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Research article

Effects of low-intensity cycle training with restricted leg blood flow on thigh muscle volume and VO_{2max} in young men

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Abstract

Concurrent improvements in aerobic capacity and muscle hypertrophy in response to a single mode of training have not been reported. We examined the effects of low-intensity cycle exercise training with and without blood flow restriction (BFR) on muscle size and maximum oxygen uptake (VO_{2max}). A group of 19 young men (mean age ± SD: 23.0 ± 1.7 years) were allocated randomly into either a BFR-training group (n=9, BFR-training) or a non-BFR control training group (n=10, CON-training), both of which trained 3 days/wk for 8 wk. Training intensity and duration were 40% of VO_{2max} and 15 min for the BFR-training group and 40% of VO_{2max} and 45 min for the CON-training group. MRI-measured thigh and quadriceps muscle cross-sectional area and muscle volume increased by 3.4–5.1% ($P < 0.01$) and isometric knee extension strength tended to increase by 7.7% ($p < 0.10$) in the BFR-training group. There was no change in muscle size (~0.6%) and strength (~1.4%) in the CON-training group. Significant improvements in VO_{2max} (6.4%) and exercise time until exhaustion (15.4%) were observed in the BFR-training group ($p < 0.05$) but not in the CON-training group (–0.1 and 3.9%, respectively). The results suggest that low-intensity, short-duration cycling exercise combined with BFR improves both muscle hypertrophy and aerobic capacity concurrently in young men.

Key words: Muscle hypertrophy, Aerobic exercise, Occlusion, Muscle strength.

Introduction

Skeletal muscle shows an enormous plasticity to adapt to stimuli such as metabolic and/or contractile activities. Based on the principle of specificity of exercise, resistance exercise elicits specific muscular adaptations, with little improvement in the physiologic adaptations experienced with typical aerobic training (Hurley et al., 1984). Conversely, aerobic training is thought to stimulate improvements in cardiovascular fitness, such as maximum oxygen uptake (VO_{2max}) and anaerobic threshold (Wenger and Bell, 1986). Within muscle, opposite morphologic and physiologic adaptive responses to the 2 types of training occur in myofibrillar protein content (Hoppeler, 1986; Luthi et al., 1986), in mitochondria volume density (Hoppeler, 1986; MacDougall et al., 1979), in capillary density (Denis et al., 1986), in enzymes reflecting aerobic energy production (Gollnick et al., 1973; Tesch et al., 1987), and in the Akt/mTOR signaling pathway (Coffey and Hawley, 2007). In addition, some studies (Bell et al., 2000; Kraemer et al., 1995) show interference in strength development when aerobic training is added to resistance training. Thus, it would be advantageous to develop a training method that can effectively and concurrently improve both cardiovascular and muscular fitness within a single mode of training.

Muscular blood flow restriction (BFR) during resistance training has been shown to elicit similar muscle hypertrophy as traditional high-intensity resistance training but much lower training intensity (Abe et al., 2005; Takarada et al., 2002). An intensity as low as that associated with walking, when combined with BFR, can lead to significant improvements in muscle strength and leg muscle hypertrophy (Abe et al., 2006; 2010). Recently, our laboratory demonstrated increased muscle activation during low-load (20% of 1 repetition maximum [1 RM]) muscle contractions with BFR such that there was a greater internal activation intensity of the muscle relative to external load (Yasuda et al., 2008). In addition, significantly greater oxygen uptake and heart rate (HR) are observed during slow treadmill walking with BFR than during walking without BFR (Abe et al., 2006). The novelty of BFR appears to be the unique combination of venous blood volume pooling and restricted arterial blood inflow, which can result in a decreased stroke volume and increased HR while maintaining cardiac output (Takano et al., 2005). Consequently, increased HR at the same systolic blood pressure (SBP) during exercise with BFR may produce high mechanical stress on the heart, as indicated by a greater rate-pressure product ([HR × SBP]/100) (Nelson et al., 1974). Furthermore, the increased oxygen uptake observed during BFR exercise may be the result of increased arterial and mixed venous blood oxygen (a-v O_2) difference since cardiac output during exercise with and without BFR is the same. We hypothesized that the potential benefits of BFR exercise could include not only an anabolic response by the muscular system (Abe et al., 2006) but also improvements in cardiovascular fitness. Thus, the purpose of the current study was to investigate the effects of low-intensity exercise training combined with BFR on muscle size and strength, as well as on VO_{2max}, in young male subjects.

