ORIGINAL ARTICLE

Increased muscle volume and strength following six days of low-intensity resistance training with restricted muscle blood flow

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Traditional high-intensity resistance training performed 2-3 times per week induces muscle hypertrophy, at least, in 5 weeks (i.e. 10-15 training sessions). To examine the effect of a higher training frequency (12 sessions in 6 days), healthy young men performed low-intensity resistance training with (n=8, LIT-BFR) and without (n=8, LIT-CON) leg blood flow restriction with cuff inflation (BFR) twice per day for 6 days. Training involved 4 sets of knee extension exercise (75 total contractions) at 20% 1-RM. Significant muscle hypertrophy was observed only in the LIT-BFR group as estimated muscle-bone cross-sectional area (CSA) (2.4%), MRI-measured mid-thigh quadriceps muscle CSA (3.5%) and quadriceps muscle volume (3.0%) increased. The resulting hypertrophic potential (% change in muscle size divided by number of training sessions; ~0.3% per session) is similar to previously reported traditional high-intensity training (0.1 to 0.5% per session). Improved 1-RM knee extension strength (6.7%) following LIT-BFR training was accounted for by increased muscle mass as relative strength (1-RM/CSA) did not change. There was no apparent muscle damage associated with the exercise training as blood levels of creatine kinase, myoglobin, and interleukin-6 remained unchanged throughout the training period in both training groups. A single bout of training exercise with and without BFR produced no signs of blood clotting as plasma thrombin-antithrombin complex, prothrombin fragment 1,2 and D-dimer were unchanged. In conclusion, changes in muscle mass and strength following 6-day (12 sessions) of low-intensity resistance training requires BFR to produce responses comparable to the effect of several weeks of high-intensity resistance training.
Key words: muscle hypertrophy, training frequency, muscle damage, blood coagulation

INTRODUCTION

It is clear that traditional high-intensity (70-80% of one-repetition maximum, 1-RM) resistance training (HIT) over a period of time causes increases in skeletal muscle mass and muscular strength in humans [Ikai & Fukunaga, 1970; MacDougall et al., 1977; Jones & Rutherford, 1987]. The recommended frequency of HIT is 2-3 sessions per week [Kraemer et al., 2002], with at least one recovery day between training sessions. The time course for increased skeletal muscle mass following HIT is on the order of 8-12 weeks, [Kraemer et al., 2002, with occasional reports of significant hypertrophy at 5-6 weeks [Abe et al., 2000; Seynnes et al., 2007]. Muscle enlargement (3-6%) coincident with HIT is observed after 9-42 training sessions with 2-4 training sessions per week. The percentage change in muscle mass (~5.0%) is quite similar among these studies. When correcting for the number of training sessions, the magnitude of the hypertrophic potential (percent increase in muscle size divided by total training sessions) in knee extensor muscle group is about 0.27% per session (range 0.11 to 0.50% per session; Table 1). Thus, longer training periods do not necessarily result in greater muscle mass gains, only dilution of the hypertrophic potential (0.11-0.23% per session; Table 1); which is most likely a result of the measurement protocol rather than physiological differences. Interestingly, muscle enlargement at the higher end of the range (5-6%) was associated with 13 training sessions (2-3 per week for 5 weeks) and thus, a greater hypertrophic potential (0.36-0.50% per session; Table 1). This suggests that the greatest changes in muscle mass occur early in training.

Thus, the theoretically most efficient training response (muscle mass and muscular strength) would involve an increased training frequency (> 3 sessions/week) and shortened training period (< 5 weeks); theoretically resulting in the greatest hypertrophic potential. However, HIT (70-80% 1-RM) produces elevated myoglobin and creatine kinase (CK) [Clarkson & Hubal, 2002], and pro-inflammatory (IL-1α and TNF-β) and anti-inflammatory cytokines (IL-6) [Pederson et al., 2001] in plasma. Although some of these markers may indicate changes which are precursors to muscle enlargement [Vierck et al., 2000], these may also indicate muscle damage and perhaps impaired

Table 1. Training studies on the effects of high-intensity resistance training and low-intensity BFR training on skeletal muscle size and strength

