

Effects of low-intensity resistance exercise with slow movement and tonic force generation on muscular function in young men

Michiya Tanimoto and Naokata Ishii

Department of Life Sciences, Graduate School of Arts and Sciences, University of Tokyo, Meguro-ku, Tokyo, Japan

Submitted 22 June 2005; accepted in final form 1 December 2005

Tanimoto, Michiya, and Naokata Ishii. Effects of low-intensity resistance exercise with slow movement and tonic force generation on muscular function in young men. *J Appl Physiol* 100: 1150–1157, 2006. First published December 8, 2005; doi:10.1152/jappphysiol.00741.2005.—We investigated the acute and long-term effects of low-intensity resistance exercise (knee extension) with slow movement and tonic force generation on muscular size and strength. This type of exercise was expected to enhance the intramuscular hypoxic environment that might be a factor for muscular hypertrophy. Twenty-four healthy young men without experience of regular exercise training were assigned into three groups ($n = 8$ for each) and performed the following resistance exercise regimens: low-intensity [$\sim 50\%$ of one-repetition maximum (1RM)] with slow movement and tonic force generation (3 s for eccentric and concentric actions, 1-s pause, and no relaxing phase; LST); high-intensity ($\sim 80\%$ 1RM) with normal speed (1 s for concentric and eccentric actions, 1 s for relaxing; HN); low-intensity with normal speed (same intensity as for LST and same speed as for HN; LN). In LST and HN, the mean repetition maximum was 8RM. In LN, both intensity and amount of work were matched with those for LST. Each exercise session consisting of three sets was performed three times a week for 12 wk. In LST and HN, exercise training caused significant ($P < 0.05$) increases in cross-sectional area determined with MRI and isometric strength (maximal voluntary contraction) of the knee extensors, whereas no significant changes were seen in LN. Electromyographic and near-infrared spectroscopic analyses showed that one bout of LST causes sustained muscular activity and the largest muscle deoxygenation among the three types of exercise. The results suggest that intramuscular oxygen environment is important for exercise-induced muscular hypertrophy.

muscular hypertrophy; continuous muscular activity; muscular blood flow; intramuscular hypoxic environment

SKELETAL MUSCLES RESPOND TO strong exercise stimuli with hypertrophy and gains in strength (2). In general, resistance exercise at middle-to-high intensity [$\sim 80\%$ one-repetition maximum (1RM)] has been regarded as optimal for gaining muscular size and strength (19). It has been shown that such a high-intensity resistance exercise does not cause orthopedic and cardiovascular problems even in older people, when appropriately performed or supervised (8). On the other hand, it has also been reported that $\sim 20\%$ of elderly (aged 70–79 yr) showed some symptoms of orthopedic injury after an exercise at 1RM (21). In addition, a marked increase in systolic blood pressure (up to 250 mmHg) has been reported to occur during a high-intensity resistance exercise (~ 8 RM) for large muscle groups (7). Therefore, developing a resistance exercise regimen that can cause substantial gain in strength with much smaller mechanical stress is to be considered for, at least,

introductory training for older people and ones with cardiovascular problems.

It has been reported that resistance exercise at intensity lower than 65% 1RM is virtually ineffective for gaining muscular size and strength (19) but causes an increase in muscular oxidative capacity (11), so large mechanical stress has often been considered essential for gaining muscular size and strength. However, some recent studies have reported that large mechanical stress is not indispensable for muscular hypertrophy. For instance, a low-intensity ($\sim 50\%$ 1RM) resistance training for the knee extensor muscles caused a marked increase in muscular size [$\sim 12\%$ gain in cross-sectional area (CSA)] and strength ($\sim 20\%$ gain) when combined with moderate vascular occlusion (28). Also, a training for the knee extensor muscles at 40% maximum voluntary contraction (MVC) under ischemia resulted in an increase in muscular strength ($\sim 25\%$ increase) (23). The effects of these exercise training regimens with restricted muscular blood flow are likely mediated by the following processes: 1) stimulated secretion of growth hormone by intramuscular accumulation of metabolic subproducts, such as lactate (27); 2) moderate production of reactive oxygen species (ROS) promoting tissue growth (29); and 3) additional recruitment of fast-twitch fibers in a hypoxic condition (24, 30). These studies suggest that the muscle-trophic effect of resistance exercise involves not only large mechanical stress but also metabolic, hormonal, and neuronal factors.

The resistance exercise with vascular occlusion is so specialized that it should not be widely used without careful monitoring of occlusive pressure and blood flow. In addition, it is often associated with pain, and its application is limited to upper limb and lower limb muscles. Exercises with sustained force generation would be one of the alternatives. Under the normal circulation, continuous force generation at $>40\%$ MVC has been shown to suppress both blood inflow to and outflow from the muscle due to an increase in intramuscular pressure in arm muscles (4) and knee extensors (16). Therefore, even without externally applied pressure, a moderate-intensity resistance exercise ($>40\%$ MVC) is expected to induce increases in muscular size and strength when performed with continuous force generation. A previous study has shown that a low-intensity resistance training ($\sim 50\%$ 1RM) with relatively tonic movement and a short interset rest period (30 s) causes increases in muscular size and strength in middle-aged women (26). Also slow-speed resistance training (10-s lifting and 4-s lowering) has been shown to effectively cause an increase in muscular strength (33). However, in these studies,

Address for reprint requests and other correspondence: M. Tanimoto, Dept. of Life Sciences, Graduate School of Arts and Sciences, Univ. of Tokyo, 3-8-1 Komaba, Meguro-ku, Tokyo 153-8902, Japan (e-mail: cc37724@mail.ecc.u-tokyo.ac.jp).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

the exercise movements were not strictly defined so as to suppress the muscular blood flow, and changes in intramuscular environment were totally unknown. The intramuscular environment that may be related to the hypertrophy, i.e., hypoxic condition and accumulation of metabolic subproducts, is likely optimized by combinations of sustained contractile force and repeated movements (work production). As one of the ways to satisfy both requirements, we propose a low-intensity (~50% 1RM) resistance exercise with relatively slow movement and tonic force generation (LST).

In the present study, we investigated the long-term (12 wk) effects of LST exercise on muscular size and strength. We also investigated the acute effects of LST on the electrical activity and the oxygenation level of the agonist muscle. The results showed that LST caused increases in muscular size and strength, as effectively as normal high-intensity training (~80% 1RM).

