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EFFECTS OF 42 WEEKS WALK TRAINING WITH BLOOD FLOW REDUCTION ON MUSCLE SIZE AND STRENGTH IN THE ELDERLY

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ABSTRACT

Short-term slow walk training combined with leg blood flow reduction (BFR-W) produces thigh muscle hypertrophy and strength gains in young and elderly adults. However, the impact of long-term BFR-W training on muscle size and function has not been explored.

PURPOSE: To determine the physiological responses to relatively long-term BFR-W training with different exercise frequencies on muscle mass and strength, as well as functional ability, in older women and men.

METHODS: Sixteen older adults (60-78 yrs) were randomized into either BFR-W (n=8: 6 women, 2 men) or non-exercise control (CON) (n=8: 6 women, 2 men) groups. BFR-W group walked on a treadmill for 20 min at 67 m/min. Initially BFR-W group exercised 5 days/wk for 6 weeks, followed by 2 days/wk for 12 weeks and then once a week for 24 weeks. The BFR-W group wore pressure cuff belts (5 cm wide) on both legs during training (external compression: 160-200 mmHg). Ultrasound estimated muscle mass, knee extension strength, and functional ability (Up & Go and chair stand tests) were assessed before (pre), at 6th week (post-1), at 18th week (post-2, BFR-walk only), and at 42nd week (post-3, BFR-walk only).

RESULTS: After the initial 6 weeks of training, thigh muscle mass increased by 12% (pre: 5.4 ± 0.6 kg; post-1: 6.0 ± 0.6 kg, P<0.05) while no change was observed in CON (pre: 5.5 ± 0.4 kg; post-1: 5.3 ± 0.4 kg, P>0.10). Isometric and isokinetic (30, 90 and 180 deg/sec) knee extension torques increased in BFR-walk (6 to 15%, P<0.05) while no significant increases were seen in CON group (P>0.10). Functional ability also increased significantly, but only in BFR-W group (P<0.05). After 12 additional weeks of reduced training frequency (2 days/wk), thigh muscle mass (6.0 ± 0.6 kg) and strength were well maintained in BFR-W group without any notable change in muscle size or function (P>0.05). However, thigh muscle mass decreased (5.6 ± 0.5 kg) following 24 weeks of reduced training frequency (once a week, post-3) compared with the 18^{th} week (post-2) period, although isometric strength was maintained.

CONCLUSION: slow walk training combined with leg blood flow reduction increased muscle size and strength when performed 5 days/wk in the elderly (post-1). Furthermore, a 2 days/wk training regimen can maintain the training response and increase bone turnover over a 12 week period (post-2). However, training-induced increases in thigh muscle size decreased during once a week training (post-3).

Keywords: Vascular Occlusion, Muscle Hypertrophy, Kaatsu Training

INTRODUCTION

A loss of skeletal muscle mass leads to an increased risk for development of insulin resistance and type-2 diabetes (13), as well as reduced levels of daily activity and physical function (22). Previously, several studies demonstrated that high-intensity resistance training leads to significant increases in muscle mass and strength in the middle-aged and the elderly (1,9,10), suggesting that high-intensity resistance training can induce muscle hypertrophy and improve insulin resistance and type-2 diabetes in the elderly (7). However, the high intensity required for muscle adaptation with traditional resistance exercise may not be practical, and may even be dangerous when carried out without proper supervision in the elderly. Therefore, it would be advantageous to develop safe and effective methods for promoting muscle hypertrophy and strength in the elderly and frail.

In the past decade, several published studies have reported that muscle hypertrophy and strength gains can be produced with low-intensity (20% of one repetition maximal, 1-RM) resistance exercise performed with restricted muscle blood flow (5,17). This training reduces arterial inflow and venous outflow from the active limb muscles and is termed KAATSU training (16). Surprisingly, slow walk training combined with leg blood flow reduction (BFR-W) produces thigh muscle hypertrophy and increased strength in young (3) and elderly (4) subjects. However, these two investigations were only 3-6 weeks in duration and the impact of long-term BFR-W training on muscle size and function is still unknown. Interestingly, a previous study (18) reported that high-intensity resistance training performed once per week is sufficient to maintain muscle strength and size in elderly men following resistance training, however, it is unknown if a reduced BFR-W training frequency can also maintain skeletal muscle mass and function after training. Thus the purpose of the present study was to examine the physiological response to relatively long-term BFR-W training with different exercise frequency on muscle mass and strength, as well as functional ability in older women and men.

