two-way interaction (Group × Mode) and no significant main effect for Time (Table 2). There were not, however, any significant follow-up analyses. Thus, there were no changes in EMG amplitude (muscle activation) as a result of either Ecc-vBFR or Con-vBFR (Fig. 6).

Electrical efficiency

There was no significant three-way interaction (Group × Time × Mode) or significant two-way interactions (Group × Time, Group × Mode, Time × Mode), but there were significant main effects for Time and Mode (Table 2). Specifically, electrical efficiency improved from baseline and 0 week to 2 weeks (20.6 and 15.0%) and improved from baseline and 0 week to 4 weeks (22.1 and 16.6%) (collapsed across Group and Mode). In addition,

Table 2 Displays the effects for each variable with the corresponding *p* value and partial eta squared effect size

Variable	ANOVA	*p* value	Partial eta squared	Effect
Torque	Group × Time × Mode	0.188	0.084	
	Group × Time	< 0.001	0.332	
	Group × Mode	0.620	0.040	
	Time × Mode	0.499	0.027	
	Mode	< 0.001	0.887	Eccentric peak torque > MVIC > Concentric peak torque
Follow-up analyses	Group × Time	< 0.001	0.317	
Baseline	Group	0.305	0.069	
0 week	Group	0.878	0.008	
2 weeks	Group	0.490	0.042	
4 weeks	Group	0.016	0.223	Ecc-vBFR and Con-vBFR > Control
Ecc-vBFR	Time	< 0.001	0.666	Baseline and 0 week < 2 weeks < 4 weeks
Con-vBFR	Time	< 0.001	0.775	Baseline and 0 week < 2 weeks < 4 weeks
Control	Time	0.559	0.051	
Muscle thickness	Group × Time	< 0.001	0.566	
Follow-up analyses baseline	Group	0.917	0.005	
0 week	Group	0.975	0.002	
2 weeks	Group	0.012	0.233	Ecc-vBFR > Control
4 weeks	Group	0.003	0.297	Ecc-vBFR and Con-vBFR > Control
Ecc-vBFR	Time	< 0.001	0.668	Baseline and 0 week < 2 weeks and 4 weeks
Con-vBFR	Time	< 0.001	0.699	Baseline and 0 week < 2 weeks and 4 weeks
Control	Time	0.777	0.032	
Echo intensity	Group × Time	0.445	0.056	
	Group	0.289	0.072	
	Time	0.084	0.065	
EMG amplitude	Group × Time × Mode	0.627	0.047	
	Group × Time	0.184	0.104	
	Group × Mode	0.016	0.167	
	Time × Mode	0.087	0.054	
	Time	0.372	0.031	
Follow-up analyses	Group × Mode	0.470	0.052	
	Group	0.275	0.075	
	Mode	0.888	0.001	
Electrical efficiency	Group × Time × Mode	0.620	0.048	
	Group × Time	0.095	0.102	
	Group × Mode	0.187	0.088	
	Group	0.503	0.041	
	Time	0.010	0.107	Baseline and 0 week > 2 weeks and 4 weeks
	Mode	< 0.001	0.699	Eccentric peak torque < Concentric peak torque < MVIC
Exercise volume	Group × Time	0.717	0.006	
	Group	< 0.001	0.763	Ecc-vBFR > Con-vBFR
	Time	0.004	0.321	2 weeks < 4 weeks

In the event of an interaction(s), only the main effect(s) not involved in the interaction(s) were provided

Ecc-vBFR eccentric venous blood flow restriction, *Con-vBFR* concentric vBFR, *MVIC* maximal voluntary isometric contraction, *EMG* electromyography

electrical efficiency was lower (more efficient) during the MVIC muscle actions (33.3 ± 10.4 μV_{RMS} per Nm) than during the concentric peak torque muscle actions (37.4 ± 12.9 μV_{RMS} per Nm), and electrical efficiency was lower (more efficient) during the eccentric peak torque muscle actions (19.7 ± 5.8 μV_{RMS} per Nm) than both MVIC and concentric peak torque muscle actions (collapsed across Group and Time) (Fig. 7).