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Methods

Subjects

Nineteen young men aged 20–26 yr volunteered to participate in the study. Subjects were randomized into either a BFR-training group (n = 9, BFR-training) or a non-BFR control training group (n = 10, CON-training). The subjects in this study were physically active, but none of the subjects had participated in regular strength/resistance and/or aerobic training (less than once a week) for a minimum of 1 yr prior to the start of the study. Volunteers who suffered from a chronic disease, such as hypertension, diabetes, an orthopedic disorder, deep venous thrombosis, or peripheral vascular disease, were excluded from the study. 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 institutional review board (IRB) of human research of Japan Aerospace Exploration Agency (JAXA) and the Ethics Committee for Human Experiments at the University of Tokyo, Japan.

Training protocol

Training was performed once a day, 3 days/wk, for 8 wk. Following measurements of body weight and mid-thigh girth, the subjects performed exercise on an electrically braked bicycle ergometer (Aerobike 900U, Combi Corporation, Tokyo, Japan) at a predetermined 40% of VO_{2max} for 15 min in the BFR training group and at a predetermined 40% of VO_{2max} for 45 min in the CON-training group. The exercise intensity and duration in each group remained constant throughout the training period. Subjects in the BFR-training group wore pressure belts (Kaatsu-Master, Sato Sports Plaza, Tokyo, Japan) on both legs during cycle exercise training. Prior to BFR training, the subjects were seated on a chair, the belt air pressure was set at 120 mmHg (the approximate SBP at heart level for each subject) for 30 s, and the air pressure was released. The air pressure was increased by 20 mmHg, held for 30 s, and then released for 10 s before the next occlusive stimulation was performed. This process was repeated until a final occlusion pressure for each training day was reached. On the first day of training, the final belt pressure (training pressure) was 160 mmHg. As subjects adapted to the occlusive stimulus during early phase of the training, the training pressure was increased by 10 mmHg each week until a final belt pressure of 210 mmHg was reached. A belt pressure of 160–210 mmHg was selected for the restriction stimulus based on a review of the data in young men (Abe et al., 2006). Blood flow to the leg muscles was restricted for a total of ~18 min (3 min preparation time and 15 min bicycling time) during each training session, with the belt pressure released immediately upon completion of the session. During all training sessions, HR was recorded at the 5th min and 15th min for the BFR-training group and CON-training group, respectively. Ratings of perceived exertion (Borg 15 Point Scale) were also recorded at the end of training session.

MRI-measured muscle cross-sectional area and volume

Multislice MRI images of the thigh were obtained using a General Electric Signa 1.5-T scanner (Milwaukee, WI). A T1-weighted, spin-echo, axial plane sequence was performed with a 1,500-ms repetition time and a 17-ms echo time (Figure 1). Subjects rested quietly in the magnet bore in a supine position with their legs extended. The great trochanter was used as the origin point, and continuous

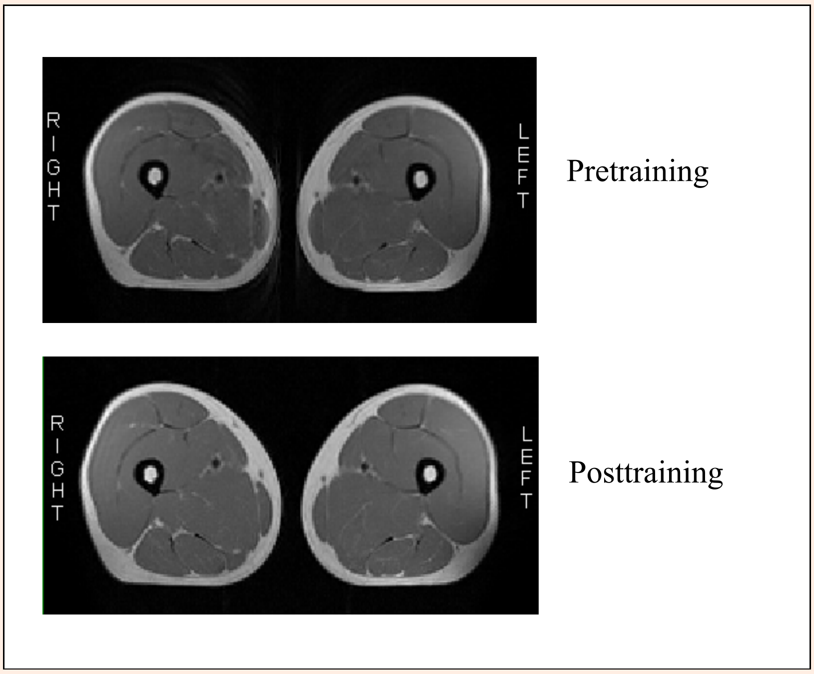

Figure 1. Typical MRI images showing transverse sections of the mid-thigh taken before (pre) and after (post) 8 wk of cycle training with BFR. The images show identical sections midway along the femur in the same subject (KK).

