

Combined effects of low-intensity blood flow restriction training and high-intensity resistance training on muscle strength and size

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Abstract We investigated the combined effect of low-intensity blood flow restriction and high-intensity resistance training on muscle adaptation. Forty young men (aged 22–32 years) were randomly divided into four groups of ten subjects each: high-intensity resistance training (HI-RT, 75% of one repetition maximum [1-RM]), low-intensity resistance training with blood flow restriction (LI-BFR, 30% 1-RM), combined HI-RT and LI-BFR (CB-RT, twice-weekly LI-BFR and once-weekly HI-RT), and nontraining control (CON). Three training groups performed bench press exercises 3 days/week for 6 weeks. During LI-BFR training sessions, subjects wore pressure cuffs on both arms that were inflated to 100–160 mmHg. Increases in 1-RM were similar in the HI-RT (19.9%) and CB-RT (15.3%) groups and lower in the LI-BFR group (8.7%, $p < 0.05$). Maximal isometric elbow extension (MVC) increased in the HI-RT (11.3%) and CB-RT (6.6%) groups; there was no change in the LI-BFR group (−0.2%). The cross-sectional area (CSA) of the triceps brachii (TB) increased ($p < 0.05$) in the HI-RT (8.6%), CB-RT (7.2%), and LI-BFR (4.4%) groups. The change in relative isometric strength (MVC divided by TB CSA) was greater ($p < 0.05$) in the HI-RT group (3.3%) than in the LI-BFR (−3.5%) and CON (−0.1%) groups. Following training, relative dynamic strength (1-RM divided by TB CSA) was increased ($p < 0.05$) by 10.5% in the HI-RT group and

6.7% in the CB-RT group. None of the variables in the CON group changed. Our results show that low-intensity resistance training with BFR-induced functional muscle adaptations is improved by combining it with HI-RT.

Keywords Vascular occlusion · Neural adaptation · Muscle hypertrophy · Muscle strength

Introduction

Resistance training is one of most fundamental ways to increase muscle strength, improve daily physical functioning and sports performance, and enhance recovery from orthopedic injuries (American College of Sports Medicine 1998, 2009; Kraemer and Ratamess 2004). Traditional high-intensity resistance training (HI-RT, 60–80% of one repetition maximum [1-RM]) produces the greatest increases in muscular strength and is associated with increased muscle size and improved neural adaptation (Folland and Williams 2007; Sale 1988). Previous studies evaluating the time course of these changes have demonstrated the importance of the nervous system in facilitating the strength gains that are observed during the early phase of HI-RT (Abe et al. 2000; Ikai and Fukunaga 1970; Moritani and deVries 1979). The relative increase in muscle strength was higher than the relative increase in muscle cross-sectional area (CSA), and, as a result, the relative strength (maximal voluntary strength per unit muscle CSA) increased significantly during the early phase (~12 weeks) of HI-RT (Goto et al. 2004; Ikai and Fukunaga 1970; Kawakami et al. 1995; Narici et al. 1996). However, the HI-RT required for muscle adaptation with traditional resistance exercise may be impractical and even dangerous if carried out without proper supervision (Haykowsky et al.

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1996; MacDougall et al. 1985; Pollock et al. 1994). In addition, a previous study (Miyachi et al. 2004) has indicated that HI-RT reduced central arterial compliance in healthy men. Low arterial compliance contributes to elevations in systolic blood pressure and coronary heart disease and reductions in arterial baroreflex sensitivity (Monahan et al. 2001; O'Rourke 1990). Therefore, it would be advantageous to develop safe and useful methods of promoting muscle hypertrophy and strength.

In the past decade, several studies have demonstrated that muscle hypertrophy can be produced with low-intensity resistance training (20–30% 1-RM) combined with blood flow restriction (BFR). Interestingly, BFR training does not require a long recovery time between training sessions (Abe et al. 2005; Yasuda et al. 2008, 2009) owing to the very low mechanical stress and minimal muscle damage associated with it (Abe et al. 2005; Fujita et al. 2008; Takarada et al. 2000a). A recent study demonstrated that BFR training, unlike HI-RT, improves muscle size as well as carotid arterial compliance (Ozaki et al. 2011). Therefore, BFR training may be a potentially useful method for promoting muscle hypertrophy with a low risk of injury. However, those same BFR training studies did not show significant increases in relative strength (Abe et al. 2005, 2006; Fujita et al. 2008; Takarada et al. 2000b, 2002; Yasuda et al. 2010b). Kubo et al. (2006) reported no significant change in relative strength or muscle activation following low-intensity BFR training, indicating that the BFR training-induced improvement in muscle strength must be attributed to muscle hypertrophy, without any change in neural adaptation. This means that low-intensity BFR training produces only an insufficient increase in muscle adaptations.

In general, combined resistance and endurance training results in the attenuation of the performance improvements and physiological adaptations typical of single-mode training (Kraemer et al. 1995; Leveritt et al. 1999; Nader 2006). Nader (2006) reported that activation of adenosine monophosphate-activated protein kinase (AMPK) by endurance exercise may inhibit signaling to the protein-synthesis machinery by inhibiting the activity of the mammalian target of rapamycin (mTOR) and its downstream targets. On the other hand, high- and low-resistance exercises combined in multiple-mode resistance training do not mutually inhibit each other and results in higher muscle adaptations compared with single-mode resistance training (Goto et al. 2004; Kraemer and Ratamess 2004; Marx et al. 2001). Notably, Fleck (1999) demonstrated that resistance training using a variety of training loads is most effective in maximizing muscle strength. Therefore, we hypothesized that the combination of HI-RT and low-intensity BFR training would achieve greater strength gains than BFR training alone. The purpose of the present study was to

investigate the combined effects of HI-RT and BFR training on muscle size and strength.