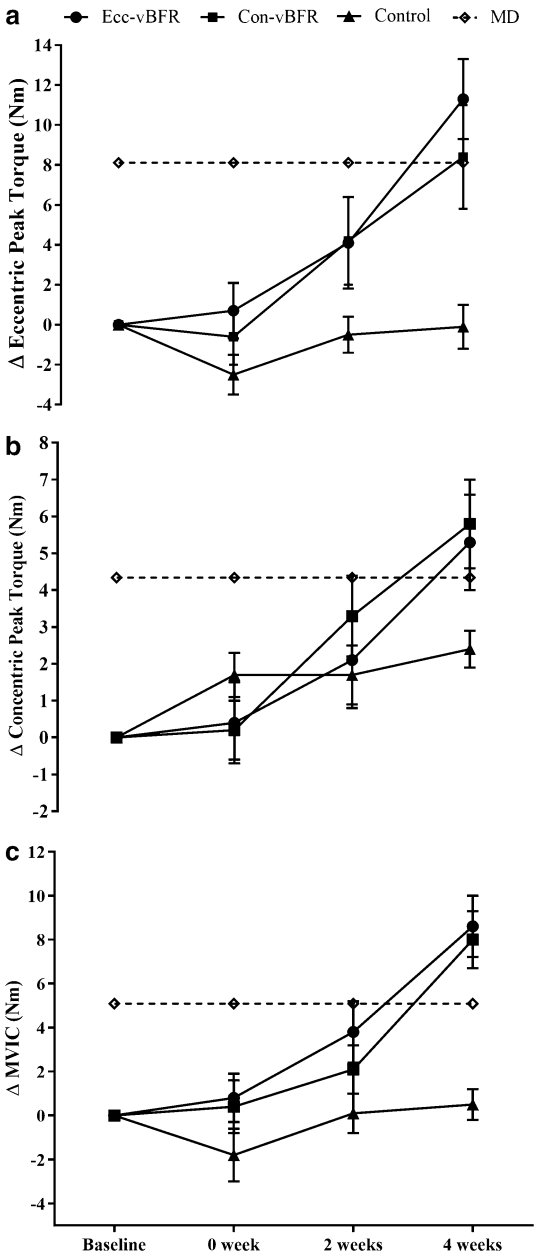

Fig. 2 Absolute (Nm) mean (±SE) changes (Δ = change) in eccentric peak torque, concentric peak torque, and maximal voluntary isometric contraction (MVIC) from baseline, 0, 2, and 4 weeks of training for the eccentric venous blood flow restriction (Ecc-vBFR = solid circles) training group, concentric vBFR (Con-vBFR = solid squares) training group, and control (solid triangles) group. For each Mode of torque measurement (eccentric peak torque, concentric peak torque, and MVIC) the minimal difference (MD = empty diamonds) needed for a change to be considered "real" is plotted and derived using standard error of measurement (SEM) values from the reliability data in Table 1 and using the equation, $MD = SEM \times 2^{1/2} \times df$ (Weir 2005)