Author (Journal, Year)	No. of subj	Sex	Type of exercise	Type of Contract	Intensity reps x sets	Frequency (per wk)	Period (wks)	Total session	M-size testing	% Change M-size	% Change per session
High-intensity Resistance Training											
Akima et al. (MSSE, 1999)	7	M7	KE	isokin	Max 5 x 10	4/5	2	9	MRI	2.8	0.31
Seynnes et al. (JAP, 2006)	7	M5 F2	KE	isokin	Max 7 x 4	2/3	5	13	MRI	5.0	0.36
Tesch et al. (Acta, 2004)	10	M7 F3	KE	isokin	Max 7 x 4	2/3	5	13	MRI	6.0	0.50
Bell et al. (JSMPF, 1992)	16	M16	KE KF	isokin	Max 20 x 3	4	5	20	CT	5.3	0.27
Wilkinson et al. (EJAP, 2006)	10	M10	KE LP	isoton	80-90% 6-10 x 3-4	3	8	24	CT	5.4	0.23
Jones et al. (JP, 1987)	12	M12	KE	isoton	80% 6 x 4	3	12	36	CT	5.0	0.14
Ahtiainen et al. (EJAP, 2003)	16	M16	KE LP	isoton	10RM all-out x 5	2	21	42	MRI	4.7	0.11
Low-intensity BFR Training (training frequency: twice per day)											
Abe et al. (IJKTR, 2005)	8	M8	SQ LC	isoton	20% 30&15 x 3	12	2	24	MRI	7.7	0.32
Present Study	8	M8	KE	isoton	20% 30&15 x 3	12	1	12	MRI	3.0 3.5	0.25 (MV) 0.29 (CSA)

M-size, muscle size; KE, knee extension; KF, knee flexsion; LP, leg press; SQ, squat; LC, leg curl
CSA, cross-sectional area; MV, muscle volume

mechanical and metabolic recovery which may limit the exercise volume (training sessions per week). Keeping the number of sessions constant but reducing the training period significantly increases the training volume (training stress) while decreasing recovery time.

Abe and colleagues [2005] reported a training study that subjects performed 24 training sessions containing squat and leg curl exercises in a period of two week. They observed significant muscle enlargement (~ 8% increase in thigh muscle volume), increased muscular strength (~ 20% increase in maximum leg strength), and a hypertrophic potential (0.32% per session; Table 1) similar in magnitude to that observed with HIT of longer duration (> 5 weeks). It appears that this effect was accomplished by concentrating the exercise volume (2x daily for two weeks) through reductions in training intensity by performing resistance exercise at 20% of 1-RM in combination with blood flow restriction (BFR). Of note in this study were that changes in muscle-bone cross-sectional area, which peaked at 7 days of training (~7% increase), leading to the conclusion that muscle mass, and perhaps muscular strength, may have increased in as early as 7 days. However, specific measurements of muscle mass (MRI) or muscular strength were not obtained and reported changes in muscle-bone CSA could have been related to increased cellular water or edema associated with muscle damage and inflammation. Therefore it would be of interest to know if these apparent rapid changes in muscle mass occur after a shorter period (6 days) of low-intensity (20% of 1-RM) resistance training with BFR, and would impact muscular strength. Thus, the purpose of this study was to examine specific changes in muscle mass and muscular strength following 6 days of twice daily BFR training (12 exercise sessions) while monitoring plasma markers of muscle damage, inflammation, and blood coagulation.

PROCEDURES and METHODS

Subjects

Sixteen healthy young men volunteered to participate in the study (Table 2). All subjects led active lives, with 6 of 16 participating in recreational sports (e.g., jogging). However, none of the subjects had participated in a regular resistance exercise training program for at least 1 yr prior to the start of the study. All subjects were informed of the procedures, risks, and benefits, and signed an informed consent document before participation.

Table 2. Physical characteristics of subjects (Experiment 2)

Variables	LIT-BFR group [N=8]	LIT-CON group [N=8]
Age (yr)	22.3 (2.9)	21.1 (3.2)
Standing height (m)	1.72 (0.05)	1.70 (0.06)
Body mass (kg)	64.5 (6.2)	62.6 (6.2)
Body mass index (kg/m^2)	21.8 (1.6)	21.8 (2.4)
Midthigh girth (cm)	50.3 (2.9)	49.6 (3.9)
Muscle-bone CSA (cm^2)	160.1 (19.7)	158.7 (24.3)

Values are means (SD); CSA, cross sectional area

The Tokyo Metropolitan University Ethics Committees for Human Experiments approved the study.

