ORIGINAL ARTICLE

Skeletal muscle size and strength are increased following walk training with restricted leg muscle blood flow: implications for training duration and frequency

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The purpose of this study was to investigate once-daily walk training with restricted leg blood flow (KAATSU) on thigh muscle size and strength. Twelve young men performed walk training: KAATSU-walk training (n=6) and control (no KAATSU-walk; n=6). Training was conducted once daily, 6 days per week, for 3 weeks. Treadmill walking (50 m/min) was performed for 5 sets of 2-min bouts interspersed with 1-min rest periods. The KAATSU-walk group wore pressure cuff belts (5 cm wide) on both legs during training, with incremental increases in external compression starting at 160 mmHg and ending at 230 mmHg. Thigh muscle volume and isometric and 1-repetition maximal (1-RM) strength were measured before and after training. In the KAATSU-walk group, quadriceps and hamstrings muscle volume increased 1.7 and 2.4% (both P<0.05), respectively, following training. One-RM leg press and leg curl increased 7.3 and 8.6% (both P<0.05), respectively, following KAATSU-walk training. Also, isometric knee extension strength (4.4%; P<0.01), but not knee flexion strength (1.7%), increased following KAATSU-walk training. There were no changes in muscle volume or strength in the control-walk group. These results confirm previous work showing that the combination of slow walk training and leg muscle blood flow restriction induces muscle hypertrophy and strength gains. However, the magnitude of change in muscle mass and strength following once-daily KAATSU-walk training was approximately one-half that reported for twice-daily KAATSU-walk training over a 3-week period. These results in combination with previous observations lead to the conclusion that the impact of KAATSU-walk training on muscle size and strength is related to an ability to accomplish a high number of training bouts within a compressed training duration. Second, frequency-dependent muscle enlargement appears to be associated with KAATSU-walk training.
Key words: blood flow restriction, muscle adaptation, training frequency, walking

INTRODUCTION

High-intensity resistance training (HIT; >70% of 1-repetition maximum [1-RM]) is one of the most common methods for achieving muscle hypertrophy and increased strength (Fry, 2004; Kraemer and Ratamess, 2004), while moderate-intensity resistance training (50-60% of 1-RM) increases muscle strength and endurance with no significant increases in muscle fiber hypertrophy (Campos et al., 2002). These data are consistent with the American College of Sports Medicine guidelines, which recommend 70-80% intensity to produce muscle hypertrophy and strength gains (American College of Sports Medicine Position Stand, 1998). In addition, HIT has been shown to be effective for a wide range of purposes, from improving weightlifting performance for athletes (Brechue and Abe, 2002) to counteracting sarcopenia in the elderly (Ferri et al., 2003; Frontera et al., 1988). 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 of promoting muscle hypertrophy and strength in the elderly and frail.

In the past decade, several published studies have reported that muscle hypertrophy can be produced with low-intensity exercise (20% of 1-RM) performed with restricted muscle blood flow. This training reduces arterial inflow and venous outflow from the active limb muscles and is termed *KAATSU* (Sato, 2005). Surprisingly, walking in combination with KAATSU blood flow reduction produced substantial muscle hypertrophy and strength gains (Abe et al., 2006). These authors observed that 3 weeks of twice-daily KAATSU-walk training produced significant muscle hypertrophy (4-7% increase in muscle volume) and increased dynamic and isometric strength (8-10% increase) in the thigh muscles despite the very low intensity of the exercise. The magnitude of muscle hypertrophy and strength gains as well as the hypertrophic potential (percent change in muscle volume divided by the number of training sessions) is comparable with previous results following HIT (Ahtiainen et al., 2003; Jones and Rutherford, 1987), although greater training effects following HIT have been reported (Akima et al., 1999; Bell et al., 1992; Seynnes et al., 2007; Tesch et al., 2004).

The novel use of walk training combined with KAATSU blood flow restriction to elicit muscle size and strength gains has reduced the required intensity of exercise training. What remains is to understand the impact of training frequency on muscle adaptations when incorporating exercise at low-intensity levels. As mentioned above, twice-daily KAATSU-walk training resulted in significant muscle adaptations. We hypothesized that the potential benefits of KAATSU-walk training to induce muscle hypertrophy and increase muscle strength would still be significant, but at a reduced magnitude, when performed once per day for the same training duration. Thus, the purpose of the present study was to investigate the effect of once-daily KAATSU-walk training on the size and strength of the upper-leg musculature and to compare the findings with those reported following twice-daily training.

