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Muscle size and arterial stiffness after blood flow-restricted low-intensity resistance training in older adults

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Previous studies have shown that blood flow-restricted low-intensity resistance training (BFR-RT) causes muscle hypertrophy while maintaining arterial function in young adults. We examined the effects of BFR-RT on muscle size and arterial stiffness in older adults. Healthy subjects (ages 61–84 years) were divided into BFR-RT ($n = 9$) or non-training control (CON; $n = 10$) groups. The BFR-RT group performed 20% and 30%, respectively, of one-repetition maximal (1-RM) knee extension and leg press exercises, 2 days/wk for 12 weeks. The BFR-RT group wore elastic cuffs (120–270 mmHg) on both legs during training. Magnetic resonance imaging-measured muscle cross-sectional area (CSA), 1-RM strength, chair stand (CS) test, and cardio-ankle vascular index testing (CAVI), an index of arterial stiffness, were measured before and 3–5 days after the final training session. Muscle CSA of the quadriceps (8.0%), adductors (6.5%), and gluteus maximus (4.4%), leg extension and leg press 1-RM strength (26.1% and 33.4%), and CS performance (18.3%) improved ($P < 0.05$) in the BFR-RT group, but not in the CON group. In CAVI testing, there were no changes in both two groups. In conclusion, BFR-RT improves muscle CSA as well as maximal muscle strength, but does not negatively affect arterial stiffness or humeral coagulation factors in older adults.

Age-related skeletal muscle loss (sarcopenia) inhibits mobility and increases the risk of developing several diseases such as diabetes, osteoporosis, and heart disease (Visser et al., 2002; Guillet & Boirie, 2005). High-intensity resistance training (HI-RT) can induce muscle hypertrophy and improve insulin resistance and type-2 diabetes in the elderly (Frontera et al., 1988; Fiatarone et al., 1990), suggesting that HI-RT leads to the prevention and/or improvement of sarcopenia in the elderly (Aagaard et al., 2010). However, HI-RT induced about a 20% reduction in arterial compliance in young and older adults (Miyachi et al., 2003, 2004). In general, reductions in arterial compliance or increases in arterial stiffness reduce the arterial buffering function of the pulsation of blood pressure and blood flow, which contribute to elevations in systolic blood pressure, left ventricular hypertrophy, coronary ischemic disease, and reductions in arterial baroreflex sensitivity (O'Rourke, 1990; Tanaka et al., 1998; Monahan et al., 2001). This means that prevention and treatment of arterial compliance or stiffness are also important. Thus, even if traditional HI-RT is an effective tool in reversing sarcopenia and/or osteoporosis, this type of training may have deleterious effect on arterial compliance or stiffness in older adults.

In the past decade, several studies have reported that low-intensity resistance training combined with blood flow restriction (BFR-RT), referred to as "KAATSU Training," elicits muscle hypertrophy and strength gains similar to those elicited during traditional HI-RT (Takarada et al., 2000; Wernbom et al., 2008; Karabulut et al., 2010). Additionally, previous studies have reported that BFR-RT could improve and/or maintain arterial compliance in young adults (Ozaki et al., 2011, 2013). Therefore, BFR-RT may be a useful method for promoting muscle hypertrophy with a low risk of increased arterial stiffness in older adults.

Recently, some studies have demonstrated that sarcopenia is muscle specific and greater quadriceps muscle loss was found in older adults (Miyatani et al., 2003; Abe et al., 2011). However, no previous studies have examined the effect of BFR-RT on lower body muscle size in older adults, and only a single study has investigated changes in skeletal muscle size with BFR-RT in older adults (Takarada et al., 2000). Thus, the purpose of the present study was to examine the effects of BFR-RT on thigh muscle size and arterial stiffness in older adults.