Experimental Protocol

Subjects were randomly divided into two training groups; low-intensity resistance training (LIT)-BFR (blood flow restricted, n = 8) or LIT-CON (control, n = 8). There were two experiments performed: experiment 1 was an acute study to investigate the blood coagulation parameters during resistance exercise with and without BFR, experiment 2 was a resistance exercise training study.

Experiment 1: Blood coagulation during exercise with BFR. Three weeks prior to the start of the training study (Experiment 2), subjects (n=6; 3 from each of the Experiment 2 groups) participated in an acute study to examine blood coagulation responses to the contraction bout with and without BFR. Individual trials of resistance exercise with and without restricted leg muscle blood flow were performed in random order, on separate days, with at least 1-wk between trials.

For the BFR trial, a pressure cuff (Kaatsu-Master, Sato Sports Plaza, Tokyo, Japan) was placed around the most proximal portion of each leg. While the subject was seated on a chair, the pressure cuff was inflated to 200 mmHg, the subjects then performed the contraction bout. Immediately after the contraction bout, the pressure cuff was released.

Venous blood samples were obtained from an antecubital vein prior to, immediately following, and 60-min following the contraction bout. Blood was collected in tubes treated with 3.2% sodium citrate. Plasma thrombin-antithrombin complex (TAT), prothrombin fragment 1, 2 (PTF1,2), and D-dimer were measured at commercially available laboratories (SRL Inc., Tokyo, Japan). Blood lactate was measured using a portable lactate analyzer (Lactate Pro, Arkray, Kyoto, Japan).

Experiment 2: Resistance exercise training study. Quadriceps cross-sectional area (CSA) and volume, thigh circumference, knee extension maximal voluntary isometric torque (right knee) and bi-lateral knee extension 1-RM were determined in each subject. Subjects participated in 6 days of supervised bi-lateral knee extension exercise training. Training was conducted twice per day (morning and afternoon sessions, with at least 4 hr between sessions) for 6 consecutive days (total 12 sessions). Following a stretching warm-up for the lower body, each subject performed the contraction bout as a training stimulus.

For the LIT-BFR group, blood flow was restricted by a pressure on both legs during training. On the first day of training (Day 1), the belt pressure was 160 mmHg, and the pressure was increased 20 mmHg each day until a final belt pressure of 220 mmHg (Day 4) was achieved [Abe et al., 2006]. The restriction of muscular blood flow was maintained for the entire exercise session, including the rest periods. The belt pressure was released immediately upon completion of the contraction bout.

Venous blood was drawn from each subject before first training session (baseline), immediately after and 24 hr and 48 hr after the first training session. Venous blood was also drawn 2-days following the final training session. All blood samples were obtained following an overnight fast (about 12 hr). The subjects were counseled to refrain from ingesting alcohol and caffeine for 12 hr before blood collection and not to perform any strenuous exercise.

METHODS

1-RM Strength Measurements. Bilateral knee extension maximum dynamic strength (1-RM) was assessed using an isotonic knee extension machine (LegEnd, Design Corporel, Salome, France) prior to and 2-days following the final training session. After warming up, the initial load was set (~80% of predicted 1-RM) and the first repetition was attempted. Following each successful lift the load was increased by 2~5% until the subject failed to lift the load 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, 5 trials were required to complete a 1-RM test. Approximately 2-3 min of rest was allotted between each attempt to ensure recovery.

Maximum Isometric Strength Measurements. Unilateral (right side) knee extension maximum voluntary isometric torque was determined (Biodex System 3) prior to and 2-days following the final training session. The subject was seated on a chair with his hip joint angle flexed at 85°. The center of rotation of the knee joint was visually aligned with the axis of the

lever arm of the dynamometer. 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 3-4 submaximal contractions (~50% of maximal torque), the subject was instructed to perform a maximal isometric knee extension (3~4 sec) at 75˚ knee joint angle (0˚ = full extension).