METHODS

Subjects and Regimes for Exercise Training

Twenty-four right-handed and healthy young men who did not have an experience of regular exercise training volunteered as subjects (Table 1). All subjects performed knee extension exercises in a seated position with a nominally isotonic leg extension machine. The range of joint motion was from 0 to 90° (0° at full extension).

The subjects were randomly assigned into three experimental groups ($n = 8$ for each group), which were matched for physical parameters, such as height, weight, and MVC of knee extension (Table 1). The subjects performed the following exercise regimens: low-intensity (~50% of 1RM) exercise with slow movement and tonic force generation [3 s for eccentric (lowering phase) and concentric (lifting phase) actions, 1-s pause, and no relaxing phase; LST], high-intensity (~80% 1RM) exercise with normal speed (1 s for concentric and eccentric actions, and 1 s for relaxing; HN), and low-intensity exercise with normal speed (same intensity as for LST and same speed as for HN; LN).

Subjects in each group repeated the movement at approximately constant speed and frequency with the aid of a metronome. The exercise session consisted of three sets with an interset rest period of 60 s and was performed three times a week for 12 wk. In the LST and HN groups, the subjects repeated the movement until exhaustion (repetition maximum; RM) at each set of exercise. The exercise intensity was determined at 8RM for each set but not at %1RM, because the former method is more commonly used in actual exercise training. The intensity was adjusted in every exercise session on the basis of the record of the previous exercise session. In the LN group, the subjects performed eight repetitions at an intensity of ~50% 1RM, to match the intensity and the number of repetitions with those for the LST group. The intensities used in the LST and HN groups (8RM) approximately corresponded to ~50% and ~80% 1RM, respectively (Table 2). It is generally known that high-intensity (~80% 1RM) exercise is highly effective for gaining muscular size and strength (18,

Table 2. Changes in 1RM and exercise intensity during the period of exercise training

| | LST | HN | LN |
|-------------------------|------------|------------|------------|
| Pretraining | | | |
| 1RM, kg | 101.0±20.7 | 104.9±18.6 | 99.6±20.9 |
| Intensity/first set, kg | 51.8±9.3 | 85.0±10.7 | 51.2±11.3 |
| % of 1RM | 51.7±3.9 | 81.8±6.4 | 51.3±1.7 |
| 1st Month | | | |
| 1RM, kg | 110.3±18.8 | 122.0±20.4 | 101.8±19.4 |
| Intensity/first set, kg | 58.5±9.0 | 96.2±10.3 | 52.9±11.4 |
| % of 1RM | 53.3±4.2 | 80.0±5.8 | 51.7±1.9 |
| 2nd Month | | | |
| 1RM, kg | 119.4±15.3 | 132.9±19.1 | 108.6±18.7 |
| Intensity/first set, kg | 65.8±8.4 | 104.1±8.8 | 57.4±8.3 |
| % of 1RM | 55.1±3.1 | 79.0±6.0 | 53.1±1.7 |
| 3rd Month | | | |
| 1RM, kg | 129.4±11.6 | 138.3±18.5 | 115.4±17.5 |
| Intensity/first set, kg | 68.1±7.9 | 108.0±8.4 | 58.5±8.1 |
| % of 1RM | 52.6±3.9 | 78.8±6.0 | 51.0±4.2 |

Values are means ± SD; $n = 8$ for each group. Intensity/first set, the weight used for leg extension at the first out of 3 sets; 1RM, 1-repetition maximum.

19). In contrast, the same 8RM intensity in LST exercise was ~50% 1RM. The difference in %1RM intensities between the LST and HN groups may be due to the difference in the type of movement.

In the HN group, the subjects performed the same RM (8RM) as in the LST group, i.e., the same RM-based intensity, whereas the exercise for the LN group was of the same intensity and amount of work (force integrated with respect to distance) as for the LST group. However, the impulse (force integrated with respect to time) in LST regimen was about three times as large as that in LN regimen. The exercise intensities actually used in all groups are summarized in Table 2.

All subjects were fully informed about the experiment procedures to be used as well as the purpose of the study and gave their written, informed consent. The study was approved by the Ethics Committee for Human Experiments, Graduate School of Arts and Sciences, University of Tokyo.

Acute Changes in Physiological Parameters During and After the Exercise

Measurement of knee angle. The knee joint movement during exercise was recorded with a two-dimensional goniometer (Biometrics, type XM180, Gwent, UK). The goniometer was placed on the lateral surface of left knee with its rotation axis aligned with the center of knee joint. The output from the goniometer was amplified, fed into a full-wave rectifier through high (30 Hz) cut filters, and stored by using a data acquisition system (Power Lab/16SP, AD Instruments).

Measurement of knee extension torque. The knee extension torque during exercise was calculated from the weight used on the knee extension machine (W), the vertical acceleration of the weight on the knee extension machine (α), the gear ratio of the machine (GR), and the lever arm length of the machine (LA) as follows:

Table 1. Physical characteristics of subjects

| | LST | | HN | | LN | |
|---------------|-------------|--------------|-------------|--------------|-------------|--------------|
| | Pretraining | Posttraining | Pretraining | Posttraining | Pretraining | Posttraining |
| Age, yr | 19.0±0.6 | | 19.5±0.5 | | 19.8±0.7 | |
| Height, cm | 169.4±3.9 | | 169.9±5.4 | | 171.6±5.4 | |
| Body mass, kg | 59.4±5.7 | 60.7±5.5 | 60.0±4.6 | 60.1±4.6 | 58.8±7.8 | 60.0±7.9 |

Values are means ± SD; $n = 8$ for each group. LST, low-intensity exercise with slow movement and tonic force generation; HN, high-intensity exercise with normal speed; LN, low-intensity exercise with normal speed.

Knee extension torque ($N \cdot m$) = $W(N) \cdot (\alpha + g) (m/s^2) \cdot GR \cdot LA (m)$

The accelerometer (AS-20GB, Kyowa Electric Instruments) was attached to the weight stack of the knee extension machine. The output from the accelerometer was processed and stored as described above.

Electromyographic recording. Electromyograph (EMG) signals were recorded from the left vastus lateralis (VL) muscle. Bipolar surface electrodes (Vitrode F, Nihon Kohden) were placed over the belly of the muscle with a constant interelectrode distance of 30 mm. The EMG signals were amplified, fed into a full-wave rectifier through both low (30 Hz) and high (1 kHz) cut filters, and stored as described above.