transverse images with 1.0-cm slice thickness (0-cm interslice gap) were obtained from the great trochanter to the lateral condyle of the femur for each subject. All MRI data were transferred to a personal computer for analysis using specially designed image analysis software (TomoVision Inc., Montreal, Canada). For each slice, skeletal muscle tissue cross-sectional area (CSA) was digitized, and the muscle tissue volume (cm^3) per slice was calculated by multiplying muscle tissue area (cm^2) by slice thickness (cm). Muscle volume of an individual muscle was defined as the sum of the slices of muscle. We have previously determined that the coefficient of variation (CV) of this measurement was less than 1% (Abe et al., 2003). This measurement, from the right side of the body, was completed at baseline and 3 days after the final training (posttesting).

Maximum isometric strength

Maximum voluntary isometric strength of the knee extensors and flexors was determined using a Biodex System 3 dynamometer (Shirley, NY). Subjects were carefully familiarized with the testing procedures of voluntary force production of the thigh muscles during several attempts of submaximal and maximal muscular contractions ~1 wk prior to baseline 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. After a warm-up consisting of submaximal contractions, the subjects were instructed to perform maximal isometric (MVC) knee extension at a knee joint angle of 75˚ and maximal isometric knee flexion at a knee joint angle of 60˚. A knee joint angle of 0˚ corresponded to full extension of the knee (Abe et al., 2000). If MVC strength for the first two trials were varied by >5%, up to an additional MVC was performed. The coefficient of variation for this test in our laboratory was 7%. The test was assessed at baseline and 3 days after the final training session (posttesting).

Maximum oxygen uptake

Graded exercise tests on an electrically braked bicycle ergometer (Aerobike 75XL-II, Combi Corporation, Tokyo, Japan) were performed in a laboratory where room-temperature was stabilized at 20–22°C. At the baseline test, seat height was noted and reproduced for posttraining testing. The exercise test was started at an initial workload of 50 W, which was increased by 15 W every minute until volitional exhaustion. (If the workload reached 200 W, the rate of increase was 10 W every minute.) During the test, HR was continuously monitored (HR monitor, Minato Medical Science Co., Ltd., Osaka, Japan). Ventilation was also monitored, and oxygen and carbon dioxide concentrations in the expired air were continuously measured to calculate of oxygen uptake (O_2), carbon dioxide output (CO_2), and the respiratory gas exchange ratio (RER; CO_2/O_2) by a calibrated breath-by-breath system (Aero monitor AE300S, Minato Medical Science Co., Ltd., Osaka, Japan). The following criteria were used to establish that maximum effort had been achieved: VO_{2max} appeared as a plateau in VO_2 despite an increase in workload (increased VO_2 within 150 ml min^{-1}), maximum heart rate within ± 11 beats·min^{-1} of the age-predicted maximum (220 minus age), and a maximum respiratory exchange ratio above 1.15. Exercise time to exhaustion was also recorded for each subject (Ozaki et al., 2010).

Statistical analyses

StatView, version 4.5, was used to compute the data, and the results are expressed as means and standard deviations (SDs) for all variables. Statistical analyses were performed by a 2-way analysis of variance (ANOVA) with repeated measures (Group [BFR-training and CON-training] × Time [pre- and posttesting]) to evaluate training effects for all dependent variables. When appropriate, post hoc paired *t* tests were used to assess within-group changes. All baseline characteristics and percentage changes in anthropometric variables, skeletal muscle volume and CSA, muscular strength, and aerobic capacity were compared between groups with a 1-way ANOVA. Statistical significance was set at $p < 0.05$.

Results

At baseline, there were no differences between the two groups for standing height, body weight, body mass index (BMI), and mid-thigh girth (Table 1). The subjects in both training groups completed all training and testing sessions, and no training-related injuries were sustained. There were no significant changes in body weight and BMI for either group following the training program;

Table 1. Changes in anthropometric variables and thigh muscle cross-sectional area and muscle volume. Values are mean(SD).