Methods

Participants

Twenty-one older men and women (aged 61–84 years) volunteered to participate in the study and were selected according to the exclusion criteria used to define "medically stable" older participants for exercise studies proposed by Greig et al. (1994). In addition, volunteers who suffered from a chronic disease such as severe hypertension, orthopedic disorders, deep venous thrombosis, peripheral vascular disease, or cognitive dysfunction were excluded from the study. None of the participants had participated in resistance-type training for a minimum of 3 years prior to the study. All participants were free of overt chronic disease as assessed by medical history, physical examination, and complete chemistry and hematologic evaluation. Subjects in the non-training control (CON) group continued their daily physical activity, but no additional exercise routine was imposed. All participants were informed of the risks associated with the methods, procedures and risks, and signed an informed consent document before participation. The principles of the World Medical Association Declaration of Helsinki and the American College of Sports Medicine Guidelines for Use of Human Subjects were adopted in this study. Twenty-one individuals (5 men, 16 women) enrolled in the study, but two participants dropped out following randomization to the BFR-RT group because of reasons unrelated to the research study. Consequently, 19 participants were randomized to either the BFR-RT group {3 men, 6 women: $n = 9$; age [mean ± standard deviation (SD)]: 71.3 ± 7.1 years} or the CON group (2 men, 8 women: $n = 10$; age: 67.7 ± 6.0 years).

Training protocol

To develop the thigh muscles especially for quadriceps muscles, the participants in the BFR-RT group performed bilateral knee extension and leg press exercise training 2 days/week for 12 weeks. This training was performed under the close supervision of those with technical knowledge in BFR training. One week before the start of the training study, both groups performed practice sessions for the functional ability test and one-repetition maximum (1-RM) test. In addition, BFR-RT participants were familiarized with the BFR stimulus. Three or four days before training, the 1-RM of both exercises was determined. Training intensity and volume were set at 20% or 30% of 1-RM and 75 repetitions (30, 20, 15, and 10 reps, with around 30-s rests between sets, respectively) for knee extension and leg press exercises (90-s rests between exercises), respectively. This protocol is typical of submaximal BFR studies (Abe et al., 2005; Yasuda et al., 2010, 2012b). Once the cuffs were inflated, they remained so for the two exercises, including rest periods between sets and exercises. During knee extension and leg press exercises, participants were seated comfortably on isotonic knee extension (13260, VR1, Cybex International, Inc., Medway, Massachusetts, USA) and leg press machines (Pro 1 Seated Leg Press, Life Fitness, Schiller Park, Illinois, USA), with the body supported in a vertical position. Knee joint range of motion (ROM) was approximately 90-0° and hip joint ROM was maintained at 110° (with 180° being full extension) during knee extension exercises, while knee joint ROM and hip joint ROM were approximately 90-0° and 125-70°, respectively during leg press exercises. The exercise duration was 2.0 s (1.0-s concentric and 1.0-s eccentric exercise cycle) for knee extension exercises and 2.6 s (1.3-s concentric and 1.3-s eccentric exercise cycle) for leg press exercises. During all training sessions, heart rate was recorded at baseline (pre) and immediately after the last set of each exercise (post; Model 9560, Onyx II, Nonin Medical Inc., Plymouth, Minnesota, USA). Ratings of perceived exertion, calculated on a scale (6–20) to measure subjective feelings of exertion and fatigue, were recorded immediately after the last set of each exercise (Borg, 1982). The training loads of each exercise for the BFR-RT group were adjusted based on 1-RM testing performed every 3 weeks.

Blood flow restriction

During the training sessions, subjects wore a specially designed elastic pressure cuff (50 mm width, KAATSU Master, Sato Sports Plaza, Tokyo, Japan) around the most proximal portion of the both legs. On the first day of training, the cuff was set at 120 mmHg. The pressure was increased by 10–20 mmHg at each subsequent training session until a pressure of approximately 270 mmHg was reached. The restriction pressure was selected in accordance with previous studies (Yasuda et al., 2012a). Immediately after the two exercises, the pressure cuff was quickly removed. The amount of time under moderate blood flow restriction was approximately 11 min.

Measurements schedule

Subject testing took place before the start of the study (pre) and 3–7 days after (post) the 12-week training period. The orders of measurements were magnetic resonance imaging (MRI), venous blood samples, arterial function [flow-mediated dilatation (FMD), cardio-ankle vascular index testing (CAVI), and ankle brachial pressure index (ABI)] tests, functional ability test, and 1-RM strength measurements. The MRI measurement was obtained between 11:00 and 12:00 h. Venous blood samples and arterial function tests (after 6–7 h fast) or functional ability test and 1-RM strength were determined on separate days (few days interval). The subjects were instructed to refrain from ingesting alcohol and caffeine for 24 h prior to pre- and post-training measurements.