Muscle-Bone Cross-Sectional Area Estimation. Muscle-bone cross-sectional area (CSA) for the mid-thigh (right leg) was estimated using following anthropometric equation:

$$\text{Muscle-bone CSA} = \pi\,[r - (\text{Q-AT} + \text{H-AT}) / 2]^2$$

where r is the radius of the thigh calculated from mid-thigh girth of the right leg, and Q-AT and H-AT are ultrasound-measured anterior and posterior thigh adipose tissue thickness, respectively. The CV of this measurement in our hands is 1.2% [Abe et al., 2006]. This measurement was completed every morning throughout Experiment 2; beginning 1-week before training, daily, prior to the morning training session, and before post-testing.

MRI-Measured Muscle CSA and Volume. Images of the quadriceps muscle group were collected using magnetic resonance imaging (MRI; General Electric Signa 1.5 Tesla scanner, Milwaukee, Wisconsin, USA). A T1 weighted, spin echo, axial plane sequence was performed with a 1500 millisecond repetition time and a 17 millisecond echo time. The subject rested quietly in the magnet bore in a supine position with the legs fully extended. Contiguous transverse images with 1.0 cm slice thickness (0 cm interslice gap) were obtained from the knee joint to the upper portion of the thigh (Figure 1). For each slice, the quadriceps muscle CSA was digitized, and the quadriceps muscle volume (cm^3) was calculated by multiplying muscle tissue area (cm^2) by slice thickness (cm). The estimated CV of quadriceps muscle CSA measurement was 0.3%. Quadriceps muscle CSA and volume was determined prior to and 2-days following the final training session.

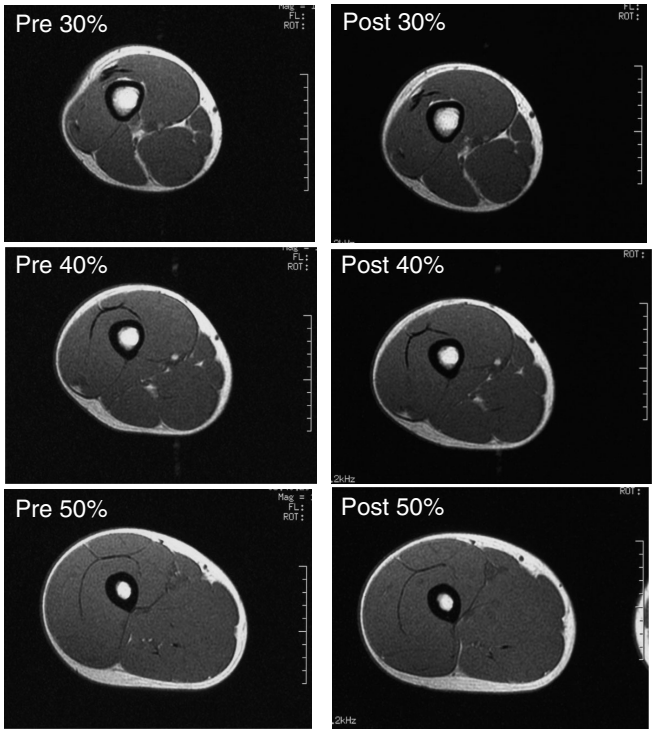

Figure 1. Typical magnetic resonance images showing transverse sections of the thigh taken before (baseline, pre) and after (post-testing) the 6 days of low-intensity knee extension training with blood flow restriction. The images show identical sections 30%, 40%, and 50% of the thigh length (starting at the lateral condyle of the femur) in the same subjects (YT).

Contraction Bout. For the acute study (Experiment 1) and the resistance exercise training protocol (Experiment 2), the contraction bout consisted of bilateral knee extension at 20% of the 1-RM. Subjects performed a set of 30 contractions followed by a 30-sec rest, followed by 3 sets of 15 contractions each with 30-sec rest intervals between sets; a total of 75 contractions requiring about 8 minutes. Individual contraction duration was 4 sec with a 2 sec:2 sec shortening-lengthening contraction duty cycle controlled by a metronome.

Blood Biomarkers. Serum activity of creatine kinase (CK) was measured at commercially available laboratories (SRL Inc., Tokyo, Japan) by the use of spectrophotometry for NADPH formed by a hexokinase and D-glucose-6-phosphate-dehydrogenase-coupled enzymic system. Serum concentration of myoglobin and interleukin-6 (IL-6) were also measured using a commercially available radioimmunoassay (Daiichi Radioisotope Laboratory, Chiba, Japan) and chemiluminescent enzyme immunoassay, respectively.