METHODS

Subjects

Twelve healthy young men aged 20-23 years volunteered to participate in the study. The subjects were physically active, but none had participated in regular (once a week or more) strength/resistance training for at least 1 year prior to inclusion in this study. Subjects were randomly divided into 2 training groups: walk training with restricted leg muscle blood flow (KAATSU-walk, n=6), and walk training without restricted leg muscle blood flow (control-walk, n=6). All subjects were informed about the procedures and the associated risks and benefits and signed an informed consent document before participating. The study was conducted according to the Declaration of Helsinki and approved by the Ethics Committee for Human Experiments of the Tokyo Metropolitan University.

Testing and Training Protocols

Upper-leg muscle volume and 1-RM leg strength were determined prior to and 3 days following the last bout of walk training, while maximal isometric leg strength was determined prior to and 4 days following the last bout of walk training. Walk training was conducted as described previously (Abe et al., 2006). Briefly, training was performed once a day, 6 days per week, for 3 weeks. Following a standardized warm-up, all subjects walked on a motor-driven treadmill at 50 m/min for five 2-min bouts, with a 1-min rest between bouts. The walking speed and duration remained constant throughout the training period. Ratings of perceived exertion (RPE) were recorded following each training session using the Borg RPE Scale (20-point scale) (Borg, 1982).

KAATSU Blood Flow Reduction

Subjects in the KAATSU-walk group wore pressure cuff belts (KAATSU Master, Sato Sports Plaza, Tokyo, Japan) on both legs during all walk training sessions. Prior to each training session, the subjects were seated on a chair, and the belt air pressure was repeatedly set (30 s) and then released (10 s) from the initial (120 mmHg) to the final (160 mmHg) pressure. On the first day of training (day 1), the final belt pressure (training pressure) was 160 mmHg. As subjects adapted to the occlusive stimulus during the early phase of the training, the pressure was increased 10 mmHg each day until a final belt pressure of 230 mmHg was achieved on day 8. Restriction of leg muscle blood flow was maintained for the entire exercise session, including the 1-min rest periods, for a total of 14 min. The belt pressure was released immediately upon completion of the session. The control-walk group performed the same exercises at the same treadmill speed but without blood flow restriction.

Upper-Leg Muscle Volume

Muscle cross-sectional area (CSA) and volume were determined using magnetic resonance imaging (MRI), as described previously (Abe et al., 2003; Abe et al., 2006; Sanada et al., 2006). MRI images were prepared using a General Electric Signa 1.5 Tesla scanner (Milwaukee, Wisconsin, USA). A T1-weighted, spin-echo, axial plane sequence was performed with a 1500-ms repetition time and a 17-ms echo time. Subjects rested quietly in the magnet bore in a supine position with their legs extended. The intervertebral space between the fourth and fifth lumbar vertebrae was used as the origin point, and contiguous transverse images with 1.0-cm slice thickness (0-cm interslice gap) were obtained from the fifth lumbar vertebra to the ankle joints for each subject. All MRI scans were segmented into 4 components (skeletal muscle, subcutaneous adipose tissue, bone, and residual tissue) by a highly trained analyst and were then traced. For each slice, the skeletal muscle tissue 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 was defined as the summation of the slices of an individual muscle. An average value of the right and left sides of the body was determined.

Lower-Body Muscle Strength

Lower-body muscle strength was determined from maximal voluntary isometric contractions and the 1-

RM strength using various lower-body exercises. One week prior to testing, all subjects were familiarized with the strength-testing equipment.

Maximum voluntary isometric strength (MVC) of the knee extensors and flexors was determined using a Biodex System 3 (Biodex Medical Systems, New York, NY, USA). Subjects were seated on a chair with the 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. 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 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 zero corresponded to full extension of the knee. Each effort was held for approximately 4-5 s.