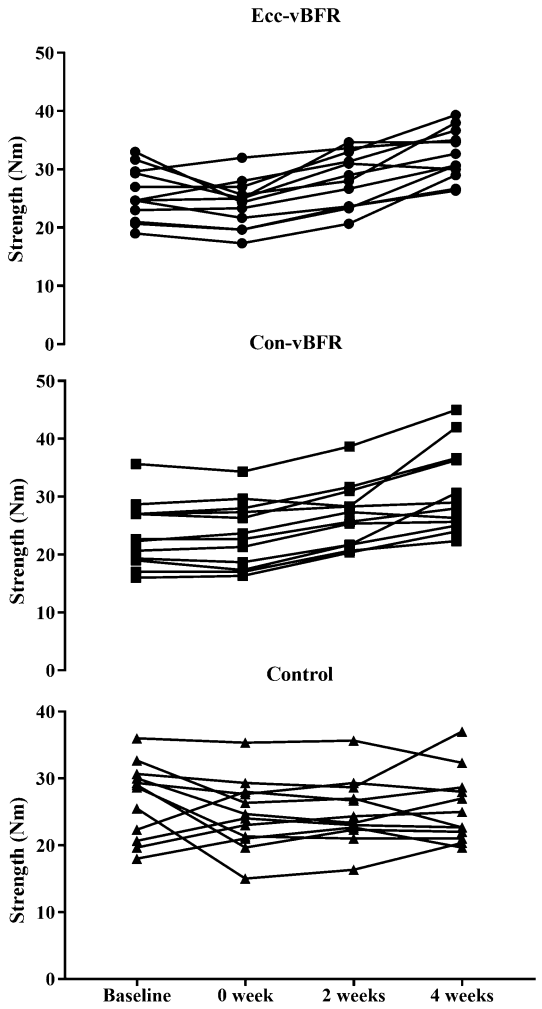

Fig. 3 Absolute (Nm) individual changes in strength [collapsed across Mode (eccentric peak torque, concentric peak torque, and maximal voluntary isometric contraction)] from baseline, 0, 2, and 4 weeks of training for the eccentric venous blood flow restriction (Ecc-vBFR = solid circles) training group, concentric vBFR (Con-vBFR = solid squares) training group, and control (solid triangles) group

Exercise volume

There was no significant two-way interaction (Group × Time), but there were significant main effects for Group and Time (Table 2). Specifically, exercise volume per session was greater during Ecc-vBFR (777.2 ± 138.2 lbs) compared Con-vBFR (449.1 ± 83.3 lbs) (collapsed across Time) and exercise volume per session increased from 2 weeks (571.9 ± 115.1 lbs) to 4 weeks (731.3 ± 144.7 lbs) (collapsed across Group). Thus, the Ecc-vBFR group performed a greater volume of exercise compared to the Con-vBFR group, but there were increases in exercise volume from 2 to 4 weeks of training for Ecc-vBFR and Con-vBFR.

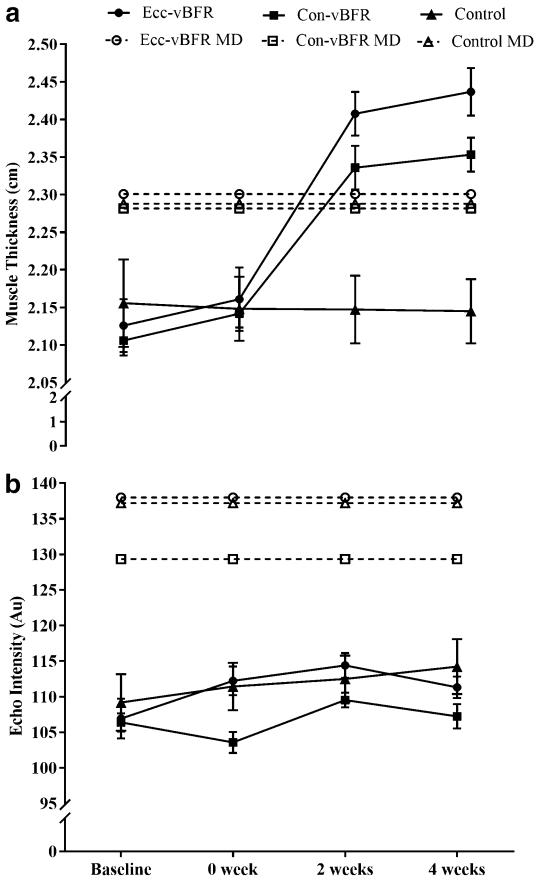

Fig. 4 Absolute (cm) mean (±SE) values for muscle thickness and echo intensity across 4 weeks of eccentric venous blood flow restriction (Ecc-vBFR = solid circles) training group, concentric vBFR (Con-vBFR = solid squares) training group, and control group (solid triangles). For each Group (Ecc-vBFR, Con-vBFR, and control), the minimal difference (MD = empty diamonds) needed for a change to be considered "real" is plotted and derived using standard error of measurement (SEM) values from the reliability data in Table 1 and using the equation, $MD = SEM \times 2^{1/2} \times df$ (Weir 2005)