Measurement of peripheral muscle (VL) oxygenation by near-infrared continuous-wave spectroscopy. A near-infrared continuous-wave spectroscopic (NIRcws) monitor (BOML1TR, Omegawave) was used to measure the peripheral muscle oxygenation in the left VL muscle during and after the exercise. The wavelengths of emission light were 780, 810, and 830 nm, and the relative concentrations of oxygenated hemoglobin and myoglobin (Oxy-Hb/Mb) in tissues were quantified according to the Beer-Lambert law (5). Because the NIRcws signals registered during exercise do not always reflect the absolute levels of oxygenation, the changes of oxygenation in working skeletal muscles are expressed as values relative to the overall changes in the signal monitored according to the arterial occlusion method (5, 9). In the present study, the resting level of Oxy-Hb/Mb was defined as 100% (baseline), and the minimum plateau level of Oxy-Hb/Mb was obtained by arterial occlusion and was defined as 0%. A pressure cuff was placed around the proximal portion of the thigh and was manually inflated up to 300 mmHg until the minimum plateau level of Oxy-Hb/Mb (3) was obtained. The distance between the incident point and the detector was 30 mm. Laser emitter and detector were fixed with a sticking tape after being shielded with a rubber sheet. The NIRcws signals were stored in a personal computer.

Measurement of blood lactate concentration. Blood samples were collected before, immediately after, and 2 and 5 min after the exercise. Approximately 5 μ l of blood were taken from the fingertip via a needle and immediately analyzed for blood lactate concentration by use of a lactate analyzer (Lactate Pro, Kyoto Primary Science).

Measurement of blood pressure. The blood pressure from the left radial artery was measured continuously during the exercise with an arterial tonometry (JENTOW-7700, Colin). During measurements, the arm was supported by an adjustable table. To minimize the mechanical effects of the contractions of upper body muscles and change of posture, the upper body was kept relaxed and was immobilized on the machine during the exercise.

Long-Term Effects of Exercise Training

Magnetic resonance imaging. Cross-sectional images of the left thigh were obtained by using a 0.2-T permanent magnet system (AIRIS mate; Hitachi Medical). Spin-echo and multislice sequences with a slice thickness of 10 mm were used with a repetition of 200 ms and an echo time of 20 ms. Each subject lay supine in the body coil with the legs fully extended and relaxed. Transverse scans were carried out with an interplaced gap of 0 mm, from the knee joint to the head of the femur. For each subject, the range of serial sections was deliberately determined on longitudinal images along the femur so as to obtain sections of identical portions before and after the period of exercise training.

To reduce errors in measurements associated with a slight mismatch between the sectional portions obtained before and after the period of exercise training and incidental deformations of muscles during the processes of MRIs, photographs for three portions near the midpoint of the thigh were used to measure the mean CSA of the knee extensor muscles. On each cross-sectional image, an outline of the quadriceps femoris muscle was traced, and the anatomical CSA was measured with Scion images. The measurements were repeated three

times for each image, and their mean values were used. Standard errors in these three sets of measurement were less than 2%.

Measurements of muscle strength. The maximum isometric torque (MVC) and isokinetic torque-angular velocity relationships of knee extensor muscles were measured by using an isokinetic dynamometer (Myoret, Kawasaki Industry, Tokyo, Japan). The subjects were familiarized with the test procedure on several occasions before the measurements. They sat on a chair with the back upright and with the left leg (nondominant side) firmly attached to the lever of the dynamometer. A pivot point of the lever was accurately aligned with the rotation axis of the knee joint, and the requisite axial alignment of joint and dynamometer axes was maintained during the movement. The isometric torque was measured at a knee angle of 80°, and the isokinetic torque was measured at preset angular velocities of 90, 200, and 300°/s. The range of angular movement of the knee joint was limited between 0 and 90° of anatomical knee angle. The value of peak torque was measured regardless of where it was developed within the range of movement. Three trials were made for isometric and each isokinetic angular velocity, and the highest value obtained was used for further analyses.

Statistical Analysis

All values are expressed as means \pm SD. One-way analysis of variance with Fisher's protected least significant difference test was used to examine differences in peripheral muscle oxygenation and blood lactate concentration between groups. Analysis of covariance with Fisher's protected least significant difference was used to examine differences in blood pressure, muscle CSA, and muscular strength between groups, considering whether the starting values may affect the magnitude of changes. Differences between two variables within the same group were examined with Student's paired *t*-test. For all statistical tests, $P < 0.05$ was considered as significant.

For examining the test-retest reliability for all variables measured, intraclass correlation coefficient (ICC) and coefficient of variation (CV) were calculated for nine subjects (three subjects from each group). In addition, differences between test-retest data were examined with Student's paired *t*-test.

RESULTS

Acute Effects of Exercises

Knee angle, knee extension torque, and muscle electric activity. Figure 1 shows typical examples of changes in knee angle, knee extension torque, and EMG signals from VL during three types of exercise. The load used for each type of exercise was 58.5 kg (~50% 1RM) for LST, 94.5 kg (~80% 1RM) for HN, and 58.5 kg (~50% 1RM) for LN. In LST, the knee extension torque was almost constant at ~50% of 1RM, which was approximately equal to 40% MVC. Accordingly, the EMG from VL exhibited almost continuous activity throughout the entire movement. In both HN and LN, the knee extension torque showed fluctuations during the lifting and lowering phases and fell to zero at the relaxing phase. In phase with these changes, the EMG signals from VL exhibited intermittent activity. The patterns of torque and EMG changes were similar between HN and LN, although their peak values were different because of the difference in load.

Before the period of exercise training, the measurements of knee angle, knee extension torque, and EMG from VL were made for all subjects ($n = 24$) assigned to the three types of exercise. Data shown in Fig. 1 were obtained from the same subject assigned into the LST group. Basically, all subjects showed the same patterns.