Methods

Subjects

Forty young men (aged 22–32 years) volunteered to participate in this study. The subjects were classified as “recreationally active”; 12 of 40 participated in regular aerobic-type exercise (walking, jogging, or cycling; 2–3 times/week for approximately 30 min). Nine of the subjects had light to moderate resistance training experience performing bench presses, but none of the subjects had participated in strength/resistance-type training for at least 6 months prior to the start of the study. All subjects were nonsmokers, normotensive (blood pressure <135/85 mmHg), nonobese (body mass index <30 kg/m²), not taking any medication, and free of overt chronic diseases as assessed by medical history. Six of the subjects had experienced both HI-RT and low-intensity BFR resistance training (LI-BFR), but none of them refused to perform either HI-RT or LI-BFR. Therefore, all subjects were randomly divided into four groups: HI-RT ($n = 10$), LI-BFR ($n = 10$), combined HI-RT and LI-BFR training (CB-RT, $n = 10$), and nontraining control (CON, $n = 10$). Each subject was informed of the risks associated with the training and measurements and gave written consent to participate in this study, which was approved by the Ethics Committee of the University of Tokyo (Japan). Testing was conducted before the initiation of training (pre) and after 6 weeks of training (post).

Training protocol

The three training groups performed a supervised free-weight flat bench press exercise 3 days/week (Monday, Wednesday, and Friday) for 6 weeks. Training intensity and volume were set at 75% of 1-RM and 30 repetitions (3 sets of 10 reps, with 2–3 min of rest between sets) for the HI-RT group and at 30% of 1-RM and 75 repetitions (30 reps followed by 3 sets of 15 reps, with 30 s of rest between sets) for the LI-BFR group. This averaged 6–10 min throughout the training during HI-RT and LI-BFR exercise. In the CB-RT group, subjects performed LI-BFR twice a week (Monday and Wednesday) and HI-RT once a week (Friday). The 1-RM strength was assessed after 3 weeks of training to adjust the training load for HI-RT exercise sessions. The training load was constant throughout the LI-BFR training period. In an attempt to minimize any potential diet-induced variability in muscle strength and muscle size measurements, subjects

were encouraged to eat similar diets throughout the experimental training period. Also, the subjects were instructed to refrain from ingesting alcohol and caffeine for 24 h before pre- and post-training measurements.

Blood flow restriction

Before the experiment, the CB-RT and LI-BFR groups were trained to wear elastic cuffs (Kaatsu-Master, Sato Sports Plaza, Tokyo, Japan) at the most proximal region of both arms. During the acclimatization period, the external pressure of the cuff (100–130 mmHg) was selected with regard to the subject's resting blood pressure as described previously (Yasuda et al. 2008). During acclimatization, no sign of discomfort or pain was observed in the subjects, which was not the case when surgical tourniquet cuffs were used.

During the LI-BFR training sessions, subjects wore elastic cuffs (Kaatsu-Master, Sato Sports Plaza, Tokyo, Japan) around the most proximal region of both arms. On the first day of training, the cuffs were inflated to a pressure of 100 mmHg. The pressure was increased by 10 mmHg at each subsequent training session until a pressure of 160 mmHg was reached. The restriction pressure was selected in accordance with previous studies (Yasuda et al. 2008, 2009, 2010a, b).

Measurement schedule

Subject testing took place before the start of the study and 3–4 days after the 6-week training period. MRI measurement was obtained first (17:00–19:00). Strength measurement (MVC and 1-RM) was determined on the same day or the following day after the MRI measurement. All measurements were balanced for the time of day. Care was taken to allow at least 10–20 min of rest between the first test (MVC) and the second test (1-RM).

1-RM strength measurement

One week before the start of training, all subjects were familiarized with the strength-testing equipment. Maximal dynamic strength (1-RM) was assessed using a free-weight flat bench press. After a warm-up period, the intensity was set at about 80% of the predicted 1-RM. Following each successful lift, the intensity was increased by about 5% until the subject failed to lift through the entire range of motion. A test was considered valid only when the subject used proper form and completed the entire lift in a controlled manner without assistance. On average, five to six trials were required to complete a 1-RM test. Approximately 2–3 min of rest were allotted between each attempt to ensure recovery (Abe et al. 2000). The coefficient

variation (CV) for this measurement from test to retest was 1.7%.

Maximum isometric strength measurement

Maximum voluntary isometric strength [maximum voluntary contraction (MVC)] of the elbow extensors was determined by using an isokinetic dynamometer (Biodex System 3, Sakai Medical Instruments, Tokyo, Japan). Each subject was comfortably seated on an adjustable chair, with the arm positioned on a stable table at chest level with the elbow bent at an angle of 90° (0° at full extension). The upper arm was maintained in the horizontal plane (at 90°), while the wrist was fixed at the end of the dynamometer lever arm in a position halfway between supination and pronation. The elbow extension force was measured with a transducer while the subject's posture was maintained in a stationary position. Subjects performed two trials separated by a 60-s rest interval. If MVC torque for the first two MVCs varied by more than 5%, up to two additional MVCs were performed. Subjects were instructed to perform an MVC as quickly as possible during a period of about 5 s. The recorded value for the MVC was taken as the highest and most stable 3 s of the 5-s contraction. The highest MVC value was used for data analysis. The CV for this measurement from test to retest was 3.1%.