METHODS

Sixteen elderly men and women, aged 60-78 years volunteered to participate in the study. Subjects were randomized into either a BFR-W training group (2 men, 6 women: n=8) or a non-exercising control (CON) group (2 men, 6 women: n=8). The elderly subjects in this study were physically active and most of them performed daily walk exercise (average 8000-20000 steps/day as assessed by pedometer). Consequently, subjects in the control group continued their daily physical activity, but no additional exercise routine was imposed. Potential subjects were required to fill out a medical history questionnaire and have a health interview by a physician. All subjects were informed of the methods, procedures and risks, and signed an informed consent document before participation. The study was conducted according to the Declaration of Helsinki and was approved by the Ethics Committee for Human Experiments of the University of Tokyo, Japan.

Training was conducted once a day, five days per week for 6 weeks, followed by 2 days per week for 3 months (12 weeks) and then once a week for 6 months (24 weeks, total 42 weeks). The subjects walked on a motor-driven treadmill at 67 m/min for 20 minutes. The walking speed and duration remained constant throughout the training period. Subjects in the BFR-W group wore pressure belts (Kaatsu-Master, Sato Sports Plaza, Tokyo) on both legs during walk training. Prior to the BFR-W training, the subjects were seated on a chair and the belt air pressure was set at 100 mmHg (the approximate mean blood pressure at heart level for each subject) for 30 sec, and then the air pressure was released. The air pressure was increased by 20 mmHg and held for 30 sec, and then it was released for 10 sec between occlusive stimulations. This process was repeated until a final occlusion pressure for each training day. On the first day of the training, the final belt pressure (training pressure) was 160 mmHg. This training pressure was increased by 10 mmHg each week until a final belt pressure of 200 mmHg was reached. A restriction pressure of 160 to 200 mmHg was selected for the restriction stimulus based on a review of the data in young men (3) and older subjects (4). Blood flow to the leg muscles was restricted for a total time of about 23 minutes (20 minutes walking and 3 minutes of preparation process) during each training session.

Lower body skeletal muscle mass was estimated from muscle thickness (MTH) and ultrasound-derived prediction equations (15). Ultrasound evaluation of MTH was performed using a real-time linear electronic scanner with a 5 MHz scanning head (SSD-500, Aloka, Tokyo), and water-soluble transmission gel, which provided acoustic contact without depression of the skin surface. The scanning head was placed perpendicular to the tissue interface at predetermined marked sites. MTHs were then measured directly from the screen with electronic calipers, and determined as the distance from the adipose tissue-muscle interface to the muscle-bone interface for the following areas: anterior and posterior thigh, midway between the lateral condyle of the femur and greater trochanter; and anterior and posterior lower leg, at 30% proximal between the lateral malleolus of the fibula and the lateral condyle of the tibia, as described previously (2). The standard error of estimates (SEE) for the predicted thigh and lower leg muscle masses ranged 1.4-1.8 kg and 0.5-0.6 kg, respectively, in men and women (15).

Maximal voluntary isometric and isokinetic strength of the knee extensors were determined

using a Biodex System-3 dynamometer. Subjects were carefully familiarized with the testing procedures of voluntary force production of the thigh muscles during several submaximal and maximal performances about one week before testing. The subjects were seated on a chair with their hip joint angle positioned at 85°. The center of rotation of the knee joint was visually aligned with the axis of the lever arm of the dynamometer and the ankle of the right leg was firmly attached to the lever arm of the dynamometer with a strap. Several warm-up contractions were performed prior to testing. Subjects were then instructed to perform maximal isometric knee extension at a fixed knee joint angle of 75° followed by maximal isokinetic knee extensions, between 0° to 90° range of motion for the knee at three different testing speeds (30, 90 and 180 deg/sec). A knee joint angle of 0° corresponded to full extension of the knee.