	BFR-Training Group			CON-Training Group		
	Pre	Post	%Δ	Pre	Post	%Δ
Anthropometric variables						
Height, m	1.72 (.07)			1.71 (.04)		
Weight, kg	61.1 (8.4)	62.0 (9.0)	1.4	61.7 (6.3)	61.4 (6.1)	–.4
BMI, kg·m^{-2}	21.2 (2.5)	21.5 (2.5)	1.4	21.0 (2.4)	20.9 (2.3)	–.4
Thigh girth, cm	49.7 (3.1)	50.5 (3.0)[a]	1.7[b]	50.0 (3.9)	49.7 (3.6)	–.6
Muscle cross-sectional area, cm^2						
Thigh at 50%	142.3 (8.7)	147.1 (9.2)[c]	3.4[d]	144.0 (17.6)	144.1 (15.0)	.1
Quadriceps at 50%	69.5 (5.4)	72.6 (5.3)[c]	4.6[b]	70.7 (7.3)	71.0 (6.5)	.6
Muscle volume, cm^3						
Thigh	3508 (283)	3641 (320)[c]	3.8[b]	3696 (447)	3689 (418)	–.1
Quadriceps	1575 (153)	1655 (132)[c]	5.1[b]	1730 (190)	1731 (180)	–.1

BMI, body mass index. Significant differences between BFR-training and CON-training: [d] $p < 0.05$, [b] $p < 0.01$. Significant differences between pre- and posttraining: [a] $p < 0.05$, [c] $p < 0.01$.

Table 2. Changes in isometric knee extension and flexion strength and specific tension. Values are mean (SD).

	BFR-Training Group			CON-Training Group		
	Pre	Post	%Δ	Pre	Post	%Δ
Isometric muscle strength, Nm						
Knee extension	194 (80)	209 (73)	7.7[a]	216 (47)	219 (45)	1.4
Knee flexion	77 (26)	79 (27)	3.3	87 (23)	84 (16)	–3.4
Specific tension, Nm/cm^2						
Knee extension/qCSA	2.79 (1.08)	2.86 (.90)	2.5	3.05 (0.51)	3.09 (0.54)	1.3

qCSA, quadriceps muscle cross-sectional area (at 50%). Significant differences between BFR-training and CON-training: [a] $p < 0.10$.

however, mid-thigh girth increased ($p < 0.05$) in the BFR-training group but not in the CON-training group (Table 1).

Muscle CSA increased ($p < 0.01$) by 3.4% for the thigh and 4.6% for the quadriceps in the BFR-training group. Thigh and quadriceps muscle volumes increased ($p < 0.01$) by 3.8 and 5.1%, respectively, for the BFR-training group. Neither muscle CSA nor volume changed for the CON-training group (Table 1).

Maximal isometric knee extension strength tended to increase ($p < 0.10$) in the BFR-training group (7.7%) but not in the CON-training group (1.4%). There was no change in isometric knee flexion strength for either group (Table 2). Relative isometric knee extension strength per unit quadriceps muscle CSA was similar at pre- and post-training in both groups.

During training sessions, heart rate (HR) ranged between 129 and 149 beats/min (50–65% heart rate reserve [HRR], mean 59%) for BFR-training subjects and between 105 and 141beats/min (37–46% HRR, mean 42%) for CON-training subjects. The ratings of perceived exertion were higher ($p < 0.01$) in the BFR-training group than in the CON-training group at the end of training session (10.5 ± 1.4 and 13.6 ± 1.3, respectively). There was no change in maximum HR attained during graded exercise test for either group. Absolute and relative VO_{2max} increased in the BFR-training group ($p < 0.05$) but did not change in the CON-training group. Increase in exercise time until exhaustion was observed in the BFR-training group (15.4%, $p < 0.01$) but not in the CON-training group (Figure 2).