Electrolomyography

Electromyograms (EMGs) were recorded from surface electrodes. The skin was shaved, rubbed with a skin preparation gel (Skinpure, Nihon Kohden, Japan), and cleaned with alcohol wipes. During all measurements, skin impedance was less than 2 k Ω . The ground electrode was positioned on the lateral epicondyle. Bipolar electrodes (Vitrode F, Ag/AgCl, 1-cm diameter, Nihon Kohden, Tokyo, Japan) were placed over the muscle belly with a constant interelectrode distance of 20 mm. The electrodes were connected to a preamplifier in a differential amplifier having a bandwidth of 0–500 kHz (AB 6216, Nihon Kohden, Tokyo, Japan). EMG signals were collected from the biceps brachii (BB) at a sampling rate of 1,024 Hz using a 12-bit analog-to-digital converter (Macintosh, Power PC 750, Apple, Japan). To determine integrated EMGs (iEMGs), signals were fully rectified and integrated (PowerLab Chart 4 software, ADInstruments, Nagoya, Japan). The EMGs were collected during each 5-s MVC and analyzed (iEMG) for the same 3-s period corresponding to the period used to select the MVC (above). To evaluate the BB antagonist muscle activity (coactivation level), we measured the iEMG of the BB during elbow extension MVC. To determine the maximal activation of the BB, the subjects performed an elbow flexion MVC at

the same angle (90°). We normalized the iEMG BB value with respect to the iEMG BB value at the same angle when acting as agonist at maximal effort. The CV for this measurement from test to retest was 1.9%.

MRI-measured muscle CSA

MRI images were prepared using a 0.2-T scanner (GE Signa, Milwaukee, Wisconsin, USA). A T1-weighted, spin-echo, axial plane sequence was performed with a 520-m s repetition time and a 20-m s echo time. Subjects rested quietly in the magnet bore in a supine position, with their arms extended along their trunk. Continuous transverse images with 10-mm slice thickness were obtained from the upper right side of the body, including the arm. All MRI data were transferred to a personal computer for analysis using specially designed image analysis software (Tomovision Inc., Montreal, Canada), and skeletal muscle tissue CSA (cm²) was digitized and calculated. Triceps brachii (TB) and pectoralis major (PM) muscle CSAs of three contiguous slices for muscle belly were averaged together for statistical analysis. The CV for this measurement from test to retest was less than 1%. All measurements were completed before (pre) and 3 days after (post) the final training session.

Ratings of perceived exertion

Ratings of perceived exertion (RPE) were measured using the Borg scale (Borg 1982) after the final repetition of 1st, 2nd, and last set of every exercise in HI-RT ($n = 20$, HI-RT and CB-RT groups) and LI-BFR programs ($n = 20$, LI-BFR and CB-RT groups).

Statistical analyses

Results are expressed as the mean \pm standard deviation (SD). A two-way ANOVA with repeated measures was used to compare four groups, with the effects being group and time (pre vs. post). Post hoc testing was performed using Tukey technique when appropriate. Percent changes from baseline were also compared among groups using Tukey's test. Statistical significance was set at $p < 0.05$. The sample size ($n = 10$) was estimated from a priori power analysis (Cohen 1988) to detect differences ($\alpha = 0.05$) in muscle size or strength measures for the interventions planned. Statistical power ranged from 0.80 to 1.00 for all comparisons reported.

Results

At baseline, there were no differences ($p > 0.05$) among the four experimental groups for age, anthropometric variables, muscular strength, and muscle CSA (Table 1). There was no change in body weight for any of the groups following training. The total training volumes (lifting weight \times repetitions) for all of the sessions were similar in the HI-RT (19,063 \pm 3,398 kg), LI-BFR (19,994 \pm 3,546 kg), and CB-RT (20,579 \pm 2,379 kg) groups.

Following training, bench press 1-RM strength increased ($p < 0.01$) in the HI-RT, LI-BFR, and CB-RT groups, but not in the CON group (Fig. 1a). Percent change in 1-RM strength was greater ($p < 0.01$) in both the HI-RT and CB-RT groups than in the LI-BFR and CON groups. Isometric MVC strength increased in the HI-RT and CB-RT groups, but not in the LI-BFR and CON groups

Table 1 Characteristics of subjects

	HI-RT	LI-BFR	CB-RT	CON
<i>n</i>	10	10	10	10
Age (year)	25.3 (2.9)	23.4 (1.3)	23.8 (2.1)	23.6 (1.6)
Standing height (cm)	172.0 (5.1)	171.7 (5.6)	172.7 (6.2)	171.1 (7.3)
Body mass (kg)	63.0 (8.9)	63.9 (7.8)	66.3 (4.6)	62.2 (8.5)
sBP (mmHg)	114.4 (6.9)	120.9 (8.7)	129.4 (11.4)	125.6 (14.6)
dBp (mmHg)	65.6 (6.3)	69.1 (4.1)	71.9 (5.0)	70.9 (9.6)
MVC (Nm)	28.9 (6.6)	31.1 (7.4)	30.5 (5.4)	31.7 (5.1)
1-RM strength (kg)	47.3 (9.5)	49.3 (8.7)	49.8 (5.9)	52.8 (11.3)
TB muscle CSA (cm ²)	21.5 (3.8)	20.5 (5.7)	21.6 (3.0)	20.7 (2.8)
PM muscle CSA (cm ²)	28.4 (6.3)	31.8 (5.2)	29.7 (2.4)	30.3 (4.7)

Data are presented as the mean with standard deviation in parentheses

CB-RT combination HI-RT and LI-BFR training, CON non-training, CSA cross-sectional area; dBp diastolic blood pressure, HI-RT high-intensity resistance training, LI-BFR low-intensity resistance training with blood flow restriction, MVC maximal voluntary contraction, *N* number of subjects, PM pectoralis major, sBP systolic blood pressure, TB triceps brachii