Statistical Analyses. Results are expressed as mean (SD) for all variables. Statistical analyses were performed by a two-way ANOVA with repeated measures [Group (LIT-BFR and LIT-CON) x time (baseline and post-testing)]. Blood parameters were analyzed with a 2 x 3 or 2 x 4 ANOVA with repeated measures. Post-hoc testing was performed by Fisher's least significant differences test. Statistical significance was set at $P < 0.05$.

RESULTS

Blood Coagulation (Experiment 1)

There were no differences in plasma lactate concentration prior to the resistance exercise bout or

Table 3. Influence of knee extension exercise with and without BFR on blood coagulation parameters (Experiment 1)

Variables	LIT-BFR [N=6]			LIT-CON [N=6]		
	Before	Immediately	1h after	Before	Immediately	1h after
Blood lactate (mmol/L)	1.1(0.1)	3.3(2.5)	1.3(0.2)	1.2(0.2)	1.5(0.6)	1.1(0.1)
TAT (ng/ml)	1.2(0.3)	1.3(0.3)	1.2(0.4)	1.5(0.8)	1.7(0.9)	1.3(0.5)
PTF 1,2 (pmol/L)	106(45)	119(38)	106(41)	109(27)	107(26)	105(32)
D-dymer (ug/ml)	0.26(0.16)	0.31(0.19)	0.24 (0.13)	0.20(0.12)	0.20(0.12)	0.17(0.07)

Values are means (SD); TAT, thrombin-antithrombin complex; PTF1,2, prothrombin fragment 1,2

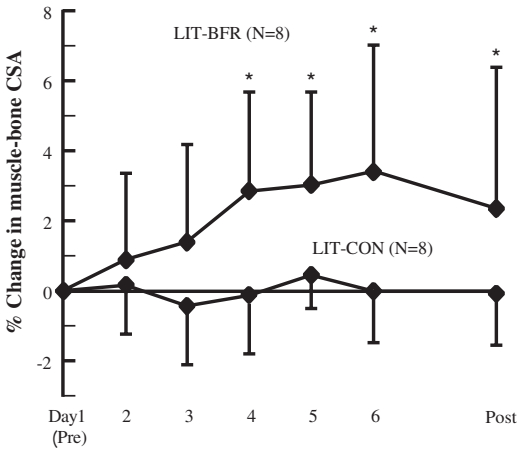

Figure 2. Relative percentage changes in muscle-bone cross-sectional area (CSA) for LIT-BFR and LIT-CON groups measured before (pre), during (every morning before the training session), and after (post) the training period. Significant differences from pre-training: * P < 0.05.

1-hour post-contraction bout. Blood lactate increased significantly following the exercise bout in LIT-BFR, but not in LIT-CON. Plasma TXT, PTF1,2 and D-dimer were not different pre-contraction bout nor were there any changes associated with the contraction bout in LIT-BFR or LIT-CON (Table 3).

Resistance Exercise Training Study (Experiment 2)

Muscle size. Muscle-bone CSA gradually increased (P<0.05) over time, reaching significance by Day 4 of training and increasing by 3.4% at the end of the training (Day 6) in LIT-BFR. At the post-testing interval, muscle-bone CSA had increased by 2.4% with BFR training. No change in muscle-bone CSA was observed with training in LIT-CON (Figure 2). MRI-measured mid-thigh quadriceps muscle CSA and quadriceps muscle volume increased by 3.5% and 3.0%, respectively, following training in LIT-BFR

Table 4. Effects of knee extension training with and without BFR on muscle size and strength (Experiment 2)

Variables	LIT-BFR group [N=8]			LIT-CON group [N=8]		
	Pre	Post	%Δ	Pre	Post	%Δ
Quadriceps femoris						
Mid-thigh CSA (cm^2)	75.1(9.1)	77.6(8.3)†	3.5	70.1(14.3)	69.5(14.7)	-1.0
Volume (cm^3)	1812(247)	1863(236)†	3.0	1797(172)	1784(175)	-0.7
Knee extension strength						
1-RM (kg)	60(9)	64(9)†	6.7	60(8)	61(8)	1.5
Isometric (Nm)	273(30)	289(35)	5.7	274(50)	279(60)	1.9
Relative strength						
1-RM/CSA (kg/cm^2)	0.80(0.08)	0.82(0.06)	3.1	0.89(0.26)	0.92(0.27)	2.6
Isometric/CSA (Nm/cm^2)	3.66(0.38)	3.74(0.48)	2.1	4.04(1.02)	4.20(1.28)	2.9