One-RM strength was determined for unilateral (right leg) leg press and bilateral leg curl (Nippyo, Tokyo, Japan). Proper lifting technique was demonstrated for the leg press and leg curl exercises, and all subjects performed practice lifts prior to attempting maximal effort lifts. After a warm-up period, the load was set at 80% of the predicted 1-RM. Following each successful lift, the load was increased by ~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

Table 1. Changes in anthropometric variables, muscle volume and dynamic (1-RM) and isometric strength for once-daily walk training combined with (KAATSU-walk) and without (Control-walk) restriction of leg blood flow

	KAATSU-walk group (n=6)		Control-walk group (n=6)	
	Pre	Post	Pre	Post
Anthropometric variables				
Standing height, m	1.77 (0.05)		1.75 (0.05)	
Body mass, kg	64.8 (2.1)	64.8 (1.8)	63.8 (4.6)	63.6 (4.4)
BMI, kg/m^2	20.7 (1.1)	20.7 (2.1)	20.8 (1.1)	20.7 (1.1)
Mid-thigh girth, cm	50.4 (2.6)	51.0 (2.7)[a]	52.0 (1.7)	51.9 (1.8)
Muscle volume, cm^3				
Quadriceps	1739 (120)	1768 (125)[a]	1686 (154)	1673 (146)
Hamstrings	622 (62)	638 (60)[a]	650 (92)	646 (88)
1-RM strength, kg				
Leg press	85 (12)	91 (8)[a]	92 (16)	92 (16)
Leg curl	57 (17)	61 (16)[a]	65 (11)	62 (9)
Isometric strength (Nm)				
Knee extension	294 (48)	307 (45)[a]	294 (60)	276 (44)
Knee flexion	119 (14)	121 (14)	119 (22)	119 (21)
Specific tension, Nm/cm^3				
Knee extension/qMV	0.17 (0.02)	0.17 (0.03)	0.17 (0.02)	0.16 (0.02)
Knee flexion/hMV	0.19 (0.02)	0.19 (0.02)	0.16 (0.02)	0.16 (0.02)

Values are mean (SD).

Abbreviations: qMV, quadriceps muscle volume; hMV, hamstrings muscle volume

[a]Significant differences between pre- and posttraining: $P<0.05$

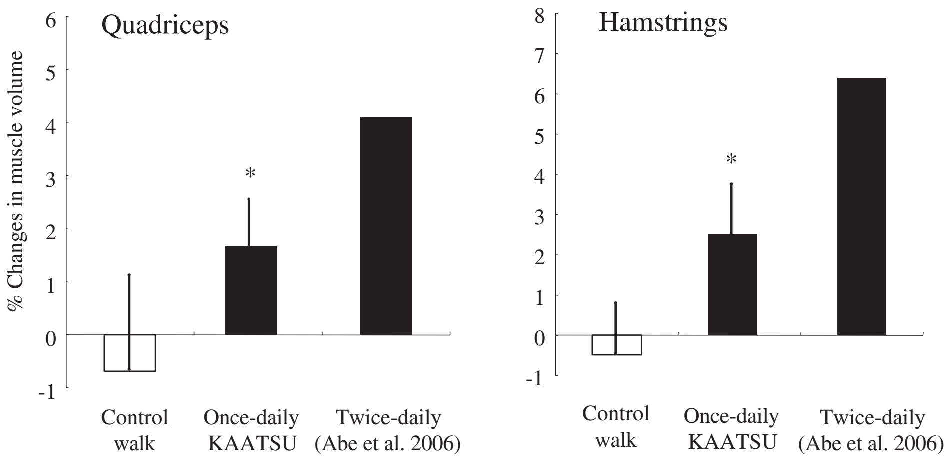

Figure 1. Percent changes in quadriceps and hamstrings muscle volume. Significant differences between once-daily KAATSU-walk training and Control-walk training: *P<0.05.

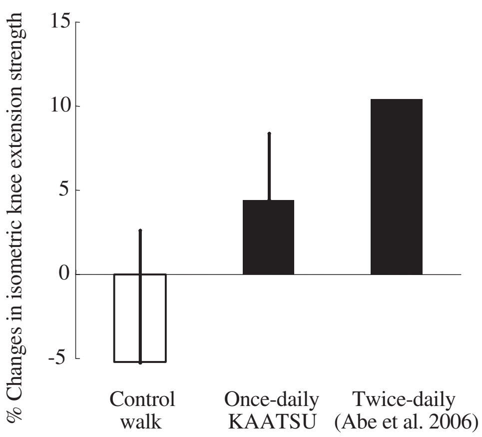

Figure 2. Percent changes in isometric knee extension strength.

required to complete a 1-RM test. To ensure recovery, approximately 2-3 min of rest was allotted between each attempt.