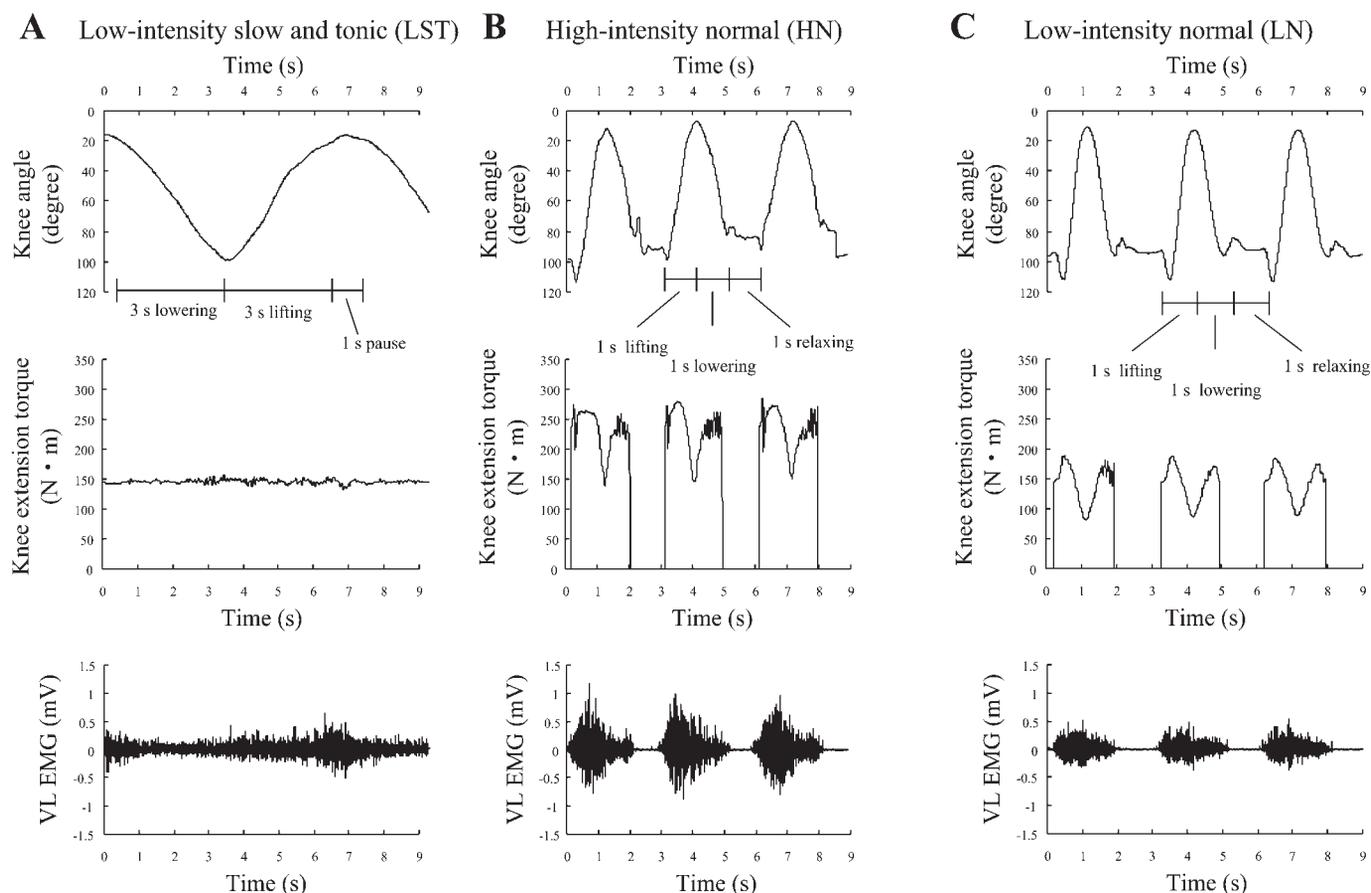


Fig. 1. Typical examples showing knee angle, knee extension torque, and electromyograph (EMG) from the left vastus lateralis (VL) recorded during low-intensity resistance exercise with relatively slow movement and tonic force generation (LST) with the load of 58.5 kg [$\sim 50\%$ 1-repetition maximum (1RM)] (A), high-intensity normal-speed (HN) exercise with the load of 94.5 kg ($\sim 80\%$ 1RM) (B), and low-intensity normal-speed (LN) exercise with the load of 58.5 kg ($\sim 50\%$ 1RM) (C). Records are from the second lifting movement in the first set for LST and the second to fourth lifting movements for both HN and LN. Data from the same subject are shown.

Peripheral muscle oxygenation. Figure 2 shows typical examples of changes in relative oxygenation level in the left VL muscle during and a few minutes after the exercises. In all three types of exercise, the oxygenation level showed an immediate decrease as the exercise repetitions started, and a rapid recovery followed by a hypercompensation after the end of the exercise repetitions. In all types of exercise, the mini-

um level of oxygenation during exercise was significantly lower than the resting level. Also, the maximum level of oxygenation after exercise was significantly higher than the resting level. The mean value of minimum oxygenation level during LST exercise was significantly lower than during HN and LN exercises, and there was no significant difference between those during HN and LN exercises (Fig. 3). The large

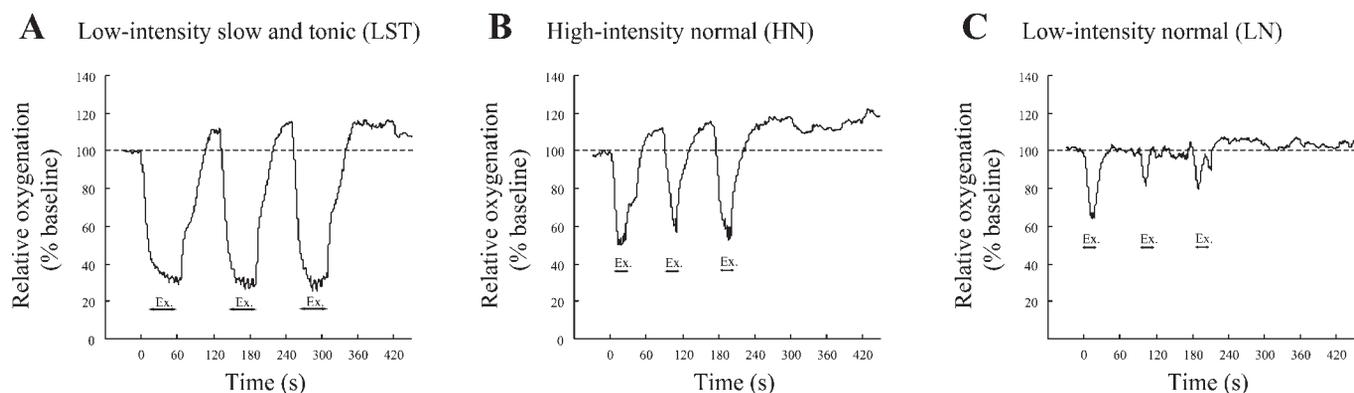


Fig. 2. Typical examples showing changes in relative oxygenation level in the left VL muscle during and after LST (A), HN (B), and LN (C) exercises. The resting and minimum levels of oxygenated hemoglobin and myoglobin (Oxy-Hb/Mb) were defined as 100% (baseline) and 0%, respectively, according to the arterial occlusion method. Ex, during exercise movement.