Discussion

This study demonstrated that a single mode of low-intensity (40% of VO_{2max}), short-duration (15 min) exercise training with BFR can elicit improvements in muscle volume in healthy young subjects. Aerobic capacity also improved concurrently following the training. Previously, concurrent improvements in muscular strength and aerobic capacity by a single mode of exercise have been achieved after high-intensity and long-duration exercise training (Hass et al., 2001; Tabata et al., 1990). However, none of the studies demonstrated significant muscular

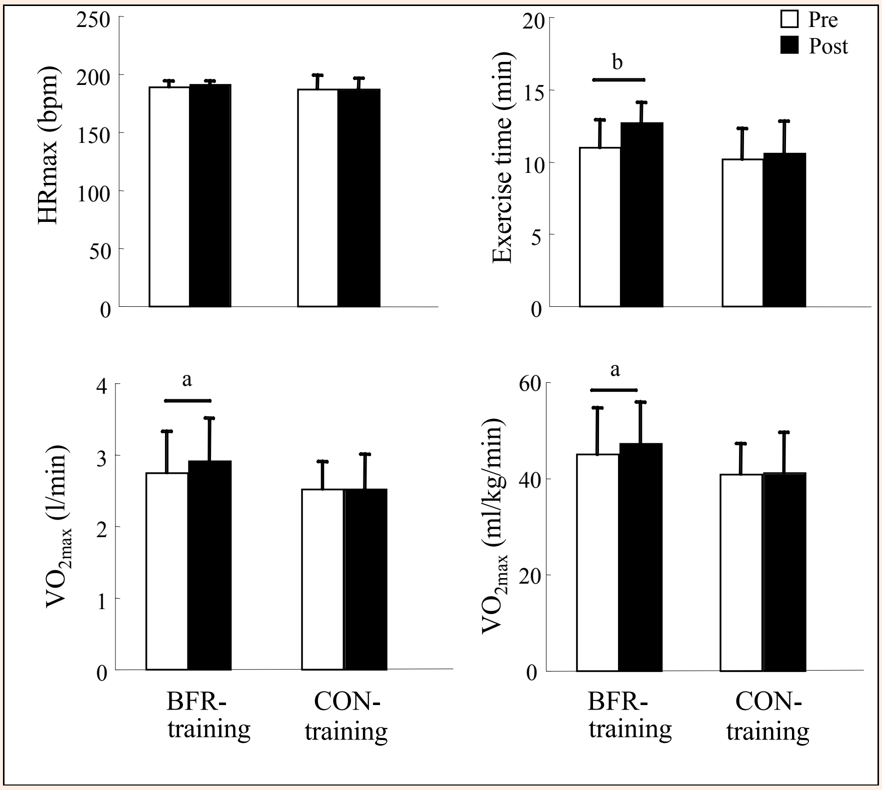

Figure 2. Changes in absolute and relative VO_{2max} and exercise time. Significant differences between pre- and post-training: [a] $p < 0.05$, [b] $p < 0.01$.

hypertrophy, which suggests that the increased strength was due mainly to neural adaptations. Thus, high-intensity, long-duration exercise training rarely produces significant muscle hypertrophy in young and middle-aged adults. Additionally, it is reported that maximal knee extension strength was reduced and the thigh muscle cross-sectional area was unchanged following 4 weeks of cycle training under conditions of local leg ischaemia, although VO_{2max} increased with this training (Nygren et al., 2000; Sundberg, 1994). However, there are few published studies documenting concurrent improvements in VO_{2max} and muscle hypertrophy after aerobic training in older and failed subjects (Harber et al., 2009; Schwartz et al., 1991).

Previous studies (Bell et al., 2000; Kraemer et al., 1995) have shown that combining aerobic training with resistance exercise negatively affected resistance training–induced muscular hypertrophy. For instance, Bell et al. (2000) reported that type I and type II muscle fiber CSA increased (27% and 28%, respectively) following 12 weeks of high-intensity resistance training (HI-RT), but the magnitude of increases in fiber CSA in the concurrent resistance and aerobic training group was less than one-half of that occurring with resistance training alone (10% and 14%, respectively). In the present study, the increases in thigh and quadriceps muscle CSA (4.1% and 5.1%, respectively) and muscle volume (3.2% and 5.3%, respectively) were similar to the increments observed in previous HI-RT studies (Jones and Rutherford, 1987; Wilkinson et al., 2006), but lower than a short (5-wk) period of HI-RT studies (Seynnes et al., 2007; Tesch et al., 2004). Although the differences in mode, intensity, and volume of exercise might have caused the variability in the training-induced muscle hypertrophy, it is clear that the magnitude of hypertrophic potential associated with BFR cycle training is comparable with that associated with HI-RT.