Values are means (SD); Pre, before training; Post, after training; Δ , change. † P < 0.05, Pre vs. Post

Table 5. Influence of knee extension training on muscle damage parameters and IL-6 (Experiment 2)

Variables	LIT-BFR group [N=8]				LIT-CON group [N=8]			
	Before	Immediately	24h after	48h after	Before	Immediately	24h after	48h after
CK (IU/L)	141(78)	135(70)	167(71)	183(89)	131(98)	131(95)	158(127)	185(203)
Myoglobin (ng/ml)	49(19)	56(15)	45(11)	65(43)	47(14)	47(15)	47(13)	44(21)
IL-6 (pg/ml)	0.7(0.3)	1.1(0.6)	0.6(0.3)	0.9(0.8)	0.8(0.5)	0.9(0.6)	1.2(1.1)	0.8(0.2)

Values are means (SD); CK, creatine kinase; IL-6, interleukin-6

(P<0.05), but not in LIT-CON (Table 4).

Muscular strength. Knee extension 1-RM strength was increased by 6.7% following training in LIT-BFR (P<0.05) but not in LIT-CON (Table 4). Maximal voluntary isometric knee extension torque did not change significantly in either group following training (Table 4). When expressed relative to quadriceps muscle CSA, both 1-RM and isometric torque were similar within and between both groups prior to and following the resistance exercise training (Table 4).

Blood markers. At baseline, all subjects had a normal CK, myoglobin and IL-6 concentrations in plasma. There were no observed changes in any of these markers (P>0.05) following training in both groups (Table 5).

DISCUSSION

The major finding of the present study was that 6 days of LIT-BFR training (total 12 training sessions) produced substantial muscle hypertrophy (muscle CSA 3.5% and muscle volume 3.0%) and muscular strength (~7%) comparable to results of studies employing longer duration and higher training intensity or volume (Table 1). Muscle hypertrophic potential calculated by percent increase in muscle size divided by total training session in the present study is 0.29% for muscle CSA and 0.25% for muscle volume per session (Table 1). These values are similar to our previous study showing that two weeks of twice-daily squat and leg curl training with BFR produce thigh muscle hypertrophy (0.32% per session) and increased strength [Abe et al., 2005]. Similarly, the hypertrophic potential in the present study is also similar as previously reported HIT for the thigh muscle (Table 1).

Cellular and molecular mechanisms of the hypertrophic response to LIT-BFR training are poorly understood. In general, skeletal muscle hypertrophy results from increased protein accretion (accumulation of contractile protein) occurring when the balance between protein synthesis and degradation shifts toward synthesis. Recently, we showed that a single bout of 20% of 1-RM intensity knee extension exercise with BFR (as utilized in the present training study) increases thigh muscle protein synthesis (~50%) through the Akt/mTOR signaling pathways in humans [Fujita et al., 2007]. Typically, the load required to stimulate this level of protein synthesis is believed to by in excess of 100 repetitions (8-10 sets of resistance exercise) at a high intensity (70-80% of 1-RM) [Dreyer et al., 2006]. Interestingly, a single bout of knee extension exercise with BFR elicits the same level of protein synthesis with a lower repetition count (75 in 4 sets of resistance exercise) and lower intensity (20% 1-RM). The unique combination of low intensity resistance exercise and BFR appears to be the stimulus for this high level of protein synthesis. Thus, BFR-exercise induced enhancement of muscle protein synthesis appears to be the basis for the increased muscle CSA/volume observed here.