MRI-measured muscle CSA

Muscle CSA was obtained using a MRI scanner (1.5-T MRI, Hitachi, Tokyo, Japan). A T-1 weighted spin-echo axial plane sequence was performed with a 540-ms repetition time and a 20-ms echo time. Subjects rested quietly in the magnet bore in a supine position with their legs extended. The top edge of the great trochanter was used as the origin point, and continuous transverse images with 10-mm slice thickness (0-mm interslice gap) were obtained from the top edge of the great trochanter to the lateral condyle of femur at pre- and post-training measurements. All MRI data were transferred to a personal computer for analysis using specially designed image analysis software (sliceOmatic, Tomovision Inc., QC, Canada). Skeletal muscle tissue cross-sectional area (CSA) data for the quadriceps, adductors and hamstrings at 50% of thigh length (Fig. 1) and for the gluteus maximus at the top edge of the great trochanter were digitized. The coefficient of variation of this measurement was less than 1.0% (Yasuda et al., 2012b).

Estimation of 1-RM strength

One RM was estimated by the 10-RM method (Baechle & Earle, 2008) using a weight stack machine. Bilateral knee extension and leg press maximum dynamic strength (1-RM) were assessed using an isotonic knee extension (VR1, Cybex International, Inc.) and leg press machines (Seated Leg Press, Life Fitness). After warming up, the testing load was set (approximately 80% of predicted 1-RM). Each subject reached muscular failure for the load, and partial repetitions (where participants failed to lift through the entire ROM) did not count as RMs. If a subject had to perform a given repetition number for a given condition again, as a result of ease in obtaining the desired repetitions or failure to attain the repetition number, a 5-min rest period was given and the condition was attempted again at an altered load. No participant had to perform a given repetition number test condition more than three times. Each participant performed the knee extension exercise, rested for 5 min, and then performed the leg press exercise. During estimated 1-RM testing as well as training sessions, the parallel leg

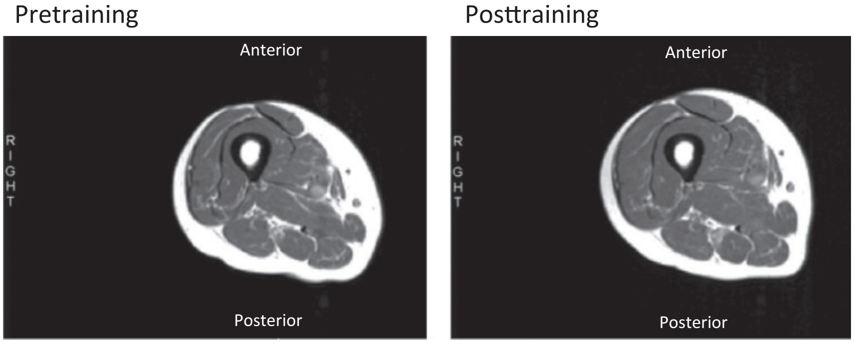

Fig. 1. Typical magnetic resonance images showing transverse sections of the thigh taken before (pre) and after (post) 12 weeks of leg extensions and leg presses with blood flow restriction. The images show identical sections at the mid-thigh in the same subjects (YN).

stance width was set at 100% of the shoulder-width for leg press exercises.