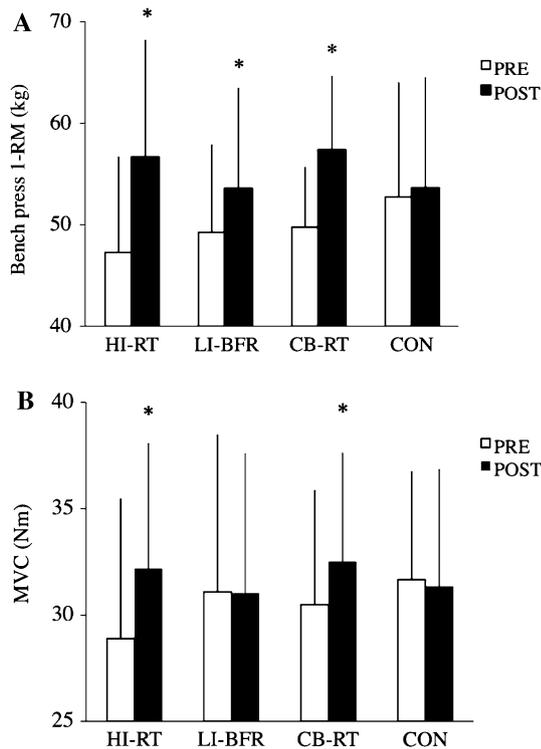


Fig. 1 Dynamic (bench press one repetition maximum [1-RM] strength) (a) and maximum isometric strength (MVC) of the elbow extensors; (b) responses following a 6-week training period. Data are presented as the mean \pm standard deviation. *CB-RT* combination HI-RT and LI-BFR resistance training; *CON* non-training; *HI-RT* high-intensity resistance training; *LI-BFR* low-intensity resistance training with blood flow restriction. *Different from pre-training, $p < 0.05$

(Fig. 1b). Percent change in MVC was greater ($p < 0.01$) in both the HI-RT and CB-RT groups than in the LI-BFR or CON groups. TB and PM muscle CSA increased ($p < 0.01$) in the HI-RT, LI-BFR and CB-RT groups, but not in the CON group (Fig. 2). Percent change in TB muscle CSA was greater ($p < 0.01$) in the HI-RT group (8.6%) than in the LI-BFR (4.9%) and CON (−1.1%) groups. Percent change in PM muscle CSA was greater ($p < 0.01$) in the HI-RT group (17.6%) than in the LI-BFR (8.3%), CB-RT (10.5%, $p < 0.05$) or CON (0.0%) groups.

Change in relative isometric strength (MVC divided by TB muscle CSA) was greater ($p < 0.05$) in the HI-RT group (3.3%) than in the LI-BFR (−3.5%) and CON (−0.1%) groups. Following training, relative dynamic strength (1-RM divided by TB muscle CSA) was increased ($p < 0.05$) 10.5% in the HI-T group and 6.7% in the CB-T group. Change in relative dynamic strength was greater ($p < 0.05$) in the HI-RT group (10.5%) than in the LI-BFR (4.0%) and CON (2.7%) groups. In the CB-RT group, change in relative dynamic strength tended to be greater ($p = 0.09$) than in the CON group (Table 2). There were no changes ($p > 0.05$) between pre- and post-training co-activation level of BB muscle (HI-RT group, 8.0 ± 4.5 vs. $8.5 \pm 4.5\%$; LI-BFR

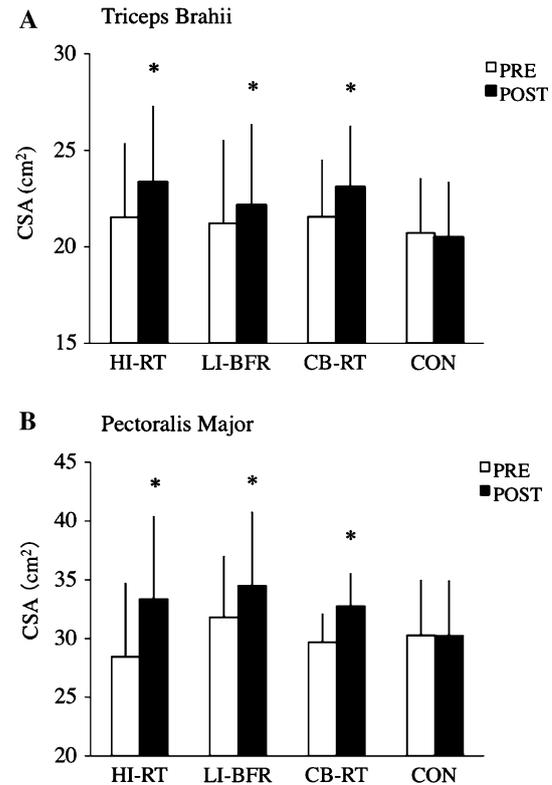


Fig. 2 Cross-sectional area (CSA) of the triceps brachii (a) and pectoralis major muscles (b) following a 6-week training period. Data are presented as the mean \pm standard deviation. *CB-RT* combination HI-RT and LI-BFR resistance training; *CON* non-training; *HI-RT* high-intensity resistance training; *LI-BFR* low-intensity resistance training with blood flow restriction. *Different from pre-training, $p < 0.05$

group, 5.9 ± 4.7 vs. 6.2 ± 2.9 ; CB-RT group, 7.4 ± 4.2 vs. $7.3 \pm 2.7\%$; CON group, 5.5 ± 2.5 vs. $6.1 \pm 3.3\%$).

RPE increased progressively in both LI-BFR and HI-RT exercises and was ($p < 0.05$) greater than LI-BFR exercise with HI-RT exercise in the 1st (12.9 ± 0.8 and 14.7 ± 1.6), 2nd (14.0 ± 0.9 and 15.8 ± 1.9), and last set (15.9 ± 1.5 and 17.6 ± 2.3).

Discussion

The findings from the present study support our hypothesis that improvement in muscle strength was significantly greater in the CB-RT combined training program (LI-BFR and HI-RT). The improvement was similar to that achieved by HI-RT alone but not to that achieved by LI-BFR alone. An increase in relative dynamic (1-RM) strength per unit muscle CSA was found in both HI-RT and CB-RT, while MVC per unit muscle CSA improved significantly with HI-RT only. The difference in improvement in relative strength between HI-RT and CB-RT may be attributed to unequal neural adaptations.