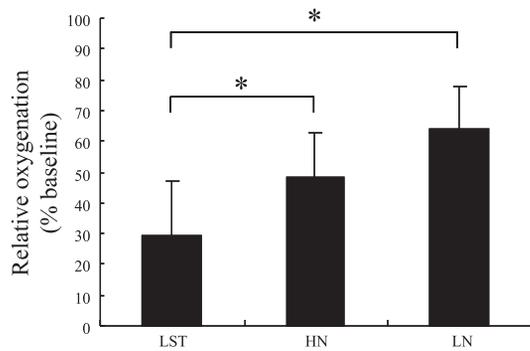


Fig. 3. Mean values of minimum oxygenation level during LST, HN, and LN exercises. Means \pm SD ($n = 8$ for each group) are shown. *Significant differences ($P < 0.05$) between groups. Compared with the resting level, the values for all types of exercise showed significant changes ($P < 0.05$).

decrease in the muscle oxygenation level during LST exercise was likely due to continuous activities of the knee extensor muscles (see Fig. 1). The mean values of maximum oxygenation level after LST and HN exercises were significantly higher than after LN, and there was no significant difference between those after LST and HN exercises (Fig. 4).

ICC and the mean CV values for the oxygenation level during exercise were 0.85 and 6.9%, respectively. There was no significant difference between test-retest data.

Blood lactate concentration. Figure 5 shows changes in blood lactate concentration measured at rest (pre), immediately after the exercise (post), and 2 and 5 min after the exercise (post 2 min, post 5 min). All types of exercise (LST, HN, and LN) caused significant increases in the blood lactate concentration at post, post 2 min, and post 5 min, compared with the resting concentration. No significant differences were observed between at post, post 2 min, and post 5 min in each group. Blood lactate concentrations after LST and HN exercises were significantly higher than after LN exercise. On the other hand, they were similar between LST and HN exercises, despite the much lower intensity and smaller amount of work in LST than in HN.

ICC and the mean CV values for the blood lactate concentration after exercise were 0.82 and 5.5%, respectively. There was no significant difference between test-retest data.

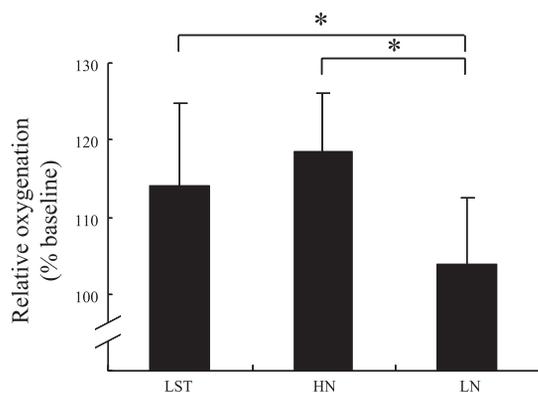


Fig. 4. Mean values of maximum oxygenation level after LST, HN, and LN exercises. Means \pm SD ($n = 8$ for each group) are shown. *Significant differences ($P < 0.05$) between groups. Compared with the resting level, the values for all types of exercise showed significant changes ($P < 0.05$).

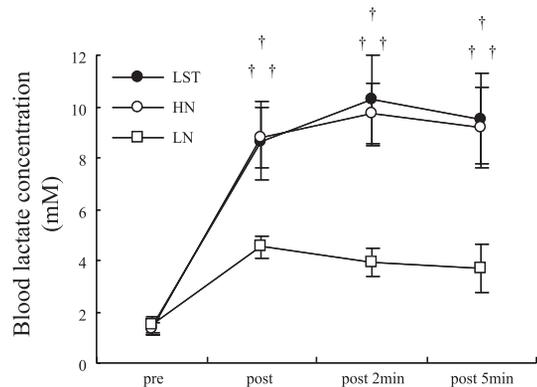


Fig. 5. Changes in blood lactate concentrations before and after LST (\square), HN (\bullet), and LN (\square) exercises. Means \pm SD ($n = 8$ for each group) are shown. †Significant difference ($P < 0.05$) between LST and LN exercises. ††Significant difference ($P < 0.05$) between HN and LN exercises. Compared with the resting level (pre), the values after exercise (post, post2min, post5min) for all types of exercise showed significant changes ($P < 0.05$).

Blood pressure during exercise. Blood pressure was measured continuously during exercises (Fig. 6). In all types of exercise, the systolic pressure reached a peak at the last repetition or the second or third from the last repetition in the first set of exercise, and it exhibited significant increases from that at resting. The peak systolic pressure during HN exercise (227.6 ± 24.9 mmHg) was significantly higher than those during LST and LN exercises, and no significant difference was seen between those during LST and LN exercises (Fig. 6A). Similar differences were seen when the values of heart rate-blood pressure product were compared between exercise groups (Fig. 6B).

ICC and the mean CV values for the peak blood pressure and for the peak values of heart rate-blood pressure product during exercise were 0.94 and 3.8% (blood pressure), 0.93 and 8.0% (heart rate-blood pressure product), respectively. There were no significant differences between test-retest data.

Long-Term Effects of Exercise Training

Changes in muscle CSA. Typical examples of cross-sectional, magnetic resonance images of an identical portion of the thigh are shown in Figure 7. These images were taken before (A) and after (B) LST exercise training for 12 wk and exhibit a marked increase (by $\sim 12\%$) in the CSA of the knee extensor muscles after the training. Both LST and HN exercises caused significant increases in the CSA of the knee extensor muscles compared with that before the training (Fig. 8). The percent increases in the CSA of the knee extensor muscles were $5.4 \pm 3.7\%$ after LST exercise training and $4.3 \pm 2.1\%$ after HN exercise training, whereas no significant change occurred after LN exercise training. The CSAs after LST and HN exercise training were significantly larger than that after LN exercise training, and there was no significant difference between the CSAs after LST and that after HN exercise training.

ICC and the mean CV values for the CSA of the knee extensor muscles were 0.99 and 1.1% respectively. There was no significant difference between test-retest data.

Changes in muscular strength. The force-velocity relations obtained before and after the 12-wk training are shown in Fig. 9. All values of the knee extension torque were normalized to the pretraining values of the isometric knee extension torque.