Arterial function tests

FMD, CAVI and ABI measurements were conducted in the supine position. The participants were instructed to fast 6–7 h before testing and refrain from ingesting alcohol, caffeine for at least 12 h prior to testing. After the participants were asked to rest in the lying position in a quiet, dark, air-conditioned room (23–25°C) for 5 min, a standard cuff was positioned around the right arm, 2–3 cm below the antecubital fossa and their systolic and diastolic blood pressures were assessed using oscillometric methods (UA-767PC, A&D Co., Ltd, Tokyo, Japan). Then, after the participants had rested again for at least 15 min in a supine position in the same room, endothelium-dependent FMD of the brachial artery was measured using an established noninvasive method (Corretti et al., 2002). Using a 10-MHz linear array transducer probe, the longitudinal image of the right brachial artery was recorded at baseline and then continuously from 30 sec before to at least 2 min after the cuff deflation that followed syprasystolic compression (50 mmHg above systolic blood pressure) of the right forearm for 5 min. The diastolic diameter of the brachial artery was determined semi-automatically using an instrument equipped with software for monitoring the brachial artery diameter (UNEX EF, Unex Co. Ltd, Nagoya, Japan). %FMD was calculated as reported previously (Tomiyama et al., 2008; Yeboah et al., 2009). Then, after a 20–30-min rest, CAVI and ABI were measured noninvasively using a VS-1500 system (Fukuda Denshi Co., Ltd, Tokyo, Japan). CAVI was obtained by substituting the stiffness parameter into an equation for determining vascular elasticity (Shirai et al., 2006).

Blood sampling and biochemical analyses

Venous blood samples were obtained from the antecubital vein and measured for fibrin/fibrinogen degradation products (FDP), D-dimer and creatine kinase (CK). The plasma concentrations of these samples were measured at a commercial laboratory (SRL Inc., Tokyo, Japan) by following latex immunoassay for FDP and D-dimer and spectrophotometry for nicotinamide adenine dinucleotide phosphate formed by a hexokinase and D-glucose-6-phosphate-dehydrogenase-coupled enzymic system for CK.

Functional ability test

A chair-stand test required participants to stand up from a seated position, as many times as possible, within 30 s (Rikli & Jones, 1990).

Statistical analyses

Results are mean ± SD. Statistical analysis was performed by a two-way analysis of variance (ANOVA) with repeated measures [trials (BFR-RT vs CON) × time (pre vs post)]. Post-hoc testing was performed using Tukey's test when a significant *F*-value was detected. Percent changes from pre were also compared between groups using Tukey's test. Statistical significance was set at $P < 0.05$.

Results

Before training, there were no significant differences between the two groups for age and anthropometric variables except for systolic blood pressure (Table 2). After the training program, mid-thigh girth was increased ($P < 0.01$) in the BFR-RT group, but not in the CON group (Table 1). There were no changes in body mass, BMI and lower leg girth in both groups. During training sessions in the BFR-RT group, heart rates were slightly higher ($P < 0.05$) in the leg press exercise [118 ± 18 beats per minute (BPM)] than in the knee extension (112 ± 19 BPM) exercise. The ratings of perceived exertion tended to be higher ($P = 0.09$) in the knee extension exercise (15.3 ± 1.5) than in the leg press (14.3 ± 1.8) exercise. During both exercises, the participants did not perform contraction efforts until exhaustion.

After 12 weeks of BFR training, CSA was increased by 8.0% (pre, 44.0 ± 9.5 cm^2; post, 45.1 ± 9.4 cm^2) in the quadriceps, 6.5% in the adductors (pre, 22.2 ± 8.4 cm^2; post, 22.6 ± 8.2 cm^2) and 4.4% in the gluteus maximus (pre, 37.5 ± 7.3 cm^2; post, 39.8 ± 4.4 cm^2), but not in the hamstrings (pre, 21.1 ± 4.6 cm^2; post, 21.1 ± 4.1 cm^2) in the BFR-RT group (Fig. 2A–D). In the CON group, no change was observed in each muscle CSA (pre, 43.5 ± 9.5 cm^2; post, 42.7 ± 9.0 cm^2 for quadriceps, pre, 21.2 ± 8.6 cm^2; post, 21.0 ± 8.6 cm^2 for adductors, pre, 19.9 ± 3.6 cm^2; post, 20.3 ± 3.6 cm^2 for hamstrings and pre, 36.4 ± 7.2 cm^2; post, 35.6 ± 7.5 cm^2 for gluteus maximus; Fig. 2A–D). Knee extension and leg press 1-RM strength were also increased 26.1% (pre, 50 ± 20 kg; post, 64 ± 26 kg) and 33.4% (pre, 145 ± 47 cm^2; post, 191 ± 56 kg) in the BFR-RT group but not in the CON group (pre, 52 ± 26 kg; post, 55 ± 27 kg for knee extension and pre, 143 ± 56 kg; post, 142 ± 51 kg for leg press; Fig. 3A,B).

