Intramuscular metabolism during low-intensity resistance exercise with blood flow restriction

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MUSCLE HYPERTROPHY AND STRENGTH gain can be achieved by high-intensity resistance training (4, 5, 23, 27). These morphological and functional muscular adaptations are generally caused by a mechanical load greater than 65% of one repetition maximum (1 RM) (24). In fact, a number of studies have shown that high mechanical stress to skeletal muscle is a potent stimulus for muscle protein synthesis (6, 43) and for endocrine (19, 20) and neuromuscular responses (12, 27). Conversely, low-intensity resistance training with a low mechanical stress does not effectively produce muscular adaptations (4). However, recent studies have reported that low-intensity resistance training with blood flow restriction dramatically leads to muscle hypertrophy and strength gain (1, 22, 25, 33, 38–40) and that it results in adaptations equal to those of high-intensity resistance training (39). The researchers suggested that the supplementation of low-intensity resistance exercise with blood flow restriction might provide additional stress and enhanced recruitment in the skeletal muscle, but the exact details were not clarified.

Metabolic stresses such as depletion of phosphocreatine (PCr), an increase in inorganic phosphate (Pi), a decrease in muscle pH, and lactate accumulation have been suggested to be potent stimuli for obtaining training effects (11, 20, 32). It was hypothesized that blood flow restriction might advance the metabolic stress and also the recruitment in the skeletal muscle even during low-intensity resistance exercise. Therefore, we used 31P-magnetic resonance spectroscopy to elucidate the intramuscular metabolites, pH and muscle fiber recruitment during a single bout of low-intensity resistance exercise with blood flow restriction, and compared the results with those from high-intensity and low-intensity resistance exercises without blood flow restriction. We also examined the difference between sexes that might have appeared in the results.

METHODS

Subjects. Twenty-six subjects (men/women 13/13, 22 ± 4 yr) participated in the study. All subjects were healthy and without orthopedic or cardiovascular diseases. Informed consent was obtained from all subjects. This study was approved by the Ethics Committee of Hokusho University.

Exercise protocols. Subjects performed unilateral plantar flexion exercises with three different exercise protocols. The experimental exercises were set for 2 min with 30 repetitions per min, lifting the weight 5 cm above ground. Each subject’s 1 RM was determined before the experiment with a successful lift without any assistance from other body parts (e.g., thigh). The workloads for each experimental protocol were calculated based on the obtained 1 RM. Exercise protocols were as follows: low-intensity resistance exercise using 20% 1 RM (L), L with blood flow restriction (LR), and high-intensity resistance exercise using 65% 1 RM. All three exercise protocols were performed in a random order on the same day with at least 48 h between trials.

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30-min intervals between protocols. Before each subsequent protocol, we confirmed the recovery in altered intramuscular metabolites and pH to baseline levels. In LR, an 18.5-cm-wide pressure cuff was placed around the thigh of the right leg. The air pressure was inflated for 10 s before the exercise protocol, and promptly released after the exercise was finished. Blood flow restriction was carried out using 130% of the subject’s resting systolic blood pressure with a pneumatic rapid inflator (E-20 rapid cuff inflator, Hokanson, Bellevue, WA), following the report by Takano et al. (36). The real-time cuff pressure was monitored digitally and precisely maintained during exercise. In a supplementary examination, we verified the changes in blood pressure during LR in 10 subjects. The systolic pressures were raised from rest at 119 ± 10 to a peak of 136 ± 11 mmHg during LR. These increases were 114.9 ± 6.2% of rest levels, sufficiently lower than 130%. We also examined the effects on intramuscular metabolism of different cuff pressures: low, at 100 mmHg; moderate, 150 mmHg; 1.3 times systolic pressure; and high 200 mmHg in 15 male subjects. There was no significant difference in metabolic stress between moderate and high cuff pressure protocols (Table 1).