Our previous study (Abe et al., 2006) demonstrated that slow walk training combined with BFR not only produced thigh muscle hypertrophy but also increased isometric and dynamic strength of the knee extensor. McCarthy et al. (1995) reported that cycle exercise training alone did not significantly change isokinetic or isometric strength, a finding that is consistent with our CON-training group results. On the other hand, an average 7.7% change in knee extension strength was observed when cycle training was combined with BFR. However, there were large individual variations in strength adaptation in response to cycle training with BFR, which resulted in a nonsignificant increase in isometric knee extension strength. The specific tension of the knee extensor muscle did not change significantly between pre- and posttraining using BFR resistance training (Takarada et al., 2002) and BFR walk training (Abe et al., 2006); nor did it change in the present study. Therefore, a main contributor of increased muscle strength after BFR training is the increase in muscle CSA, which surpasses the neural adaptation, such as fiber recruitment patterns.

Our results showed that BFR cycle training produced a 6.4% increase ($p < 0.05$) in absolute VO_{2max} and a 15.4% increase ($p < 0.01$) in exercise time until exhaustion. The magnitude of change in VO_{2max} (percentage increase in VO_{2max} divided by total training sessions) in the BFR-training group (0.25%) is similar to that reported in some studies (0.25%–0.26%) (Gaesser and Rich, 1984; Wilmore et al., 1980), but lower than that reported in another study (0.60%) (McCarthy et al., 1995). Studies (Gaesser and Rich, 1984; Wenger and Bell, 1986) have demonstrated that the magnitude of change in VO_{2max} increases as exercise intensity increases from 50% to 100% of VO_{2max}. The minimum stimulus necessary to evoke change is ~50% of VO_{2max}, although 1 study (Gaesser and Rich, 1984) reported the increase in VO_{2max} after cycle training to be 45% of VO_{2max}. If exercise intensity is low, longer-duration efforts (>35 min) can be more effective than shorter-duration efforts at higher intensity (Wenger and Bell, 1986). During low-intensity exercise with BFR, stroke volume (SV) decreased and HR increased without changes in cardiac output (Ozaki et al., 2010; Takano et al., 2005). In the present study, exercise intensity and duration were set at 40% of VO_{2max} and 15 min in the BFR-training group. During the training sessions, however, the exercise intensity estimated from maximum HRR was 59% on average, which is within the effective exercise intensity for improvements in VO_{2max}.

The exercise training–induced increase in VO_{2max} is known to be due to central cardiovascular and/or peripheral metabolic adaptations, and the VO_{2max} is the product of cardiac output and arterial and mixed venous blood oxygen (a-v O_2) difference at maximal exercise workload. However, there is a lack of studies investigating the cardiovascular hemodynamic and muscle metabolic responses to BFR exercise training (Ozaki et al., 2010). Although the BFR method is different, Sundberg (1994) found an increase in VO_{2max} by utilizing supine one-legged cycle training with 50 mmHg chamber pressure (reduced leg blood flow by 16%) for 4 weeks (4 sessions/wk). In that study, muscle enzyme of oxidative metabolism and capillary density are increased in the ischaemically-trained leg, but cardiovascular adaptations to the ischaemic exercise training were not reported. Recently, a study reported that increases in VO_{2max} and submaximal exercise SV were observed after 2 weeks of twice–daily, 6 days/wk BFR walk training, while resting SV remain unchanged (Park et al., 2010). Therefore, the increase in VO_{2max} by BFR training may be due to adaptations in muscle oxidative capacity (a-v O_2 difference) and SV. In addition, increase in lower body muscle mass may be associated with improvements in VO_{2max} in the BFR training group.

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 and Clark, 2009). Our previous studies demonstrated that a single bout of 20% of 1-RM intensity knee extension exercise with BFR increased both vastus lateralis muscle protein synthesis and the Akt/mTOR signaling pathway in young (Fujita et al., 2007) and old (Fry et al., 2010) men, although the rate of muscle protein breakdown was not measured. These anabolic responses may contribute significantly to BFR training–induced muscle hypertrophy. However, there have not been any studies assessing the changes in mitochondrial and capillary density and muscle enzymes reflecting aerobic energy production, as well as cardiac function in response to BFR exercise training. Further research is needed to clarify the mechanisms of the BFR training–induced concurrent improvement in both types of physical fitness.

Conclusion

In conclusion, low-intensity (40% VO_{2max}) cycle training of short duration (15 min) combined with blood flow restriction can produce a significant increase in thigh muscle volume and aerobic capacity in young men.

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Key points

- Concurrent improvements in aerobic capacity and muscle hypertrophy in response to a single mode of training have not been reported.
- In the present study, low-intensity (40% of VO_{2max}) cycle training with BFR can elicit concurrent improvement in muscle hypertrophy and aerobic capacity.

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