There were no changes ($P > 0.05$) between pre- and post-training in heart rate, systolic and diastolic blood

Table 1. Changes in anthropometric variables and skeletal muscle size after 12 weeks of training period

	BFR-RT			CON		
	Pre	Post	%	Pre	Post	%
Anthropometric variables						
Age, years	71 (7)			68 (6)		
Standing height, m	1.61 (0.08)			1.58 (0.06)		
Body mass, kg	53.9 (9.3)	54.0 (9.0)	0.4	53.4 (9.1)	53.4 (9.0)	0.1
BMI, kg/m^2	20.8 (2.6)	20.9 (2.5)	0.4	21.3 (2.9)	21.3 (2.8)	0.1
Mid-thigh girth, cm	44.0 (3.7)	44.7 (1.5)**	1.5##	46.5 (3.7)	46.3 (3.9)	–0.5
Lower leg girth, cm	33.7 (3.0)	33.5 (3.1)	–0.7	34.0 (2.9)	33.9 (2.9)	–0.4

Notes: Data are given as mean (±standard deviation). BFR-RT, blood flow-restricted resistance training; BMI, body mass index; CON, non-resistance training; mid-thigh girth, at 50% thigh length; lower leg girth, at 30% lower leg length. **$P < 0.01$, Pre vs Post; ##$P < 0.01$, BFR-RT vs CON.

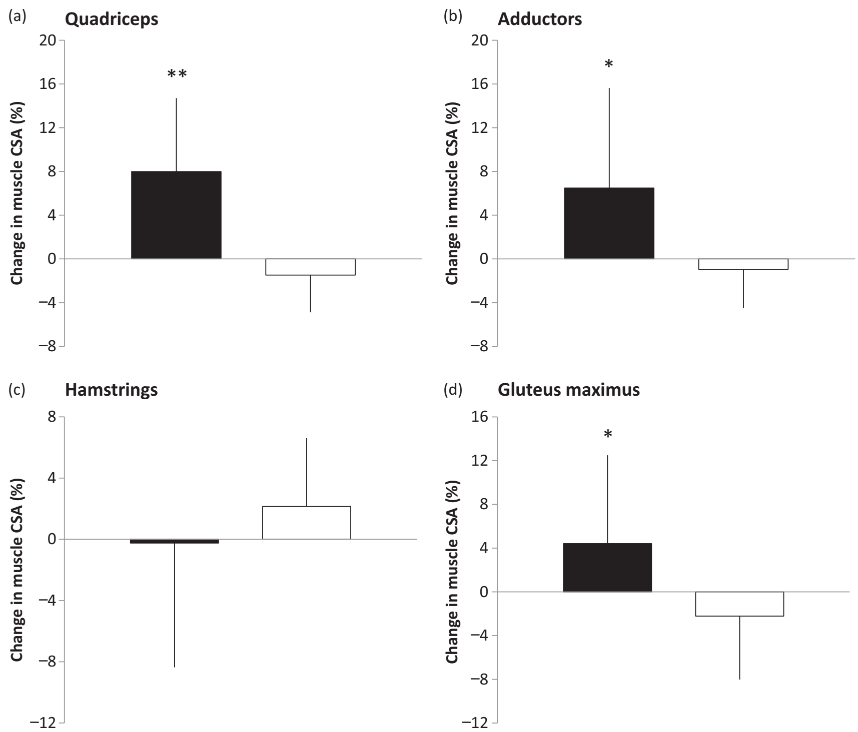

Fig. 2. Percent changes in quadriceps (a), adductors (b), hamstrings, (c) and gluteus maximus (d) muscle cross-sectional area (CSA). Data are given as mean (±standard deviation). **$P < 0.01$, *$P < 0.05$. Blood flow-restricted resistance training (filled symbols) vs non-resistance training (unfilled symbols).

pressures, CAVI, ABI, FDP, D-dimer and CK for either group; however, the BFR-RT group tended to improve ($P = 0.09$) in FMD, whereas the CON group did not change (Table 2).