Statistical Analysis

Results are expressed as means ± the standard deviations (SDs) for all variables. A one-way analysis of variance (ANOVA) was performed to examine differences between the groups before the training. A two-way repeated measures ANOVA (group x time) was used to evaluate training effects for all dependent variables. When appropriate, post hoc paired t tests were used to assess within-group differences. Percent changes between baseline and posttesting were evaluated with a one-way ANOVA. Statistical significance was set at P<0.05.

RESULTS

At baseline, there were no differences (P>0.05) between the 2 groups (KAATSU-walk and control-walk) for height, body weight, body mass index (BMI), and mid-thigh girth.

All subjects completed all prescribed training bouts. The daily posttraining RPE scores were significantly higher in the KAATSU-walk group (range: 11-14) than in the control-walk group (range: 9-11).

Following 3 weeks of walk training, there were no significant (P>0.05) changes in body weight or BMI for either group. However the mid-thigh girth was greater (P<0.01) in the KAATSU-walk group (1.2%) than in the control-walk group (-0.2%). Muscle volume increased 1.7% (P<0.05) for the quadriceps and 2.4% (P<0.01) for the hamstrings in the KAATSU-walk group (Figure 1). Neither quadriceps nor hamstrings muscle volume changed (P>0.05) for the control-walk group (-0.8 and -0.6%, respectively).

One-RM strength increased 7.3% for the leg press (P<0.05) and 8.6% for the leg curl (P<0.01) in the KAATSU-walk group. Also, isometric knee extension strength (4.4%; P<0.01) but not knee flexion strength (1.7%) increased following KAATSU-walk training (Figure 2). There were no changes in isometric (knee extension and flexion: -5.2 and -0.1%, respectively) or 1-RM strength (leg press and leg curl: 0.7 and -4.5%, respectively) in the control-walk group.

Relative isometric knee extension strength per unit of quadriceps muscle volume or knee flexion strength per unit of hamstrings muscle volume was not different (P > 0.05) between pre- and posttraining in both groups (Table 1). Leg press and leg curl 1-RM strength per unit of muscle volume was also similar at pre- and posttraining in both groups.

DISCUSSION

Three weeks of once-daily KAATSU-walk training resulted in significant increases in muscle volume and muscle strength. This is a surprising observation given the very low-intensity training, but it supports previous findings that KAATSU-walk training leads to such adaptations (Abe et al., 2006). However, the present study employed a 50% reduction in training frequency, and the magnitude of the muscle volume changes (1.7-2.4%) was more moderate than that observed with twice-daily training (4-7%). Hence, the hypertrophic changes (muscle volume) reflect a frequency-dependent dose response. While the muscle size and strength gains of the KAATSU-walk training are not as robust as those associated with HIT, they are physiologically significant and consistent.

In general, skeletal muscle hypertrophy results from increased protein accretion and the accumulation of contractile protein, which occurs when the balance between protein synthesis and degradation shifts toward synthesis. The mammalian target of the rapamycin (mTOR) signaling pathway has been shown to play a significant role in stimulating messenger RNA translation initiation and muscle protein synthesis. Recently, Fujita et al. (2007) demonstrated that a single bout of 20% of 1-RM intensity knee extension exercise with KAATSU 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. Similar anabolic responses likely contribute to the presently observed increase in muscle volume following once-daily KAATSU-walk training.

Muscle adaptation to training is controlled by the intensity and volume of training, which are inversely related. Training volume is dictated by the number of sets and repetitions, training frequency (per day and per week), and total duration of training (total number of training bouts over the training period). While each of these factors is important, the training stimulus and ultimate level of adaptation are related to the total number of training bouts. A method for evaluating the impact of training on muscle growth is the determination of the hypertrophic potential (Fujita et al., 2008). Determining the hypertrophic potential is a theoretical attempt to evaluate muscle growth per training session by dividing the percent change in muscle volume by the number of training bouts. Maximal-intensity training 3 times a week for 5 weeks results in significant increases in muscle size (5-6%) and a hypertrophic potential of 0.3-0.5% (Akima et al., 1999; Bell et al., 1992; Seynnes et al., 2007; Tesch et al., 2004). Studies that have incorporated high-intensity (but not maximal effort) resistance training (e.g., 80% 1-RM or 10-RM) and similar training frequencies produce similar hypertrophic responses (~5% increase in muscle size; Ahtiainen et al., 2003; Jones and Rutherford, 1987). However, given the greater number of training bouts, the resultant hypertrophic potential is significantly lower (~0.15%). Presumably, the increased number of training bouts is required to attain the 5% increase in muscle size.