Table 2 Changes in relative isometric or dynamic strength following a 6-week training or control period

	HI-RT	LI-BFR	CB-RT	CON
Relative isometric strength (Nm/cm ²)				
Pre	1.34 (0.11)	1.59 (0.42)	1.43 (0.18)	1.53 (0.17)
Post	1.38 (0.10)	1.53 (0.45)	1.42 (0.21)	1.53 (0.20)
%Δ	3.3 ^{#,†}	−3.5	−0.7	−0.1
Relative dynamic strength (kg/cm ²)				
Pre	2.20 (0.21)	2.53 (0.61)	2.34 (0.29)	2.54 (0.35)
Post	2.43 (0.25)*	2.63 (0.63)	2.50 (0.26)*	2.61 (0.32)
%Δ	10.5 ^{#,†}	4.0	6.7	2.7

Data are presented as the mean with standard deviation in parentheses. *CB-RT* combination HI-RT and LI-BFR training, *CON* non-training, *HI-RT* high-load resistance training, *Relative dynamic strength* 1-RM strength divided by triceps brachii muscle cross-sectional area, *Relative isometric strength* maximum voluntary contraction divided by triceps brachii muscle cross-sectional area, *LI-BFR* low-load resistance training with blood flow restriction

* Different from Pre, $p < 0.05$; #Different from CON, $p < 0.05$; †Different from LI-BFR, $p < 0.05$

Muscle adaptations through HI-RT or LI-BFR training alone

Our results showed that HI-RT-induced muscle adaptations are consistent with the results of previous HI-RT studies (Abe et al. 2000; Hartmann et al. 2009; McLester et al. 2000), namely that there are similar magnitudes of increases in muscle size and isometric and 1-RM strength. Increases in muscle protein synthesis after a single bout of exercise are observed in high-intensity resistance exercise (Phillips et al. 1997; Yarasheski et al. 1999) as well as in low-intensity BFR resistance exercise (Fry et al. 2010; Fujita et al. 2007). Interestingly, the same laboratory using the same technique reported that 70% 1-RM intensity knee extension exercise without BFR increased vastus lateralis muscle protein synthesis (48% at 2 h post-exercise) through the mTOR signaling pathway in young men (Dreyer et al. 2006). It also reported that 20% 1-RM intensity knee extension exercise with BFR increased muscle protein synthesis (40–50% at 3 h post-exercise) through the mTOR pathway in both young and old men (Fry et al. 2010; Fujita et al. 2007). These anabolic responses may contribute to LI-BFR- and HI-RT-induced muscle hypertrophy. Therefore, it would seem that a similar magnitude of significant muscle hypertrophy was achieved by HI-RT and LI-BFR training.

Most previous studies (Abe et al. 2000; Ikai and Fukunaga 1970; Moritani and deVries 1979) as well as the current study indicated that HI-RT increased relative strength, but LI-BFR training did not. Our results showed that muscle size and dynamic 1-RM strength are increased following 6 weeks of LI-BFR training. These findings are

similar to results from previously reported low-intensity BFR training studies (Abe et al. 2006; Fujita et al. 2008; Kubo et al. 2006; Takarada et al. 2000b, 2002). A finding of no change in relative strength in the LI-BFR group was also similar to the findings of previous studies (Abe et al. 2006; Fujita et al. 2008; Kubo et al. 2006; Takarada et al. 2000b, 2002). For previously untrained subjects, the training load required to increase maximal strength is fairly low since they are not proficient in the proper form and technique. In general, training loads of 45–50% 1-RM are needed to increase dynamic muscle strength for untrained subjects (ACSM 2009; Rhea et al. 2003). In fact, relative strength was increased when BFR training was performed at a training load of 50% 1-RM (Moore et al. 2004). Thus, it appears that LI-BFR training of 20–30% 1-RM rarely produces increases in neural adaptation. These findings indicated that the LI-BFR training-induced increase in muscle strength was due to the muscle hypertrophy only, unlike HI-RT training.

Muscle adaptations through combined HI-RT and LI-BFR training

To the best of our knowledge, this is the first study to investigate the combined effects of LI-BFR and HI-RT training (CB-RT) on relative strength per unit muscle CSA. Most previous studies (Abe et al. 2006; Fujita et al. 2008; Kubo et al. 2006; Takarada et al. 2000b, 2002) as well as the current study indicated that LI-BFR alone did not change relative isometric and dynamic strength. Following the CB-RT program in the present study, improvement in relative dynamic strength, but not relative isometric strength, was elicited. In contrast, increases in relative isometric and dynamic strength were observed following HI-RT in previous studies as well as ours. The difference between CB-RT and HI-RT was the frequency of HI-RT sessions—once a week for CB-RT and 3 times a week for HI-RT—which may be associated with the relative strength results. To improve dynamic strength, once-weekly dynamic resistance training is effective, as reported previously (Hunter et al. 2001; McLester et al. 2000). Rutherford and Jones (1986) demonstrated that dynamic resistance training produces a greater relative increase in dynamic strength compared with isometric strength, since there is task specificity involved in neural adaptation. Therefore, it would appear that the CB-RT-induced increase in relative dynamic strength was due to the task specificity of the HI-RT program.

On the other hand, relative isometric strength was improved following the dynamic HI-RT program, suggesting that task specificity alone does not fully account for neural adaptation. Previously, resistance training-induced improvement in relative isometric strength was thought to

be due to changes in agonist and/or antagonist co-activation levels (Folland and Williams 2007). In the present study, the antagonist co-activation level was unchanged after the training in each group, although the agonist activation was not evaluated. Previous studies have reported that untrained subjects cannot maximally activate their agonist during MVC even when fully motivated (Dudley et al. 1990; Moritani and deVries 1979; Westing et al. 1988), and the level of agonist activation was increased following an HI-RT program, with a training frequency of three times a week (Erskine et al. 2010). It is possible that improvement in relative isometric strength in the HI-RT group may be caused by the increase in agonist activation (i.e., motor unit recruitment, firing frequency, and synchronization), while the CB-RT program, with its once-weekly HI-RT session, may not lead to significant change. More work is needed to understand how different training programs affect improvement in relative strength.