Chair-stand performance improved ($P < 0.05$) 18.3% in the BFR-RT group (pre, 14.8 ± 3.1 times; post, 17.4 ± 4.2 times), but not in the CON group (pre, 18.0 ± 3.3 times; post, 18.4 ± 3.9 times). The change in the chair-stand test results correlated with the change in muscle CSA for the quadriceps ($r = 0.53$, $P < 0.05$) and gluteus maximus ($r = 0.50$, $P < 0.05$), but not for the adductors ($r = 0.27$, $P > 0.05$), as well as changes in muscle strength for knee extension ($r = 0.55$, $P < 0.05$) and leg press ($r = 0.47$, $P < 0.05$).

Discussion

It has previously been observed that BFR-RT leads to increased muscle size and maintenance of arterial compliance in young adults (Ozaki et al., 2013). However, there are no published data investigating thigh muscle size and arterial stiffness following BFR-RT in older adults. Our findings show that low-intensity knee extension and leg press training with BFR can lead to a significant increases in thigh (quadriceps and adductors) and hip (gluteus maximus) muscle CSA as well as maximal contractile strength in older adults. In addition, we observed no changes in hemodynamic parameters (heart rate, systolic and diastolic blood pressures), arte-

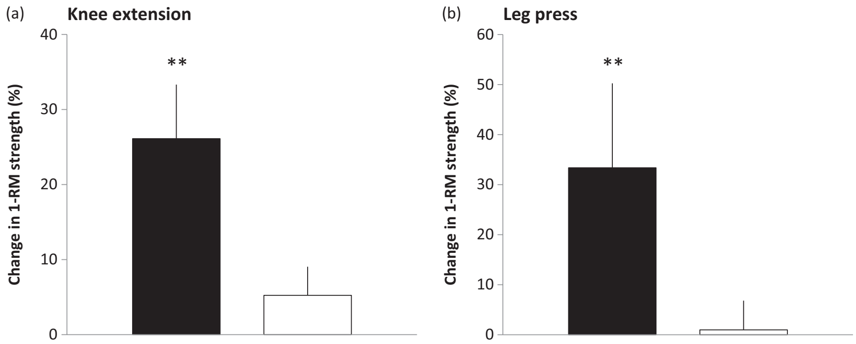

Fig. 3. Percent changes in knee extension (a) and leg press (b) one-repetition maximal (1-RM) strength. Data are given as mean (±standard deviation). $^{**}P < 0.01$, Blood flow-restricted resistance training (filled symbols) vs non-resistance training (unfilled symbols).

Table 2. Changes in hemodynamic parameter, arterial function, coagulation system and muscle damage after 12 weeks of training period

	BFR-RT		CON	
	Pre	Post	Pre	Post
Heart rate, bpm	62 (11)	62 (8)	58 (7)	59 (7)
Systolic BP, mmHg	151 (15)$^{\#\#}$	143 (20)$^{\#}$	126 (10)	121 (12)
Diastolic BP, mmHg	90 (9)	91 (11)	79 (10)	80 (12)
CAVI, m/sec	9.1 (1.4)	9.0 (1.5)	8.7 (0.8)	8.5 (1.1)
ABI, unit	1.13 (0.07)	1.15 (0.06)	1.13 (0.10)	1.13 (0.09)
FMD, %	2.8 (2.0)	4.4 (2.5)§	4.4 (1.8)	3.9 (2.5)
FDP, 10^{-5} g/L	2.9 (1.1)	3.7 (3.0)	2.7 (0.7)	3.0 (2.0)
D-dimer, 10^{-5} g/L	0.5 (0.4)	1.2 (1.6)	0.3 (0.3)	0.4 (0.2)
CK, IU/l	165 (145)	137 (63)	108 (53)	115 (54)

Notes: Data are given as mean (± standard deviation). BFR-RT, blood flow-restricted resistance training; CON, non-resistance training; BP, blood pressure; CAVI, cardio-ankle vascular index; ABI, ankle-brachial pressure index; FMD, flow-mediated dilation; FDP, fibrin/fibrinogen degradation products; CK, creatine kinase. $^{\#\#}P < 0.01$, $^{\#}P < 0.05$, BFR-RT vs CON; $^{\S}P$, 0.09, Pre vs Post.

rial stiffness (CAVI), coagulation factors (FDP and δ-dimer) and muscle damage (CK), suggesting that BFR-RT was an useful method for preventing and/or improving sarcopenia in old healthy adults.