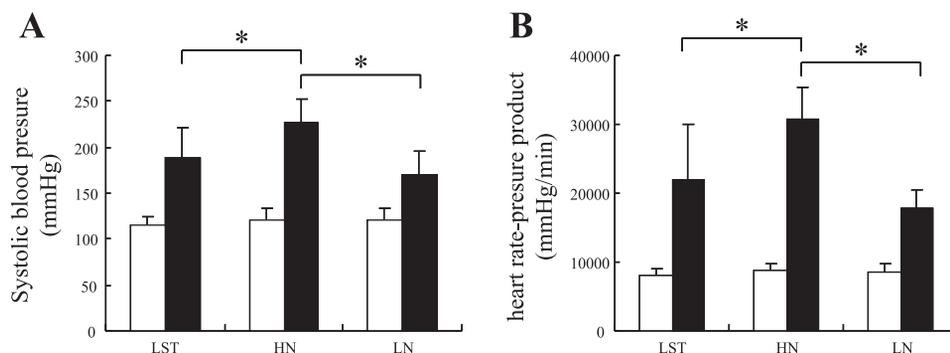


Fig. 6. Peak blood systolic pressure (A) and peak heart rate-pressure product (B) during LST, HN, and LN exercises (solid bars) and at resting (open bars). Means \pm SD ($n = 8$ for each group) are shown. *Significant differences ($P < 0.05$) between groups. Compared with the resting level, the values for all types of exercise showed significant changes ($P < 0.05$).

LST exercise training caused a significant increase in isometric strength but no significant changes in isokinetic strengths at 90, 200, and 300°/s (Fig. 9A). HN exercise training caused significant increases in isometric strength and isokinetic strength at 90°/s but no significant changes in isokinetic strengths at 200 and 300°/s (Fig. 9B). On the other hand, LN exercise training caused small but significant increases in isokinetic strengths at 90 and 200°/s and no significant changes in isometric strength and isokinetic strength at 300°/s (Fig. 9C). Isometric strength after HN exercise training was significantly larger than that after LST exercise training. Also, isometric strength after LST exercise training was significantly larger than that after LN exercise training. There were no significant differences between isokinetic strengths after LST, HN, and LN exercise training. The maximal isometric torque per unit CSA of the knee extensor muscles (in N/m) did not change significantly after the exercise training in all three groups: from 2.58 ± 0.29 to 2.67 ± 0.28 in LST, from 2.63 ± 0.29 to 2.90 ± 0.39 in HN, and from 2.73 ± 0.56 to 2.79 ± 0.44 in LN. These results indicate that the increases in isometric strength after LST and HN exercise training are due primarily to the muscular hypertrophy.

All types of exercise caused significant increases in 1RM strength compared with that before the training: from 101.0 ± 20.7 to 129.4 ± 11.6 kg in LST, from 104.9 ± 18.6 to 138.3 ± 18.6 kg in HN, and from 99.6 ± 20.9 to 115.4 ± 17.6 kg in LN (Table 2). There was no significant difference between the three types of exercise in 1RM after exercise training.

ICC and the mean CV values for the muscular strength were 0.97 and 2.4%, respectively. There was no significant difference between test-retest data.

DISCUSSION

The present study showed an increase in muscular size and concomitant increase in muscular strength after a 12-wk low-

intensity ($\sim 50\%$ 1RM) resistance exercise training with slow movement and tonic force generation (LST). The gains in muscular size and strength were similar to those after a high-intensity ($\sim 80\%$ 1RM) exercise training with normal speed (HN), whereas no significant increases in muscular size and strength were seen after a low-intensity ($\sim 50\%$ 1RM) exercise training with normal speed (LN). The primary factors responsible for the effect of LST exercise would be the slow movement and tonic force generation, because the intensity and the amount of work for LST exercise were the same as those for LN exercise.

The present LST exercise was physiologically characterized as 1) knee extension torque kept constant at $\sim 40\%$ MVC; 2) activity of VL kept constant throughout the entire exercise movement; 3) lowered peripheral muscle oxygenation level during exercise; and 4) increased blood lactate concentration (Figs. 1–5). The lowered muscle oxygenation level and the increased blood lactate concentration are likely due, at least partially, to the restriction of muscular blood flow during exercise and may be related to the mechanisms for muscular hypertrophy.

Takarada et al. (27) have shown that a low-intensity exercise combined with moderate vascular occlusion gives rise to a marked increase in plasma growth hormone (GH) concentration. It has been speculated that local accumulation of metabolic subproducts, such as lactate and proton, stimulate the hypophyseal secretion of GH (18, 27) and the local secretion of growth factors such as IGF-I (22). It has also been shown that plasma GH stimulates synthesis and secretion of IGF-I within a muscle, which then may act on the muscle itself and promote growth (6, 13, 27). In a separate set of experiments, we recently measured plasma GH concentrations and found that LST exercise caused GH response similar to that after HN exercise, whereas LN exercise did not (31). This suggests that the long-term effect of LST exercise is mediated by GH.

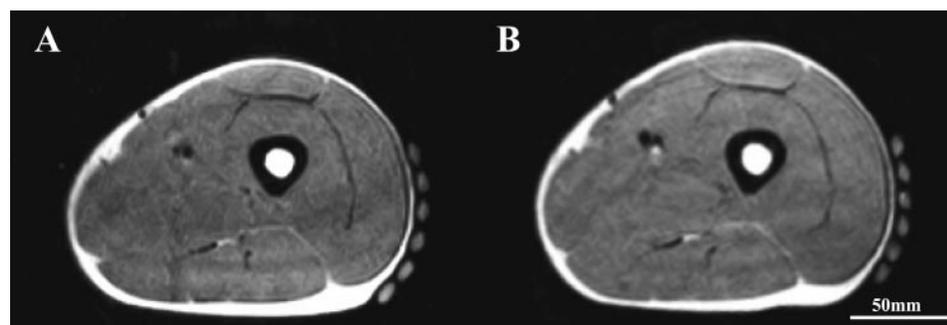


Fig. 7. Typical MRIs showing transverse sections of the mid thigh taken before (A) and after (B) LST exercise training for 12 wk.