Perceived pain and safety of LI-BFR training

Apart from the beneficial effects of LI-BFR training, there exists the concern that LI-BFR may only be limited to highly motivated individuals (Hollander et al. 2010; Loenneke et al. 2010; Wernbom et al. 2006, 2008, 2009). In general, wide and/or non-elastic cuffs around the limbs are used in orthopedic surgeries to maintain complete occlusion of the blood flow. Therefore, LI-BFR by a surgical tourniquet (i.e., 135 mm width for thighs) may cause neural impairment and a suppression of lactate clearance, resulting in serious perceptual pain (Wernbom et al. 2006, 2009). On the other hand, a previous study reported that narrow and elastic cuffs (30 mm width) at 300 mmHg for arms also caused a complete occlusion of blood flow and serious perceptual pain (Yasuda et al. 2009). However, since most LI-BFR studies were using narrow and elastic cuffs (30 mm width for arms, 33–50 mm width for thighs) to compress at 100–160 mmHg for arms and at 160–240 mmHg for thighs, the arterial blood flow was reduced by no more than 40–70% of the baseline value (Iida et al. 2007; Takano et al. 2005; Yasuda et al. 2010a). In the present study, we did not record the perceptual pain using a pain scale, but there were no incidents of any pain reported. In addition, RPE was lower in LI-BFR compared with HI-RT. Furthermore, LI-BFR was performed by narrow and elastic cuffs at 100–160 mmHg, which suggests that our LI-BFR moderately restricted the blood flow. Therefore, in the present study, it can be speculated that LI-BFR with the use of narrow and elastic cuffs does not require any special effort from the subjects due to the absence of pain unlike LI-BFR with the use of surgical tourniquets which induces perceptual pain and is only accepted by willing subjects who are capable of tolerating the discomfort.

Since the mechanisms of muscle adaptation by LI-BFR are not fully understood, there is a controversy concerning the safety of the LI-BFR method. Previous studies have shown that severe restrictions or complete occlusions of blood flow may cause the thrombus formation, and induce microvascular occlusions after releasing the BFR, which results in muscle cell damage and necrosis (Harmon 1948, Kawada and Ishii 2005; Strock and Majno 1969). Therefore, LI-BFR always requires paying attention to the side effects. Recently, it has been demonstrated that LI-BFR has no impact on the blood clotting function as assessed by the changes in fibrin D-dimer and fibrin degradation products after exercise or training (Clark et al. 2010; Fujita et al. 2008; Madarame et al. 2010). Also, Clark et al. (2010) reported that in several clinical assessments, LI-BFR did not negatively alter peripheral vascular stiffness and peripheral nerve conduction after 4 weeks of training. Furthermore, Nakajima et al. (2006) surveyed 13,000 people (45.4% males and 54.6% females) that the use of BFR training on a population of different age groups, including ages of over 70 years, to examine the observed incidences and occurrences of side effects in BFR training. In total, more than 30,000 BFR training sessions were conducted, where the most frequent side effects were subcutaneous hemorrhage (13.1%), temporary numbness (1.3%), and lightheadedness (0.3%). Only in very few cases, more serious adverse effects were observed: venous thrombosis (0.06%), deterioration of ischemic heart disease (0.016%), cerebral infarction (0.008%), rhabdomyolysis (0.008%), and pulmonary embolism (0.008%). All these findings suggest that LI-BFR is a relatively safe training method, but it should be noted that the possibilities of side effects cannot be denied completely.

Conclusion

Training-induced improvements in isometric and dynamic strength brought about by combining LI-BFR with HI-RT (CB-RT program) were higher than those seen with LI-BFR alone, which were similar to those of HI-RT alone. Although the TB and PM muscle CSA increased significantly following three training sessions, relative strength improved with HI-RT and CB-RT, but not with LI-BFR. Therefore, BFR training-induced functional muscle adaptations are improved by combining BFR with HI-RT. Given the health risks and strength improvement associated with resistance training, a combination of HI-RT and LI-BFR may be an effective training program for promoting strength adaptations in practical applications.