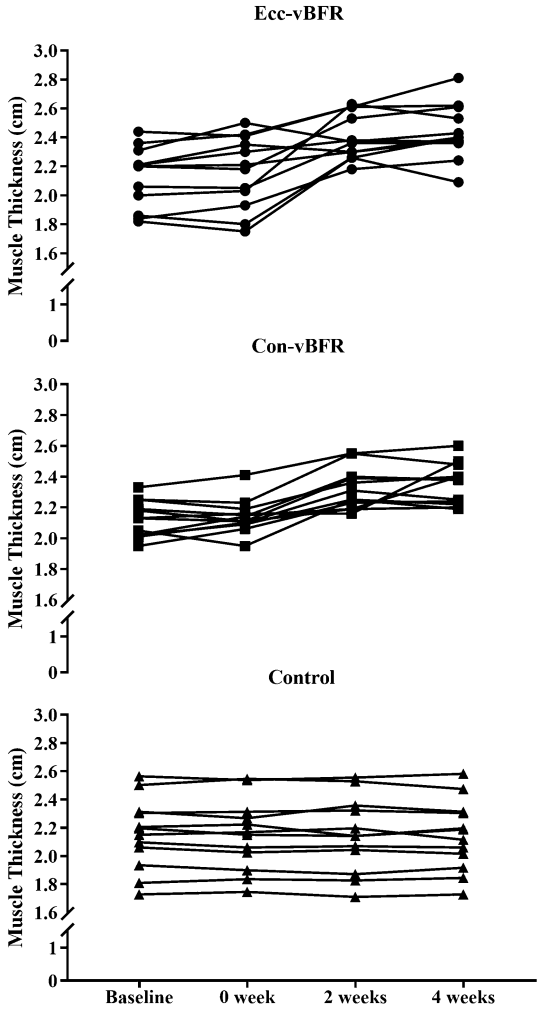

Fig. 5 Absolute (cm) individual changes in muscle thickness from baseline, 0, 2, and 4 weeks of training for the eccentric venous blood flow restriction (Ecc-vBFR = solid circles) training group, concentric vBFR (Con-vBFR = solid squares) training group, and control (solid triangles) group

Discussion

Muscle strength and size

In the present study, there were no mode-specific (eccentric peak torque vs. concentric peak torque vs. MVIC) increases in strength as a result of the Ecc-vBFR or Con-vBFR training. There were increases in eccentric peak torque of 34.6 and 28.2%, concentric peak torque of 26.0 and 30.2%, and MVIC of 35.0 and 37.6% as a result of the Ecc-vBFR and Con-vBFR training, respectively (Figs. 2, 3). For both modes of training, the increases in eccentric peak torque, concentric peak torque, and MVIC exceeded the MD necessary to be considered "real" (Weir 2005) after 4 weeks of training. Thus, contrary to our hypothesis, the increases in muscle strength were similar as a result of the Ecc-vBFR and Con-vBFR training interventions. No previous investigations have compared the strength increases from isokinetic Ecc-vBFR vs. Con-vBFR training, but Yasuda et al. (2013) examined the effects of isotonic Ecc-vBFR vs. Con-vBFR training. Yasuda et al. (2013) reported a smaller increase in MVIC strength as a result of Ecc-vBFR (3.8%) than Con-vBFR (8.6%) following 6 weeks of training. In the study by Yasuda et al. (2013), the Ecc-vBFR training group trained at an intensity of 30% of 1RM which corresponded to approximately 10% of eccentric peak torque, compared to the 30% of eccentric peak that was used in the present study. These findings indicated that Ecc-vBFR training at 30% of 1RM (Yasuda et al. 2013) did not elicit increases in muscle strength that were comparable to isokinetic Ecc-vBFR training at 30% of eccentric peak torque. In