As an index of perceived effort, the rating of perceived exertion (RPE) was evaluated with the 10-point Borg scale, with the lowest rating at 0.5 point. The RPE was taken immediately after the exercise was finished.

\[31P\] magnetic resonance spectroscopy. Subjects lay in the supine position on an original apparatus equipped with a magnetic resonance device, and the right foot was coupled to the pedal by a Velcro strap. \[31P\]-magnetic resonance spectroscopy (MRS) was performed using a 55-cm-bore, 1.5-T superconducting magnet (Magnetom Vision VB33G, Siemens Erlangen, Germany). An 80-mm surface coil was placed under the muscle belly of the right gastrocnemius. Shimming was adjusted by using the proton signal from water. Spectra of high-energy phosphate were acquired at a pulse width of 500 \(\mu\)s, a transmitter voltage of 20 V, and a repetition time of 2,000 ms. The spectra were obtained at rest and every 30 sec during exercise. Each spectrum consisted of an average of eight scans during 16 s before each time point. Peaks corresponding to high-energy phosphates were determined based on the chemical shifts. Peak areas were automatically calculated by peak fitting and integration after baseline correction using magnetic resonance software. A millimolar concentration of PCr ([PCr]) assumed that [PCr] + creatine concentration ([Cr]) = 42.5 mM (13) when it is unchanged, and supposed that P\(_i\) concentration [P\(_i\)] is equal to [Cr] (17, 21). Diprotonated phosphate (\(H_2PO_4^-\)) was calculated using the obtained [P\(_i\)] (8, 21). Intramuscular pH was calculated from the chemical shift of P\(_i\) relative to PCr. When distinct P\(_i\) splitting was shown, the pH was calculated by standardizing the observed individual pH on the basis of peaks corresponding to each P\(_i\) (21).

**Statistical analyses.** The values are presented as means ± SD in the text and means ± SE in figures. Interaction effects (protocol × time) were examined by two-way ANOVA with repeated measures. For sex difference, interaction effects were evaluated by three-way ANOVA (protocol × sex × time). The post hoc test was examined by Bonferroni’s test. The level of significance was set at \(P < 0.05\). All statistical tests were performed using SPSS 13.0 for Windows software.

**RESULTS**

Mean resistance loads of 20% 1 RM and 65% 1 RM were 8.3 ± 2.4 and 26.9 ± 7.8 kg, respectively. The applied pressure for blood flow restriction in LR was 150.0 ± 16.7 mmHg on average.

Figure 1 shows two representative spectrum patterns at rest and at the end of the three exercise protocols. There was no significant difference in intramuscular metabolites and pH among protocols at rest. PCr was significantly decreased and \(H_2PO_4^-\) was significantly increased in all three protocols compared with those at rest (\(P < 0.001\)). Intramuscular pH was significantly decreased in LR and H (\(P < 0.001\)), but not in L. Changes of intramuscular metabolites and pH in LR were significantly greater than those in L. However, those in LR were significantly lower than those in H (Fig. 2).

The RPE in LR was significantly higher than that in L (\(P < 0.001\)), but significantly lower than that in H (L: 3.0 ± 1.6, LR: 6.6 ± 1.8, H: 8.2 ± 1.5, \(P < 0.001\) vs. LR and H, \(P < 0.05\) vs. H). Although splits in P\(_i\) were observed during LR and H, none were observed during L. The number of observed Pi splitting in LR and H are shown in Fig. 3. Splits in P\(_i\) were observed in only 31% of the subjects in LR compared with 70% in H. Fifty-six percent of the subjects who showed P\(_i\) splitting in H did not have a split P\(_i\) in LR.

Figure 4 shows the changes of intramuscular metabolites and pH among men and women in all protocols. Subjects were similar in age (men: 22 ± 4 vs. women: 21 ± 4 yr; not significant). Naturally, body height (171 ± 4 vs. 160 ± 4 cm), weight (65 ± 6 vs. 53 ± 6 kg) and 1 RM (50 ± 6 vs. 31 ± 8 kg) were greater in men than in women (men vs. women, respectively, \(P < 0.001\)). Men also showed higher systolic blood pressure than women (124 ± 8 vs. 106 ± 6 mmHg, \(P < 0.001\)); thus men had higher applying pressure for blood flow restriction (161 ± 8 vs. 138 ± 8 mmHg; \(P < 0.001\)). Although the changes of intramuscular metabolites and pH in LR and H tended to be smaller in women than in men, no statistical difference was obtained. No significant difference between sexes was observed in L.