In this study, BFR-RT (at 20–30% 1-RM) produced a hypertrophic potential of 0.33% per session (8.0% increase in quadriceps muscle CSA over 24 training sessions), which is similar to that observed following HI-RT at 80% 1-RM (0.26–0.45%) in elderly adults (Frontera et al., 1988; Fiatarone et al., 1990). Additionally, the observed gains in knee extension and leg press 1-RM strength (1.09% and 1.39% per session, respectively) were comparable with the previous BFR-RT study (Karabulut et al., 2010) at 20% 1-RM (1.06% and 1.07% per session, respectively), which thus appears equally effective as HI-RT at 80% 1-RM for improving thigh muscle strength in older adults. Therefore, our data suggested that BFR-RT (at 20–30% 1-RM) as well as HI-RT (at 80% 1-RM) can provide an effective hypertrophic stimulus on selected thigh muscles in older adults.

Few studies have attempted to elucidate the cellular and molecular mechanisms of adaptation in skeletal muscle as well as the cardiorespiratory system in response to low-intensity BFR exercise (Manini & Clark, 2009). Previous studies demonstrated that a single session of low-intensity (at 20% 1-RM) knee extension exercise with BFR increased both vastus lateralis (VL) muscle protein synthesis (40–50% at 3 h post-exercise) and the Akt/mammalian target of rapamycin (mTOR) signaling pathway in young and older men (Fujita et al., 2007; Fry et al., 2010). These anabolic responses may contribute significantly to BFR training–induced muscle hypertrophy and strength gain. On the other hand, the same laboratory using the same technique reported that high-intensity (at 70% 1-RM) knee extension exercise increased VL muscle protein synthesis (48% at 2 h post-exercise) through the mTOR pathway in young men (Dreyer et al., 2006). This means that increases in post-exercise muscle protein synthesis are probably similar between high-intensity resistance exercise and low-intensity BFR resistance exercise. Recently, Nielsen *et al*. (2012) revealed that BFR-RT (23 training sessions) leads to marked proliferation of myogenic stem cells and resulting myonuclei addition in skeletal muscle, which is accompanied by substantial myofiber hypertrophy. Therefore, BFR-RT as well as HI-RT indicates that myogenic stem cell-derived myonuclei provides an improved capacity for myofibrillar gene transcription, which is likely to contribute to an enhanced activity of muscle protein synthesis.

Previous cross-sectional studies found that individuals who performed HI-RT on a regular basis demonstrated lower levels of arterial compliance than their sedentary peers (Bertovic et al., 1999; Miyachi et al., 2003). Consistent with the cross-sectional studies, 8–16 weeks of HI-RT induced approximately 20% reductions in arterial compliance (Miyachi et al., 2004). On the other hand, our results show that arterial stiffness was maintained following 12 weeks of BFR-RT in older adults. The finding is consistent with previous observations of an unaffected arterial stiffness following BFR-RT in young adults (Ozaki et al., 2013). It is not clear what physiological mechanisms explain the reduced arterial compliance following resistance training, but previous HI-RT and BFR-RT studies reported that resistance training-reduced arterial compliance was associated with elevations of systolic arterial pressure during training sessions (London & Guerin, 1999; Ozaki et al., 2013). The training load, the number of repetitions, and the rest time between sets during BFR training sessions were similar between this study and a previous BFR-RT study (Ozaki et al., 2013). Therefore, we speculate that the magnitude of change in blood pressure responses during BFR exercise is an influencing factor for resistance training-induced arterial compliance in older adults as well as young adults.

Recently Yoshizawa *et al*. (2009) demonstrated that moderate-intensity resistance training (at 60% 1-RM) did not increase arterial stiffness in middle-aged women, which may have great importance for health promotion with resistance training. However, they did not mention the changes for muscle size. In addition, the magnitude of increase in 1-RM leg press strength following training period was less than one-half that reported for current study (14.8 vs. 33.4%) although the training frequency and period (2 days/week for a 12-week period) were same between two studies. This means that moderate-intensity resistance training is not enough method for preventing and/or improving sarcopenia in old healthy adults.