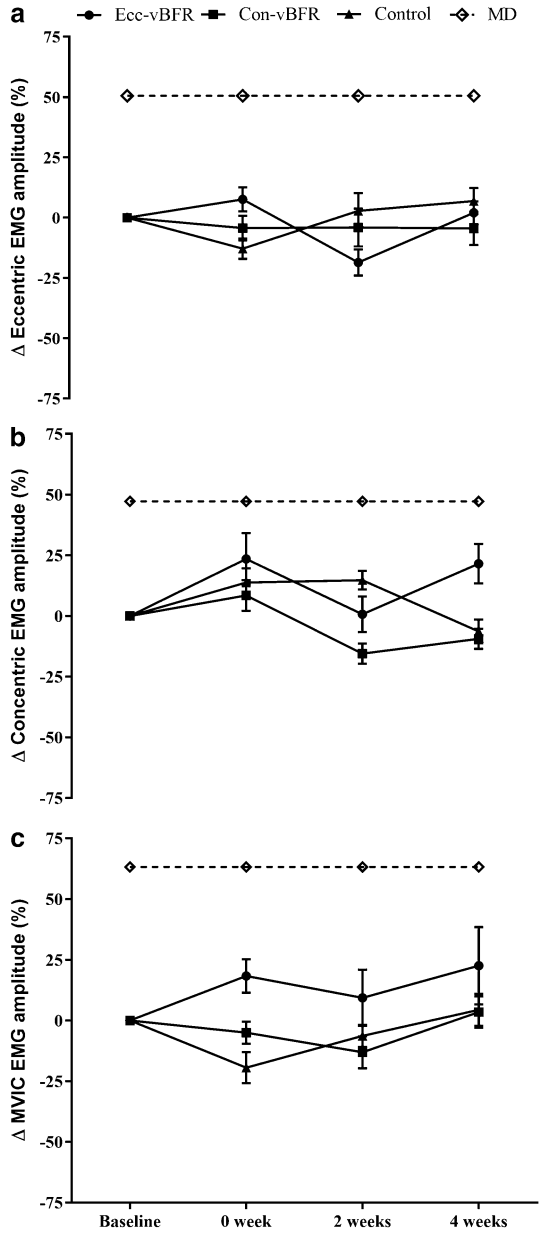

Fig. 6 Normalized (to baseline maximal voluntary isometric contraction [MVIC]) mean (±SE) changes (Δ = change) in electromyographic (EMG) amplitude during the eccentric peak torque, concentric peak torque, and MVIC muscle actions from baseline, 0, 2, and 4 weeks of training for the eccentric venous blood flow restriction (Ecc-vBFR = solid circles) training group, concentric vBFR (Con-vBFR = solid squares) training group, and control (solid triangles) group. For each Mode of EMG amplitude measurement (eccentric peak torque, concentric peak torque, and MVIC) the minimal difference (MD = empty diamonds) needed for a change to be considered "real" is plotted and derived using standard error of measurement (SEM) values from the reliability data in Table 1 and using the equation, $MD = SEM \times 2^{1/2} \times df$ and normalized to baseline MVIC (MD/baseline MVIC EMG amplitude) (Weir 2005)