**DISCUSSION**

**Major findings.** In the present study, we compared metabolic stress, intramuscular metabolites and pH measured with \[31P\].

<table>
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<th>Table 1. Effects of different cuff pressures on intramuscular metabolism during low-intensity resistance exercise with blood flow restriction</th>
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<tr>
<td>PCr breakdown, %</td>
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<td>Intramuscular pH decrease</td>
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Values are means ± SD. L, 20% of 1 repetition maximum without blood flow restriction; PCr, phosphocreatine. *\(P < 0.05\) vs. L, †\(P < 0.05\), vs. L + 100 mmHg.
MRS, during a single bout of low-intensity resistance exercise with blood flow restriction with those of high-intensity and low-intensity resistance exercises without blood flow restriction. During low-intensity resistance exercise, additional changes of intramuscular metabolites and pH were obtained by applying blood flow restriction. However, these changes did not reach the level of those during high-intensity resistance exercise. Contrary to the speculations in previous studies, the results of the present study have suggested that the metabolic stress in skeletal muscle during low-intensity resistance exercise with blood flow restriction is not equivalent to that in high-intensity resistance exercise.

Our study found that recruitment of fast-twitch (FT) fiber evaluated by Pi splitting was induced by supplementing the low-intensity resistance exercise with blood flow restriction. However, the recruitment of FT fiber during this exercise was observed in only 31% of the subjects, significantly lower than the rate (70%) during high-intensity resistance exercise. Moreover, 56% of the subjects who showed FT fiber recruitment during high-intensity resistance exercise did not show it during low-intensity resistance exercise with blood flow restriction. Therefore, this new method of resistance training might not generally be applied to replace high-intensity training.

Comparison between the present study and previous studies. Recently, some researchers have reported that training effects such as muscle hypertrophy and strength gain were effectively provided by low-intensity resistance training with blood flow restriction (1, 22, 25, 33, 38–40), and that those effects were equivalent to those of high-intensity resistance training (39). Moreover, the postexercise growth hormone response showed a greater elevation in low-intensity resistance training with blood flow restriction than in high-intensity resistance training (30). Some researchers have advocated that increased metabolic stress by restricting blood flow during low-intensity resistance training might equal the metabolic stress induced by high-intensity resistance training (9, 29, 30, 33, 37–40). However, the results of our study were not consistent with the prediction of previous researchers. The discrepancy could be due to a number of factors.

First, there is inconsistency in the protocols for low-intensity resistance training with blood flow restriction between the...
Distributed. The gastrocnemius muscle has been known to be muscle (2, 23), slow-twitch (ST) and FT fibers are equally brachii muscle) of the knee extensor (34, 35) and elbow flexor 39). In the key muscles (i.e., vastus lateralis muscle and biceps 22, 29, 33, 36, 37, 38, 40) and elbow flexor muscles (25, 30, 9, 22, 25, 29, 30, 33, 36–40). For example, Takarada et al. (39) set the low-intensity resistance exercise as 50% 1 RM and high-intensity as 80% 1 RM. Similarly, Reeves et al. (30) set low-intensity resistance exercise as 30% 1 RM and high-intensity as 70% 1 RM. By contrast, the present study employed 20% 1 RM as low-intensity resistance exercise and 65% 1 RM as high-intensity resistance exercise, in accord with the majority of previous studies (1, 9, 29, 36, 37, 40) and the recommendation of the American College of Sports Medicine (3). However, the relative difference between low intensity and high intensity might be greater in the present study than that in the previous studies (30, 39). To obtain metabolic stress equal to that of high-intensity resistance exercise, more intensity in the low-intensity resistance exercise might be needed. Second, although the pressure for blood flow restriction in the present study was 150 mmHg on average by applying 130% of resting systolic blood pressure based on the report by Takano et al. (36), some previous studies used an applied pressure of ≥200 mmHg (29, 33, 37, 40). Further study might be needed to optimize this training method.