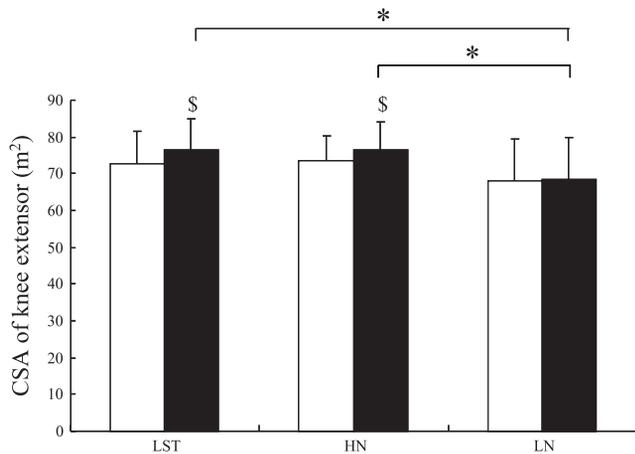


Fig. 8. Cross-sectional area (CSA) of the knee extensor muscles before (open bars) and after (solid bars) LST, HN, and LN exercise training for 12 wk. Means \pm SD ($n = 8$ for each group) are shown. $\$$ Significant differences between pre- and posttraining values ($P < 0.05$). $*$ Significant differences between groups ($P < 0.05$).

The production of reactive oxygen species is another factor to consider. It may play a more direct role in inducing muscular hypertrophy. The activity of ROS within the muscle has been shown to increase in a hypoxic environment (17). Therefore, a considerable amount of ROS could be produced when the muscle is kept hypoxic and subsequently exposed to reperfusion. Although ROS often cause an injurious or even lethal effect in cardiac muscles, nerve cells, and transplanted tissues (10, 25), they have also been shown to play an important role in signal transduction for the growth of vascular smooth muscle. Nitric oxide, one of the ROS, was observed to mediate activation and proliferation of muscle satellite cells, which are muscle fiber stem cells (1). Therefore, both lowered and elevated muscle oxygenation levels during and after LST exercise, respectively, may cause an enhanced production of ROS, thereby stimulating the growth of muscle (Figs. 3 and 4). Using an animal model, we have recently shown that the tissue nitric oxide level is elevated in hypertrophied muscle after chronic restriction of venous blood flow (15).

The intensity and the amount of work in LST exercise are the same as those in LN exercise, but the impulse (force integrated with respect to time) in LST exercise was about three times as large as that in LN exercise. However, the

impulse may not be a major determinant of the exercise quantity, because isometric contraction, even with large impulse, theoretically produces no mechanical work in addition to maintenance heat. Our recent study showed that blood lactate and plasma GH concentrations after isometric exercise with the same impulse as LST were lower than after LST and HN exercises (31). Therefore, larger impulse in LST exercise may not be a primary factor responsible for the present effect of LST exercise.

In knee extension exercise with normal speed [1 s for concentric (lifting phase) and eccentric (lowering phase) actions], it is difficult to maintain a constant muscular tension. The knee extension torque and the activity of VL during HN and LN exercises (Fig. 1, B and C) rapidly decreased at the end of lifting phase and at the beginning of the lowering phase. Maintaining slow movement speed in both lifting and lowering actions may be necessary to achieve constant tension. In a pilot study, we examined several patterns of exercise movement to determine the most appropriate movement pattern for maintaining constant tension. In the exercise movement consisting of 2-s lifting and 2-s lowering, it appeared to be difficult for the subjects to maintain constant tension, whereas in the exercise movement consisting of 4-s lifting and 4-s lowering, the subjects could maintain constant tension but it was almost impossible for them to perform several repetitions at $\sim 50\%$ 1RM. Taking 1-s pause at the fully extended position seemed to effectively prevent the decline of knee extension torque at the end of lifting phase and at the beginning of lowering phase. The isometric exercise appeared to be a superior method for maintaining constant tension, and the oxygenation level in VL was lowered during an isometric exercise. As mentioned above, however, the isometric exercise caused much smaller increase in the blood lactate concentration than did LST exercise, owing possibly to its small energy expenditure (31). On the basis of these observations, we had chosen the present LST exercise as an optimal way to make the muscle hypoxic without large mechanical stress.

After LST exercise training, only isometric strength increased significantly, but isokinetic strengths at 90, 200, and 300°/s did not (Fig. 9). Muscular strength is primarily determined by both muscular size and neural factors (12). Because LST exercise training caused effectively the increase in muscular size (Fig. 8), it might not effectively improve neural functions for dynamic movement. This result agrees with

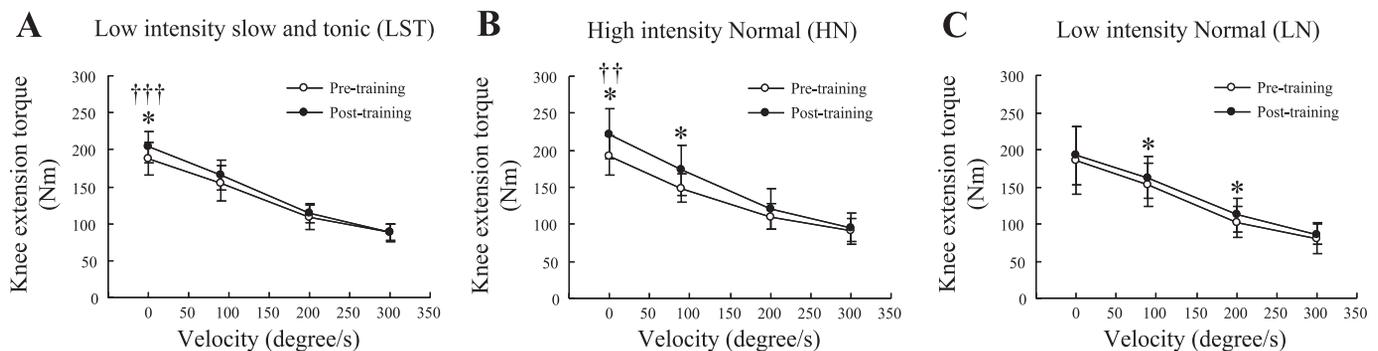


Fig. 9. Effects of exercise training on force-velocity relations. Isometric torque and isokinetic torque-angular velocity relations of knee extensor muscles were obtained before (pretraining: \circ) and after (posttraining: \bullet) the 12-wk exercise training. Means \pm SD ($n = 8$ for each group) are shown. $*$ Significant difference ($P < 0.05$) between pretraining and posttraining. \dagger Posttraining in LST significantly higher ($P < 0.05$) than in LN. $\dagger\dagger$ Posttraining in HN significantly higher ($P < 0.05$) than in LST and in LN.

previous studies showing that muscular strength gains are specific to the movement speed used in the training regimens (14). According to the study by Toji and Kaneko (32), multiple-load, multiple-speed training programs are effective for improving muscular power over a wide range of movement speeds. In the present study, LN exercise training caused small but significant increases in isokinetic strengths at 90 and 200°/s (Fig. 9). This may be due, at least partially, to movement-associated changes in neuromotor control, e.g., a rapid acceleration of light load may improve the motor unit recruitment at high movement velocities.