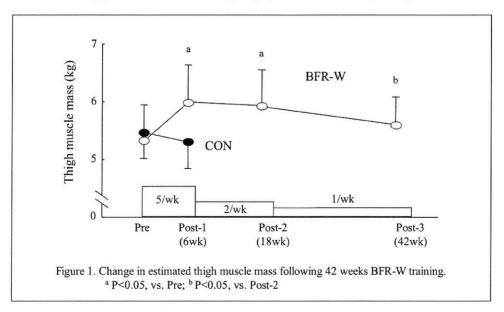
Two tests were used to assess functional ability for each subject (14). The Timed Up and Go Test required the time to be measured for the subject to stand from a chair without the use of their arms, walk 2.4 meters (8 feet), turn around, walk back to the chair, and return to the seated position. The second functional test required the subject to stand up from a seated position, as many times as possible, in 30 seconds.

Resting venous blood samples by venipuncture from the antecubital vein were obtained between 09:00 and 10:00, following an overnight fast. Blood hemoglobin was determined by the cyanomethemoglobin method (Coulter hemoglobinometer) and hematocrit by the micro-hematocrit ultra centrifugation technique. Serum growth hormone (GH), insulin-like growth factor-1 (IGF-1) and IGF binding protein-3 (IGFBP-3) concentrations were determined using commercially available kits (at S.R.L. Inc., Tokyo, Japan).

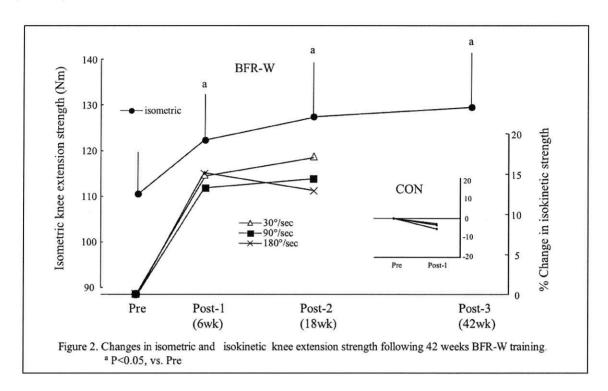
StatView, version 4.5, was used to compute the data and the results are expressed as means and standard errors (SE) for all variables. Statistical analyses were performed by a two-way analysis of variance (ANOVA) with repeated measures [Group (BFR-W and CON) x Time (pre and post)]. Baseline differences and percent changes between BFR-W and CON were evaluated with a one-way ANOVA. Statistical significance was set at P < 0.05.

RESULTS

At baseline, prior to training, there were no significant differences between BFR-W and CON groups for age $(67.8\pm4.6 \text{ and } 65.4\pm6.1 \text{ yr}, \text{ respectively})$, standing height $(1.52\pm0.06 \text{ and } 1.55\pm0.08 \text{ m})$, body weight $(54.4\pm9.4 \text{ and } 54.4\pm7.3 \text{ kg})$, body mass index (BMI, $23.4\pm2.8 \text{ and } 22.4\pm1.4 \text{ kg/m}^2)$, and mid-thigh girth $(46.8\pm3.8 \text{ and } 47.0\pm1.6 \text{ cm})$. There were no significant changes in body weight and BMI for either group following initial 6 weeks of the training, and also throughout the additional training period in the BFR-W group (post-2, $53.2\pm9.0 \text{ kg}$ and post-3, $53.3\pm9.4 \text{ kg}$).



After the initial 6 weeks of training (post-1), mid-thigh girth increased (P<0.05) significantly in the BFR-W group (pre, 46.8 ± 3.8 cm and post-1, 47.6 ± 3.9 cm), but not in the CON group (pre, 47.0 ± 1.6 cm and post-1, 46.7 ± 1.9 cm). Thigh muscle mass increased by 12% (pre, 5.4 ± 0.6 kg and post-1, 6.0 ± 0.6 kg; P<0.05) while no change was observed in CON (pre, 5.5 ± 0.4 kg and post-1, 5.3 ± 0.4 kg; P>0.10). Isometric and isokinetic (30, 90 and 180 deg/sec) knee extension torques increased in BFR-W (6 to 15%, P<0.05) while no significant increase (P>0.10) was seen in CON group (Figs. 1 & 2). Functional ability also increased (P<0.05) significantly only in the BFR-W group (Table 1).



After 12 additional weeks of reduced training frequency (2 days per week, post-2), thigh muscle mass (6.0 ± 0.6 kg) and isometric and isokinetic knee extension strength were well maintained in BFR-W group without any notable change (P>0.05) in muscle size or function (Fig. 1). However, thigh muscle mass decreased (5.6 ± 0.5 kg) following 24 weeks of additional reduced training frequency (once a week, post-3) compared with the 18^{th} week (post-2) period, although isometric strength was maintained (Figs. 1 & 2).