Finally, the exercised muscles in the present study were the plantar flexor muscles (i.e., gastrocnemius and soleus), while many previous studies have examined the knee extensor (1, 9, 22, 29, 33, 36, 37, 38, 40) and elbow flexor muscles (25, 30, 39). In the key muscles (i.e., vastus lateralis muscle and biceps brachii muscle) of the knee extensor (34, 35) and elbow flexor muscle (2, 23), slow-twitch (ST) and FT fibers are equally distributed. The gastrocnemius muscle has been known to be similar to the aforementioned muscles; however, in the soleus muscle, ST fibers predominate (10, 41). The relatively large proportion of ST fiber might contribute to lowering the effects by blood flow restriction compared with the knee extensor and elbow flexor muscles.

Recruitment of fast-twitch fiber. According to Henneman’s size principle (14), during low-level muscular activity, ST fibers with small motor units are predominantly recruited, while increasing muscular force causes FT fibers to gradually be recruited. However, several studies have suggested that early recruitment of FT fibers might occur to maintain the muscular force during low-intensity resistance exercise with blood flow restriction because of an inadequate oxygen supply for ST fibers (26, 39). Previous studies using 31P-MRS have demonstrated that the split in Pi indicates remarkable recruitment of FT fibers as well as ST fibers (15, 28, 42). In the present study, some subjects showed Pi splitting due to blood flow restriction during low-intensity resistance exercise. The increased anaerobic stress by blood flow restriction might be a stimulus for additional recruitment of FT fibers. However, the incidence of Pi splitting was significantly lower during low-intensity resistance exercise with blood flow restriction than during high-intensity resistance exercise. Moreover, around half the subjects who showed Pi splitting (i.e., FT fiber recruitment) during high-intensity resistance exercise did not show Pi splitting during low-intensity resistance exercise with blood flow restriction. Previous studies have reported that resistance training-induced muscle fiber hypertrophy was greater in FT fiber than in ST fiber (5, 23). To achieve effective muscle hypertrophy, therefore, FT fiber recruitment during exercise is apparently required. The results of our study suggested that around one-third of our subjects could obtain successful training effects by combining low-intensity resistance exercise with blood flow restriction, but that the others could not. The combined effects of blood flow restriction might be influenced by physiological background including neural control, muscle fiber composition and metabolic capacity.

Sex difference. Women might have higher muscular fatigue resistance and endurance performance compared with men (7, 16). Furthermore, a few studies using 31P-MRS have demonstrated that the changes in intramuscular metabolites and pH in fatiguing muscle were lower in women than in men (8, 18). The lower metabolic responses during fatiguing exercise might relate to relatively high muscular fatigue resistance in women. However, other studies found that the muscular fatigue resistance during exercise with blood flow restriction (or ischemia)
was similar in women and men, while that during exercise without blood flow restriction was significantly higher in women than in men (7, 31). Some previous studies have reported that ST fiber distribution is greater in women than in men (34, 35). In the present study, the changes in intramuscular metabolites and pH during low-intensity resistance exercise with blood flow restriction tended to be lower in women than in men, but the difference did not reach statistical significance. The small difference between the sexes might be possibly due to the muscular property and/or significantly lower pressure for blood flow restriction in women than in men. Further studies would be needed to resolve this aspect of this new resistance training method.

LIMITATIONS

There might be a number of factors inducing muscle hypertrophy and strengthening, including some that have not yet been elucidated. The present study only examined the intramuscular metabolic stress, which is an important mechanism. Although training effects are obtained by long-term exercise, the present study examined only the acute effects of this type of exercise. Nevertheless, based on our findings it is inconceivable that everyone would get the same favorable training effects from a uniform procedure of resistance exercise with blood flow restriction. There might be a wide range of response to this type of training.

In conclusion, the results of the present study demonstrated that the metabolic stress in skeletal muscle during low-intensity resistance exercise was significantly increased by applying blood flow restriction, but did not necessarily reach the level of that during high-intensity resistance exercise without blood flow restriction. However, it appears that additional recruitment of FT fibers during low-intensity resistance exercise may occur with the application of blood flow restriction. This new method of resistance training needs to be examined for optimization of the protocol to reach equivalence with the high-intensity resistance training.

GRANTS

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REFERENCES