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References

- Abe T, deHoyos DV, Pollock ML, Garzarella L (2000) Time course for strength and muscle thickness changes following upper and lower body resistance training in men and women. *Eur J Appl Physiol* 81:174–180
- Abe T, Yasuda T, Midorikawa T, Sato Y, Kearns CF, Inoue K, Koizumi K, Ishii N (2005) Skeletal muscle size and circulating IGF-1 are increased after two weeks of twice daily “KAATSU” resistance training. *Int J Kaatsu Training Res* 1:6–12
- Abe T, Kearns CF, Sato Y (2006) Muscle size and strength are increased following walk training with restricted venous blood flow from the leg muscle, Kaatsu-walk training. *J Appl Physiol* 100:1460–1466
- American College of Sports Medicine (1998) American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc* 30:992–1008
- American College of Sports Medicine (2009) American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 41:687–708
- Borg GA (1982) Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 14:377–381
- Clark BC, Manini TM, Hoffman RL, Williams PS, Guiler MK, Knutson MJ, McGlynn ML, Kushnick MR (2010) Relative safety of 4 weeks of blood flow-restricted resistance exercise in young, healthy adults. *Scand J Med Sci Sports* [Epub ahead of print]
- Cohen J (1988) Statistical power analysis for the behavioral sciences. 2nd edn. Lawrence Erlbaum Associates Inc., Hillsdale, NJ pp 19–39
- Dreyer HC, Fujita S, Cadenas JG, Chinkes DL, Volpi E, Rasmussen BB (2006) Resistance exercise increases AMPK activity and reduces 4E-BP1 phosphorylation and protein synthesis in human skeletal muscle. *J Physiol* 576:613–624
- Dudley GA, Harris RT, Duvoisin MR, Hather BM, Buchanan P (1990) Effect of voluntary vs. artificial activation on the relationship of muscle torque to speed. *J Appl Physiol* 69:2215–2221
- Erschine RM, Jones DA, Williams AG, Stewart CE, Degens H (2010) Resistance training increases in vivo quadriceps femoris muscle specific tension in young men. *Acta Physiol (Oxf)* 199:83–89
- Fleck SJ (1999) Periodized strength training: a critical review. *J Strength Cond Res* 13:82–89
- Folland JP, Williams AG (2007) The adaptations to strength training: morphological and neurological contributions to increased strength. *Sports Med* 37:145–168
- Fry CS, Glynn EL, Drummond MJ, Timmerman KL, Fujita S, Abe T, Dhanani S, Volpi E, Rasmussen BB (2010) Blood flow restriction exercise stimulates mTORC1 signaling and muscle protein synthesis in older men. *J Appl Physiol* 108:1199–1209
- Fujita S, Abe T, Drummond MJ, Cadenas JG, Dreyer HC, Sato Y, Volpi E, Rasmussen BB (2007) Blood flow restriction during low-intensity resistance exercise increases S6K1 phosphorylation and muscle protein synthesis. *J Appl Physiol* 103:903–910
- Fujita T, Brechue WF, Kurita K, Sato Y, Abe T (2008) Increased muscle volume and strength following six days of low-intensity resistance training with restricted muscle blood flow. *Int J Kaatsu Training Res* 4:1–8
- Goto K, Nagasawa M, Yanagisawa O, Kizuka T, Ishii N, Takamatsu K (2004) Muscular adaptations to combinations of high- and low-intensity resistance exercises. *J Strength Cond Res* 18:730–737
- Harmon JW (1948) The significance of local vascular phenomena in production of ischemic necrosis in skeletal muscle. *Am J Pathol* 24:625–641
- Hartmann H, Bob A, Wirth K, Schmidtbleicher D (2009) Effects of different periodization models on rate of force development and power ability of the upper extremity. *J Strength Cond Res* 23:1921–1932
- Haykowsky MJ, Findlay JM, Ignaszewski AP (1996) Aneurysmal subarachnoid hemorrhage associated with weight training: three case reports. *Clin J Sport Med* 6:52–55
- Hollander DB, Reeves GV, Clavier JD, Francois MR, Thomas C, Kraemer RR (2010) Partial occlusion during resistance exercise alters effort sense and pain. *J Strength Cond Res* 24:235–243
- Hunter GR, Wetzstein CJ, McLafferty CL Jr, Zuckerman PA, Landers KA, Bamman MM (2001) High-resistance versus variable-resistance training in older adults. *Med Sci Sports Exerc* 33:1759–1764
- Iida H, Kurano M, Takano H, Kubota N, Morita T, Meguro K, Sato Y, Abe T, Yamazaki Y, Uno K, Takenaka K, Hirose K, Nakajima T (2007) Hemodynamic and neurohumoral responses to the restriction of femoral blood flow by KAATSU in healthy subjects. *Eur J Appl Physiol* 100:275–285
- Ikai M, Fukunaga T (1970) A study on training effect on strength per unit cross-sectional area of muscle by means of ultrasonic measurement. *Int Z Angew Physiol* 28:173–180
- Kawada S, Ishii N (2005) Skeletal muscle hypertrophy after chronic restriction of venous blood flow in rats. *Med Sci Sports Exerc* 37:1144–1150
- Kawakami Y, Abe T, Kuno SY, Fukunaga T (1995) Training-induced changes in muscle architecture and specific tension. *Eur J Appl Physiol Occup Physiol* 72:37–43
- Kraemer WJ, Ratamess NA (2004) Fundamentals of resistance training: progression and exercise prescription. *Med Sci Sports Exerc* 36:674–688
- Kraemer WJ, Patton JF, Gordon SE, Harman EA, Deschenes MR, Reynolds K, Newton RU, Triplett NT, Dziados JE (1995) Compatibility of high-intensity strength and endurance training on hormonal and skeletal muscle adaptations. *J Appl Physiol* 78:976–989
- Kubo K, Komuro T, Ishiguro N, Tsunoda N, Sato Y, Ishii N, Kanehisa H, Fukunaga T (2006) Effects of low-load resistance training with vascular occlusion on the mechanical properties of muscle and tendon. *J Appl Biomech* 22:112–119
- Leveritt M, Abernethy PJ, Barry BK, Logan PA (1999) Concurrent strength and endurance training: a review. *Sports Med* 28:413–427
- Loenneke JP, Balapur A, Thrower AD, Barnes JT, Pujol TJ (2010) The perceptual responses to occluded exercise. *Int J Sports Med* [Epub ahead of print]
- MacDougall JD, Tuxen D, Sale DG, Moroz JR, Sutton JR (1985) Arterial blood pressure response to heavy resistance exercise. *J Appl Physiol* 58:785–790
- Madarame H, Kurano M, Takano H, Iida H, Sato Y, Ohshima H, Abe T, Ishii N, Morita T, Nakajima T (2010) Effects of low-intensity resistance exercise with blood flow restriction on coagulation system in healthy subjects. *Clin Physiol Funct Imaging* 30:210–213
- Marx JO, Ratamess NA, Nindl BC, Gotshalk LA, Volek JS, Dohi K, Bush JA, Gómez AL, Mazzetti SA, Fleck SJ, Häkkinen K, Newton RU, Kraemer WJ (2001) Low-volume circuit versus high-volume periodized resistance training in women. *Med Sci Sports Exerc* 33:635–643
- McLester JR Jr, Bishop P, Williams ME (2000) Comparison of 1 day and 3 days per week of equal-volume resistance training in experienced subjects. *J Strength Cond Res* 14:273–281
- Miyachi M, Kawano H, Sugawara J, Takahashi K, Hayashi K, Yamazaki K, Tabata I, Tanaka H (2004) Unfavorable effects of resistance training on central arterial compliance: a randomized intervention study. *Circulation* 110:2858–2863