In the present study, KAATSU-walk training produced a hypertrophic potential of 0.14% per session (~2% increase in muscle volume over 18 training sessions), which is similar to that observed following high-intensity resistance exercise training (Ahtiainen et al., 2003; Jones and Rutherford, 1987). The similarity in hypertrophic potential highlights the importance of the compressed training duration employed during KAATSU-walk training with very low exercise intensities. While the muscle enlargement resulting from KAATSU-walk was one-half that observed with resistance exercise, it was achieved in significantly less time (3 weeks vs. >12 weeks) and fewer total training bouts (18 vs. >36). Interestingly, a previous study (Abe et al., 2006) reported that KAATSU-walk training performed at a higher frequency (twice daily) but of the same duration (3 weeks) resulted in a significantly greater increase in muscle volume (4.7%) comparable with that of the HIT studies and about 2 times greater than that of the present study. The resultant hypertrophic potential (0.17%) in this study is likewise comparable with that seen in the HIT studies (Ahtiainen et al., 2003; Jones and Rutherford, 1987) and also in the previous study (Abe et al., 2006). Given the level of muscle volume change and the hypertrophic potential, the KAATSU-walk training response exhibits a frequency dependency, but in either case (once- or twice-daily frequency) KAATSU-walk training produces physiologically significant muscle enlargement.

Muscle strength was increased following KAATSU-walk training. The importance of the hypertrophic response associated with KAATSU-walk training is reflected in the fact that specific tension (force per unit of muscle) was not altered. This is intriguing as neither muscle enlargement nor increased muscle strength is typically expected following walk training (as observed in controls). This is in agreement with previous studies showing that specific tension did not change significantly following KAATSU resistance training (Takarada et al., 2002) or twice-daily KAATSU-walk training (Abe et al., 2006). Overall, these data lead to the conclusion that the increased muscle strength following KAATSU training is more closely tied to changes in muscle hypertrophy (i.e., increases in muscle contractile protein) than to changes in neural adaptations. This finding highlights the importance of the hypertrophic response (increased muscle volume) to KAATSU-walk training.

Interestingly, KAATSU-walk training achieved its hypertrophic results with the participants experiencing minimal muscle fatigue and/or discomfort. This finding is critical considering the importance of a compressed training duration and, to an extent, training frequency, which was discussed above and appears central to KAATSU low-intensity training. The ability to compress the training duration is certainly related to the use of low-intensity exercise, which does not appear to cause significant muscle damage or delayed recovery, as indicated by a lack of change in the blood markers of muscle damage or immune stress (Fujita et al., 2008; Goldfarb et al. 2008; Takarada et al., 2000), while still promoting muscle adaptations. Further, the average reported score for intensity and discomfort (including pain) for all participants was 11-14 on a scale of 6-20, using the Borg RPE Scale (Borg, 1982). These scores are significantly lower than those reported in previous KAATSU resistance training studies (Takarada et al., 2002; Yasuda et al., 2009) and in HIT studies, which reported intense muscle fatigue and discomfort (Campos et al., 2002; Hurley et al., 1984 [Borg RPE scores were reported as 18 ± 1]). This contrast makes KAATSU-walk training ideal for elderly or frail individuals.

In conclusion, once-daily KAATSU-walk training produced physiologically significant increases in thigh muscle volume and knee joint strength in young men. The magnitude of change in muscle volume and muscle strength appears to be due to a compressed training duration (3 weeks) and is frequency dependent; once-daily training results in about half the magnitude of muscle changes resulting from a twice-daily training regimen. These gains in muscle size and strength are achieved with minimal to no muscle fatigue or discomfort, making KAATSU-walk a reasonable inclusion in the exercise rehabilitation regimen for frail, elderly, or other similarly debilitated patient populations who cannot tolerate even moderate-intensity exercise.

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