Arterial compliance is influenced by vascular endothelial function (Wilkinson et al., 2004). In general, vascular endothelial cells play an important role in the regulation of vascular activity by producing vasoactive substances such as nitric oxide (NO), but the endothelial function is not improved by HI-RT (Okamoto et al., 2009). In this study, NO-dependent brachial artery FMD tended to improve following BFR-RT. Moreover, a previous study demonstrated that NO production in muscle is enhanced following BFR exercise (Larkin et al., 2012). Therefore, there is a high possibility that BFR-RT has a beneficial effect on endothelial function, unlike HI-RT. In this study, interestingly, brachial artery FMD was tended to improve following leg exercise training. This is in agreement with previous study showing that cycle exercise improves brachial artery FMD (Schmidt et al., 2002). Previously, Madarame *et al*. (2008) demonstrated that "cross-transfer" effect for the endogenous anabolic hormones of blood flow-restricted muscles was observed in non-restricted muscles. These findings indicate that a beneficial effect on endothelial function following BFR-RT could be expected to affect both blood flow-restricted and non-restricted sites.

Previous studies reported that resistance training increases muscle size and strength, and improves functional performance in daily tasks for older adults (Hunter et al., 2001; Suetta et al., 2004; Bottaro et al., 2007; Kryger & Andersen, 2007). Additionally, it is well known that knee extension muscle CSA and strength play important role in the chair-stand performance for older adults (Corrigan & Bohannon, 2001; Takai et al., 2009). In the present study, we showed that 12-week BFR-RT led to improved chair-stand performance where the magnitude of improvement was associated with the change in the muscle CSA and strength for both the quadriceps and gluteus muscles, respectively. Recently, Yoshioka *et al*. (2012) revealed that hip extensors (gluteus maximus, etc.) as well as knee extensors are fundamental muscles in the chair-stand task. Taken together, the present improvement in the chair-stand task likely was due to the observed increases in muscle size and strength for the quadriceps and gluteus maximus.

The present results showed that muscle hypertrophy occurring not only in the thigh muscles directly affected BFR, but also in the gluteus maximus muscle proximal to the area directly affected by BFR. This finding is consistent with that of previous investigations in young adults (Abe et al., 2005; Yasuda et al., 2010). The mechanisms behind trunk (non-restricted blood flow) muscle hypertrophy following BFR-RT are not completely known, but have been hypothesized to occur from an accumulation of metabolites leading to increased muscle fiber recruitment (Yasuda et al., 2009) and the "cross-transfer" effect for the growth of restricted-blood flow skeletal muscles (Madarame et al., 2008) in older adults as well as young adults.

Some potential limitations of this study may be mentioned. We measured CAVI, which reflects changes in both central and peripheral muscle arterial compliance, although previous studies measured central and/or peripheral arterial compliance. Hence, more work is needed to understand the relationship between BFR-RT and arterial function.

In conclusion, low-intensity knee extension and leg press training with BFR elicited marked gains in thigh muscle CSA and strength, and did not negatively affect arterial stiffness in older healthy adults. Also, chair-stand ability was improved by this training, which may be mainly due to an increase in quadriceps and gluteus maximus muscle size. Thus, our results demonstrated that low-intensity resistance training with BFR was an useful method for preventing and/or improving sarcopenia in old healthy adults.

Perspective

BFR-RT leads to improve lower body muscle size and strength and improve and/or maintain arterial compliance in young healthy adults. However, the effect of BFR-RT on lower body muscle size and arterial function in old healthy adults was unclear. As previous BFR-RT studies in young healthy adults, our results suggested that BFR-RT (20–30% of 1-RM) could improve lower body muscle size and maintain arterial stiffness in old healthy adults. Thus, BFR-RT is an useful method for preventing and/or improving not only sarcopenia in old healthy adults, but also disuse muscle atrophy in elderly patients capable of tolerating only low-load resistance training (i.e., multiple sclerosis patients, hip/knee arthritis patients, etc).

Key words: sarcopenia, vascular occlusion, muscle hypertrophy, arterial stiffness, strength.

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