- Monahan KD, Tanaka H, Dinunno FA, Seals DR (2001) Central arterial compliance is associated with age- and habitual exercise-related differences in cardiovascular baroreflex sensitivity. *Circulation* 104:1627–1632
- Moore DR, Burgomaster KA, Schofield LM, Gibala MJ, Sale DG, Phillips SM (2004) Neuromuscular adaptations in human muscle following low intensity resistance training with vascular occlusion. *Eur J Appl Physiol* 92:399–406
- Moritani T, deVries HA (1979) Neural factors versus hypertrophy in the time course of muscle strength gain. *Am J Phys Med* 58:115–130
- Nader GA (2006) Concurrent strength and endurance training: from molecules to man. *Med Sci Sports Exerc* 38:1965–1970
- Nakajima T, Kurano M, Iida H, Takano H, Oonuma H, Morita T, Meguro K, Sato Y, Nagata T (2006) Use and safety of KAATSU training: results of a national survey. *Int J KAATSU Training Res* 2:5–13
- Narici MV, Hoppeler H, Kayser B, Landoni L, Claassen H, Gavardi C, Conti M, Cerretelli P (1996) Human quadriceps cross-sectional area, torque and neural activation during 6 months strength training. *Acta Physiol Scand* 157:175–186
- O'Rourke M (1990) Arterial stiffness, systolic blood pressure, and logical treatment of arterial hypertension. *Hypertension* 15:339–347
- Ozaki H, Miyachi M, Nakajima T, Abe T (2011) Effects of 10-weeks walk training with leg blood flow reduction on carotid arterial compliance and muscle size in the elderly adults. *Angiology* 62:81–86
- Phillips SM, Tipton KD, Aarsland A, Wolf SE, Wolfe RR (1997) Mixed muscle protein synthesis and breakdown after resistance exercise in humans. *Am J Physiol* 273:E99–E107
- Pollock ML, Graves JE, Swart DL, Lowenthal DT (1994) Exercise training and prescription for the elderly. *South Med J* 87:S88–S95
- Rhea MR, Alvar BA, Burkett LN, Ball SD (2003) A meta-analysis to determine the dose response for strength development. *Med Sci Sports Exerc* 35:456–464
- Rutherford OM, Jones DA (1986) The role of learning and coordination in strength training. *Eur J Appl Physiol Occup Physiol* 55:100–105
- Sale DG (1988) Neural adaptation to resistance training. *Med Sci Sports Exerc* 20:S135–S145
- Strock PE, Majno G (1969) Microvascular changes in acutely ischemic rat muscle. *Surg Gynecol Obstet* 129:1213–1224
- Takano H, Morita T, Iida H, Asada K, Kato M, Uno K, Hirose K, Matsumoto A, Takenaka K, Hirata Y, Eto F, Nagai R, Sato Y, Nakajima T (2005) Hemodynamic and hormonal responses to a short-term low-intensity resistance exercise with the reduction of muscle blood flow. *Eur J Appl Physiol* 95:65–73
- Takarada Y, Nakamura Y, Aruga S, Onda T, Miyazaki S, Ishii N (2000a) Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. *J Appl Physiol* 88:61–65
- Takarada Y, Takazawa H, Sato Y, Takebayashi S, Tanaka Y, Ishii N (2000b) Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. *J Appl Physiol* 88:2097–2106
- Takarada Y, Sato Y, Ishii N (2002) Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. *Eur J Appl Physiol* 86:308–314
- Wernbom M, Augustsson J, Thomeé R (2006) Effects of vascular occlusion on muscular endurance in dynamic knee extension exercise at different submaximal loads. *J Strength Cond Res* 20:372–377
- Wernbom M, Augustsson J, Raastad T (2008) Ischemic strength training: a low-load alternative to heavy resistance exercise? *Scand J Med Sci Sports* 18:401–416
- Wernbom M, Järrebring R, Andreasson MA, Augustsson J (2009) Acute effects of blood flow restriction on muscle activity and endurance during fatiguing dynamic knee extensions at low load. *J Strength Cond Res* 23:2389–2395
- Westing SH, Seger JY, Karlson E, Ekblom B (1988) Eccentric and concentric torque-velocity characteristics of the quadriceps femoris in man. *Eur J Appl Physiol Occup Physiol* 58:100–104
- Yarasheski KE, Pak-Loduca J, Hasten DL, Obert KA, Brown MB, Sinacore DR (1999) Resistance exercise training increases mixed muscle protein synthesis rate in frail women and men ≥ 76 yr old. *Am J Physiol* 277:E118–E125
- Yasuda T, Brechue WF, Fujita T, Sato Y, Abe T (2008) Muscle activation during low-intensity muscle contractions with varying levels of external limb compression. *J Sports Sci Med* 7:467–474
- Yasuda T, Brechue WF, Fujita T, Shirakawa J, Sato Y, Abe T (2009) Muscle activation during low-intensity muscle contractions with restricted blood flow. *J Sports Sci* 27:479–489
- Yasuda T, Abe T, Brechue WF, Iida H, Takano H, Meguro K, Kurano M, Fujita S, Nakajima T (2010a) Venous blood gas and metabolite response to low-intensity muscle contractions with external limb compression. *Metabolism* 59:1510–1519
- Yasuda T, Fujita S, Ogasawara R, Sato Y, Abe T (2010b) Effects of low-intensity bench press training with restricted arm muscle blood flow on chest muscle hypertrophy: a pilot study. *Clin Physiol Funct Imaging* 30:338–343