In contrast, it could be hypothesized that the changes muscle CSA/volume are the result of increased muscle water; either in the inter- or intra-vascular space or within the muscle itself due to the BFR technique. Indeed, resistance exercise with a cuff belt leads to venous pooling and significant cell/muscle swelling [Abe et al., 2005]. However, the 2 cm increase in mid-thigh girth following a single bout BFR exercise dissipates quickly (~3 hours) and thus is not likely part of the muscle enlargement reported here. One interesting possibility between acute muscle volume swelling and the muscle enlargement is the relationship noted between cell swelling (i.e. via saline infusion) and reduced proteolysis [Berneis et al., 1999]. A reduction in proteolysis, secondary to BFR exerecise-induced acute cell/muscle swelling, could contribute to net increase protein balance and subsequently an anabolic response of skeletal muscle. This may be due to activation of a signaling mechanism like h-sgk, which has been shown to be triggered by cell swelling in vitro [Waldegger et al., 1997]. Additionally, if

changes in the water content of the muscle or surrounding area were responsible for some or the entire muscle enlargement observed, the expectation would be a reduction in relative muscular strength (isometric torque or 1-RM relative to muscle CSA/volume); there were no such changes (Table 4). Thus it would appear that the quadriceps muscle hypertrophy observed in the LIT-BFR group was likely due to changes in either or both protein synthesis or proteolysis rather than water accumulation.

Another possible factor for the training effects observed in the LIT-BFR group may be increased muscle activation and apparent elevation in contraction intensity during training session [Takarada et al., 2000]. With complete blood flow occlusion, muscle activation is progressively increased during repetitive low-intensity muscle contractions [Moritani et al., 1992], and there is a reduction in reflex inhibition of alpha motoneurons and inappropriate increases in motor unit recruitment [Leonard et al., 1994]. Our recent work reveals that moderate blood flow restriction and neural compression with cuff inflation results in similar neural manifestations as exercise with complete blood flow occlusion [Yasuda et al., 2008]. Thus, increased muscle activation associated with low external load (20% of 1-RM) caused by blood flow restriction and/or neural compression appears to result in greater internal activation intensity such that activation is comparable to that observed when training at 50-60% external load while controls were training with 20% 1-RM.

Further, it would appear that the hypertrophic response observed in the LIT-BFR trained group was elicited independent of muscle damage or inflammation as plasma levels of CK, myoglobin and IL-6 were unaltered in both groups, but hypertrophy was observed in the LIT-BFR group. Although these indicators (CK and myoglobin) are not definitive measures of skeletal muscle damage, it is commonly expected that these markers of skeletal muscle damage rise by over 100% after one bout of high intensity exercise in previously untrained individuals [Clarkson & Hubal, 2002]. These markers can remain elevated for several days [Clarkson & Hubal, 2002]. There was no change in CK or myoglobin in either group 24 hr or 48 hr from the first training session, even though the subjects were training twice per day. This also confirms the observation that it is the intensity of the resistance exercise, and not the number of training sessions, that is the trigger for muscle damage and release of these indicators [Abe et al., 2005].

Use of a tourniquet and blood pooling, as in the present study, certainly present risks for blood clot formation and venous emboli [Jrrett et al., 2004]. No indication of activation of blood clotting mechanisms are apparent in the present study as there were no changes in circulating levels of coagulation parameters (TAT, PTF1,2 and D-dimer). In general, exercise has been shown to result in a transient, but balanced, activation of coagulation and fibrinolytic cascades [Herren et al., 1992]. TAT and PTF1,2 are increased after long duration of high-intensity (over 70% of VO_2max) aerobic exercise, but not after high-intensity resistance exercise [Weiss et al., 1998]. Further, exercise duration of BFR exercise protocol is about 6 min including rest period between sets. Thus, the low-intensity and short duration of training protocol may explain the lack of blood coagulation response during resistance exercise and/or BFR. The conclusion drawn from these data is that in healthy individual's blood flow restriction imposed during muscle contractions of low-intensity poses minimal risk of a thrombolytic event as there are no apparent changes in activation of coagulation.

In conclusion, low-intensity resistance exercise training combined with BFR provides a sufficient stimulus for muscle adaptation as there were significant increases in quadriceps muscle CSA/volume and knee extension muscular strength following only 6 days (12 sessions) of training. The unique combination (low-intensity exercise/blood flow restriction) appears to allow for faster recovery from training (no indications of muscle damage/inflammation) and thus an ability to train more frequently (12 training bouts in 6 days). These data, together with previous BFR training data, leads to the conclusion that low-intensity exercise BFR training is an effective method to rapidly induce skeletal muscle hypertrophy.

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