There were no changes (P>0.05) in resting serum GH, IGF-1 and IGFBP-3, as well as hemoglobin, hematocrit, and red blood cell count for either group. On the other hand, blood concentration of bone-specific alkaline phosphatase (pre, 23.7 ± 9.4 U/l) increased significantly (P<0.05) at 18^{th} week in BFR-W group (post-2, 31.2 ± 13.8 U/l), but not in the CON (22.7 ± 2.1 and 23.0 ± 1.9 U/l, respectively).

DISCUSSION

In the present study, we examined the effects of reduced training frequency (twice or once per week) for 9 months after 6-weeks of BFR-W training on muscle size and function. The main finding was that when training frequency was decreased from 5 days per week to twice per week that muscle size and strength were maintained, however, training only 1 day per week failed to maintain muscle size, even though strength was maintained.

Our findings showed that the relative increase in thigh muscle size that occurred during the initial 6-week BFR-W training was higher than that of previously reported BFR-W training results in young subjects (3), and is comparable to the results of high-intensity resistance training for the elderly (9,10). Similar to the increases in muscle size, muscle strength of knee extensors also increased after

6-weeks of BFR-W training. The relative increases in isometric and isokinetic strength are similar to the improvements observed in high-intensity resistance training studies (8,9). Cellular and molecular mechanisms of hypertrophic responses and strength gains to the BFR-W training are still poorly understood. Skeletal muscle hypertrophy occurs from increased protein accretion and the accumulation of contractile protein, or when the balance between protein synthesis and degradation shifts toward synthesis. A recently published study (12) demonstrated that a single bout of 20% of 1-RM intensity knee extension exercise with BFR increased both thigh muscle protein synthesis and the Akt/mTOR signaling pathway in young men, although the rate of muscle protein breakdown was not measured. More recently, low-intensity BFR exercise-induced increases in muscle protein synthesis was also confirmed in the elderly (11). Similar anabolic responses may have contributed to the presently observed increases in muscle size following BFR-W training.

Our results showed that muscle hypertrophy and strength gains achieved after the 6-week BFR-W training were able to be maintained after reducing the training frequency to twice per week for 3 months. In fact, Trappe et al. (18) reported that high-intensity resistance training performed once per week for 6 months was sufficient to maintain muscle strength and size in elderly men following a 12-week of 3 days per week resistance training. However, thigh muscle size in the current study decreased 7% when the training frequency was further reduced to once per week. The 7% decline over 6 months in muscle size was relatively modest compared with the 12% increase achieved after 6-week of BFR-W training, since a number of studies have shown that 3 months of detraining resulted in the total loss of muscle mass gains (19, 20).

	BFR-W			CON	
_	Pre	Post-1	Post-2	Pre	Post-1
Up & go (sec)	4.4 ± 0.2	3.8 ± 0.2^{-8}	3.5 ± 0.1^{a}	4.5 ± 0.2	4.4 ± 0.2
Chair stand (reps/30-s)	28.3 ± 2.5	31.8 ± 2.6^{a}	$34.8 \pm 1.8^{\ a}$	27.6 ± 2.4	27.0 ± 3.0

Multicomponent exercise programs, consisting of aerobic, strength, and flexibility training, can improve functional ability (chair stand and up-and-go performance) in the elderly (21). In the present study, we also found improvements in the chair stand and up-and-go performance measures after the initial 6-weeks of BFR-W training. These improvements were maintained throughout the 9 months of reduced training frequency and were probably due in part to the significant increases in maximal isometric and isokinetic strength.

Bone-specific alkaline phosphatase (BAP) has a role in the mineralization of newly formed bone (23). Beekley et al. (6) reported that BFR-W training was associated with significant increases in resting levels of serum BAP in young men. Our results also demonstrated increased serum levels of BAP following BFR-W training in the elderly which may indicate increased bone remodeling.

CONCLUSION

Slow walk training combined with leg blood flow reduction increased muscle size and strength when performed 5 days per week in the elderly. Furthermore, decreasing the training frequency to 2 days per week maintained the training response and increased bone turnover but that a further reduction in training frequency to once per week was no longer adequate.

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