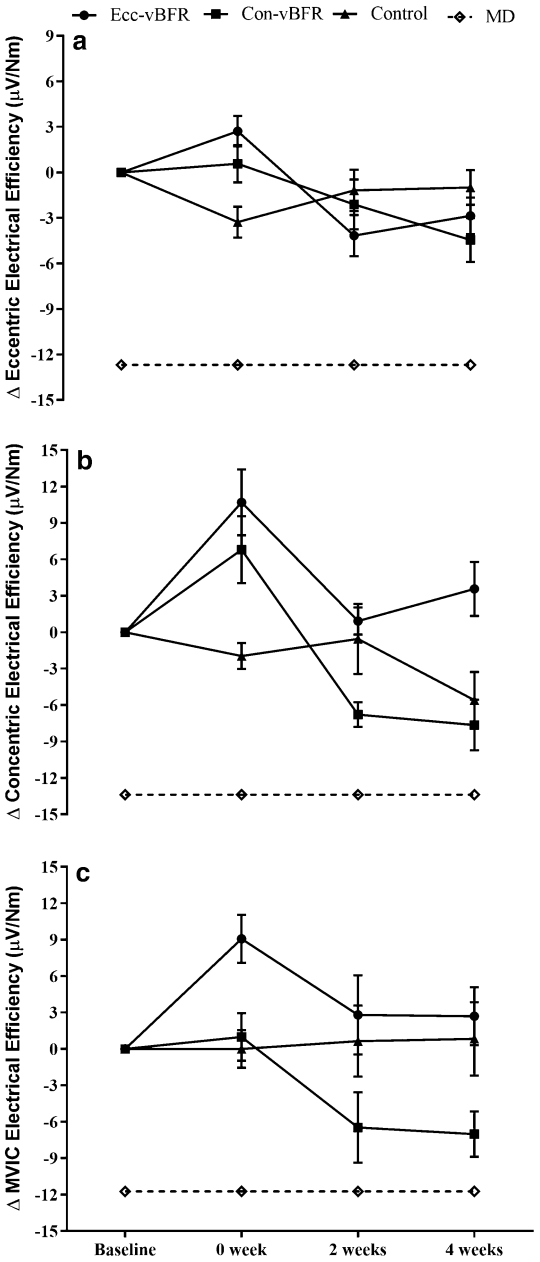

Fig. 7 Absolute (μV_{RMS}/Nm) mean (±SE) changes (Δ = change) in electrical efficiency during the eccentric peak torque, concentric peak torque, and maximal voluntary isometric contraction (MVIC) muscle actions from baseline, 0, 2, and 4 weeks of training for the eccentric venous blood flow restriction (Ecc-vBFR = solid circles) training group, concentric vBFR (Con-vBFR = solid squares) training group, and control (solid triangle) group. For each Mode of EMG amplitude measurement (eccentric peak torque, concentric peak torque, and MVIC), the minimal difference (MD = empty diamond) needed for a change to be considered "real" is plotted and derived using standard error of measurement (SEM) values from the reliability data in Table 1 and using the equation, $MD = SEM \times 2^{1/2} \times df$ (Weir 2005)

addition, vBFR resistance training at 30% of isokinetic peak torque elicited comparable increases in muscle strength, regardless of training modality (Ecc-vBFR or Con-vBFR) when the relative training intensity, velocity and tempo, number of repetitions performed, and rest between sets were identical.

The increase in MVIC as a result of Con-vBFR training in the present study was also greater (37.6 vs. 8.6%) than that reported by Yasuda et al. (2013). The differences in training adaptations associated with Con-vBFR in the present study vs. those of Yasuda et al. (2013) may have been due to the type of training (isokinetic vs. isotonic) (Guilhem et al. 2010; Pipes and Wilmore 1975) and/or the joint angle at which MVIC was assessed (120° vs. 90°, where 180° corresponds to full extension at the elbow) (Kang et al. 2013; Yang et al. 2014). Thus, the present findings indicated that 4 weeks of low-intensity isokinetic Ecc-vBFR and Con-vBFR resulted in similar increases in strength across all modes of assessment (eccentric peak torque, concentric peak torque, and MVIC).

As a result of both the Ecc-vBFR and Con-vBFR training in the present study, there were increases in muscle thickness that exceeded the MD at 2 weeks and continued to increase to 4 weeks of training (Fig. 4a). The increases in muscle thickness, however, were not accompanied by changes in echo intensity which is thought to be related to edema (DeFreitas et al. 2011; Damas et al. 2016) (Fig. 4b). Therefore, the increases in muscle thickness were likely the result of muscle hypertrophy and not attributable to exercise-induced edema (DeFreitas et al. 2011; Damas et al. 2016). The present findings indicated that low-intensity vBFR training resulted in early phase increases in muscle hypertrophy within 2 weeks of training that was earlier than the 3.9–11.7% increases in muscle thickness reported by Yasuda et al. (2013) following 6 weeks of isotonic, forearm flexion Ecc-vBFR and Con-vBFR training. Like the effects of Ecc-vBFR training on MVIC strength, the smaller increases in muscle thickness after 6 weeks of training reported by Yasuda et al. (2013) compared to those of the present study at 2 and 4 weeks were likely due to the lower intensity of Ecc-vBFR training (approximately 10% of eccentric peak torque) compared to 30% of eccentric peak torque. Thus, the present findings indicated that both low-intensity Ecc-vBFR and Con-vBFR stimulated muscle hypertrophy during the early phases of training as evidenced by the increases in muscle thickness and lack of changes in exercise-induced edema.

Neuromuscular adaptations

In the present study, EMG amplitude remained unchanged (collapsed across modes of testing) from baseline to 0, 2, and 4 weeks as a result of low-intensity Ecc-vBFR and Con-vBFR training, and EMG amplitude was not different between the Ecc-vBFR group, Con-vBFR group, or control group (collapsed across Time). Furthermore, there were no "real" changes in electrical efficiency which has been used to track training-induced improvements in force production per unit of muscle activation ($Nm/\mu V_{RMS}$) (Lenman 1959; deVries 1968). Together, these findings indicated that the training-induced increases in muscle strength in the present study were not associated with neural changes as assessed by EMG amplitude and electrical efficiency.

The present findings were consistent with previous investigations (Takarada et al. 2002, 2000; Fujita et al. 2008; Yasuda et al. 2011) that have also reported increases in muscle strength as a result of low-intensity vBFR training that were associated with increases in muscle size, but were not associated with neural changes. For example, Yasuda et al. (2011) reported increases in muscle strength as a result of 30% of 1RM vBFR bench press resistance training that were not associated with neural adaptations, but were likely the result of muscle hypertrophy. It is possible that low-intensity vBFR resistance training is not sufficient to elicit comparable neural adaptions as high-intensity non-BFR resistance training (Loenneke et al. 2012b). In support of this, previous investigations (Jenkins et al. 2016, 2017) have reported a dissociation in the training-induced increases in muscle strength and neural adaptations that were greater as a result of high-intensity non-vBFR vs. low-intensity non-vBFR resistance training. In addition, there were no significant increases in muscle strength per unit of muscle cross-sectional area during the early phases (< 8 weeks) of low-intensity vBFR resistance training studies (Loenneke et al. 2012b). Thus, the early phase increases in muscle strength as a result of low-intensity vBFR resistance training were coupled with or could be explained by muscle hypertrophy. The training-induced increases in muscle strength and size, but lack of neural changes may be a unique characteristic of low-intensity vBFR resistance training. Loenneke et al. (2012b) postulated that "…the traditional training adaption paradigm is reversed with low-intensity BFR exercise" (page 1856) as indicated by early phase increases in muscle strength and muscle hypertrophy, without neural changes. It is plausible, however, that neural adaptations may facilitate increases in muscle strength during longer duration low-intensity vBFR resistance training studies or that low-intensity vBFR and low-intensity non-vBFR resistance training is not of sufficient intensity to induce neural adaptations (Loenneke et al. 2012b). Collectively, the present findings indicated that there were no differences between low-intensity Ecc-vBFR and Con-vBFR training for the early phase changes in muscle strength, size, and muscle activation. Therefore, in conjunction with previous investigations (Takarada et al. 2002, 2000; Fujita et al. 2008; Yasuda et al. 2011), the present findings indicated the low-intensity Ecc-vBFR and Con-vBFR

training resulted in early phase increases in muscle strength and size, without changes in muscle activation or efficiency.

Summary

The present findings indicated that 4 weeks of low-intensity isokinetic Ecc-vBFR and Con-vBFR resulted in similar increases in strength across all modes of assessment (eccentric peak torque, concentric peak torque, and MVIC). In addition, as a result of both the Ecc-vBFR and Con-vBFR training in the present study, there were increases in muscle thickness that exceeded the MD at 2 weeks and continued to increase to 4 weeks of training. There were, however, no changes in muscle activation (EMG amplitude) or electrical efficiency at any of the time points. Together, these findings indicated that the training-induced increases in muscle strength in the present study were not associated with neural changes as assessed by EMG amplitude and electrical efficiency, but were likely due to muscle hypertrophy (as indicated by the increases in muscle thickness without changes in echo intensity). Therefore, unlike non-vBFR resistance training, the present findings indicated that early phase increases in muscle strength as a result of low-intensity Ecc-vBFR and Con-vBFR training were due to increases in muscle size and not neural adaptations.

Limitations

In the present study, the women were not asked to provide information regarding their phase within the ovarian cycle or if they were using a contraceptive. It has been suggested (Wikstrom-Frisen et al. 2017; Sung et al. 2014; Sakamaki et al. 2012; Gil et al. 2017) that different phases of the ovarian cycle may enhance the effects of resistance training. For example, previous investigations (Wikstrom-Frisen et al. 2017; Sung et al. 2014) have reported that training-induced increases in muscle strength and size were greatest during the follicular phase, while other investigations (Sakamaki et al. 2012; Gil et al. 2017) have reported that training-induced increases in muscle strength and size were greatest during luteal phase. It has been suggested (Wikstrom-Frisen et al. 2017; Sung et al. 2014) that estrogen, which is highest during the follicular phase promotes anabolic signaling pathways, while progesterone, which is highest during the luteal phase supports catabolic activities. There were, however, no correlations for estrogen or progesterone and training-induced increases in muscle strength or size (Sakamaki et al. 2012). For women taking contraceptives, however, there appears to be no effect on the training induces increases in muscle strength or size (Nichols et al. 2008; Sarwar et al. 1996).

In the present study, all testings were performed within 30 ± 2 days that were consistent with the typical ovarian cycle of 27–31 days (Sung et al. 2014). Therefore, it is likely that all women completed the initial and final testing procedures at similar phases within their ovarian cycle across the 4 weeks of testing and training. Furthermore, the women were randomly assigned to each condition (Ecc-vBFR, Con-vBFR, and control group) to counterbalance the potential effects of the phase of ovarian cycle on the training-induced adaptations to muscle strength and size.

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