In conclusion, a low-intensity resistance exercise with slow movement and tonic force generation was effective for gaining muscular size and strength. This exercise was not associated with the generation of large force and considerable elevation of blood pressure (Fig. 6), so it would be useful for introductory strength training and rehabilitation from orthopedic injuries. However, a combination of low-intensity resistance exercise with slow movement and tonic force generation and an exercise with higher velocity may be ideal for further improvement in dynamic strength.

REFERENCES

- Anderson JE. A role for nitric oxide in muscle repair: nitric oxide-mediated activation of muscle satellite cells. *Mol Biol Cell* 11: 1859–1874, 2000.
- Aniansson A, Grimby G, Hedberg M, and Krotkiewski M. Muscle morphology, enzyme activity and muscle strength in elderly men and women. *Clin Physiol* 1: 73–86, 1981.
- Bae SY, Hamaoka T, Katsumura T, Shiga T, Ohno H, and Haga S. Comparison of muscle oxygen consumption measured by near infrared continuous wave spectroscopy during supramaximal and intermittent pedalling exercise. *Int J Sports Med* 21: 168–174, 2000.
- Bonde-Petersen F, Mork AL, and Nielsen E. Local muscle blood flow and sustained contractions of human arm and back muscles. *Eur J Appl Physiol* 34: 43–50, 1975.
- Chance B, Dait MT, Zhang C, Hamaoka T, and Hagerman F. Recovery from exercise-induced desaturation in the quadriceps muscles of elite competitive rowers. *Am J Physiol Cell Physiol* 262: C766–C775, 1992.
- DeVol DL, Rotwein P, Sadow JL, Novakofski J, and Bechtel PJ. Activation of insulin-like growth factor gene expression during work-induced skeletal muscle growth. *Am J Physiol Endocrinol Metab* 259: E89–E95, 1990.
- Fleck SJ. Cardiovascular adaptations to resistance training. *Med Sci Sports Exerc* 20: S146–S151, 1988.
- Hakkinen K, Kraemer WJ, Pakarinen A, Triplett-McBride T, McBride JM, Hakkinen A, Alen M, McGuigan MR, Bronks R, and Newton RU. Effects of heavy resistance/power training on maximal strength, muscle morphology, and hormonal response patterns in 60–75-year-old men and women. *Can J Appl Physiol* 27: 213–231, 2002.
- Hampson NB and Piantadosi CA. Near infrared monitoring of human skeletal muscle oxygenation during forearm ischemia. *J Appl Physiol* 64: 2449–2457, 1988.
- Hearse DJ, Manning AS, Downey TM, and Yellon DM. Xanthine oxidase: a critical mediator of myocardial injury during ischaemia and reperfusion? *Acta Physiol Scand Suppl* 548: 65–78, 1986.
- Holloszy JO and Booth FW. Biochemical adaptations to endurance exercise in muscle. *Annu Rev Physiol* 18: 273–291, 1976.
- Ikai M and Fukunaga T. A study on training effect on strength per unit cross-sectional area of muscle by means of ultrasonic measurement. *Int Z Angew Physiol Einschl Arbeitsphysiol* 28: 173–180, 1970.
- Isgaard J, Nilsson A, Vikman K, and Isaksson OG. Growth hormone regulates the level of insulin-like growth factor-I mRNA in rat skeletal muscle. *J Endocrinol* 120: 107–112, 1989.
- Kaneko M, Fuchimoto T, Toji H, and Sueti K. Training effect of different loads on the force-velocity relationship and mechanical power output in human muscle. *Scand J Sports Sci* 5: 50–55, 1983.
- Kawada S and Ishii N. Skeletal muscle hypertrophy after chronic restriction of venous blood flow in rats. *Med Sci Sports Exerc* 37: 1144–1150, 2005.
- Koba S, Hayashi N, Miura A, Endo M, Fukuba Y, and Yoshida T. Pressor response to static and dynamic knee extensions at equivalent workload in humans. *Jpn J Physiol* 54: 471–481, 2004.
- Korthius RJ, Granger DN, Townsley MI, and Taylor AE. The role of oxygen derived free radicals in ischaemia-induced increases in skeletal muscle vascular permeability. *Circ Res* 57: 599–609, 1985.
- Kraemer WJ and Ratamess NA. Hormonal responses and adaptations to resistance exercise and training. *Sports Med* 35: 339–361, 2005.
- McDonagh MJN and Davies CTM. Adaptive response of mammalian skeletal muscle to exercise with high loads. *Eur J Appl Physiol* 52: 139–155, 1984.
- Newton RU, Hakkinen K, Hakkinen A, McCormick M, Volek J, and Kraemer WJ. Mixed-methods resistance training increases power and strength of young and older men. *Med Sci Sports Exerc* 34: 1367–1375, 2002.
- Pollock ML, Carroll JF, Graves JE, Leggett SH, Braith RW, Lima-cher M, and Hagberg JM. Injuries and adherence to walk/jog and resistance training programs in the elderly. *Med Sci Sports Exerc* 23: 1194–1200, 1991.
- Schott J, McCully K, and Rutherford OM. The role of metabolites in strength training. II. Short versus long isometric contractions. *Eur J Appl Physiol* 71: 337–341, 1995.
- Shinohara M, Kouzaki M, Yoshihisa T, and Fukunaga T. Efficacy of tourniquet ischemia for strength training with low resistance. *Eur J Appl Physiol* 77: 189–191, 1998.
- Shinohara M and Moritani T. Increase in neuromuscular activity and oxygen uptake during heavy exercise. *Ann Physiol Anthropol* 11: 257–262, 1992.
- Southard JM, Marsh DC, McAnulty JF, and Belzer FO. The importance of O₂ derived free radical injury to organ preservation and transplantation. *Transplant Proc* 19: 1380–1381, 1987.
- Takarada Y and Ishii N. Effects of low-intensity resistance exercise with short inter-set rest period on muscular function in middle-aged women. *J Strength Cond Res* 16: 123–128, 2002.
- Takarada Y, Nakamura Y, Aruga S, Onda T, Miyazaki S, and Ishii N. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. *J Appl Physiol* 88: 61–65, 2000.
- Takarada Y, Sato Y, and Ishii N. Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. *Eur J Appl Physiol* 86: 308–314, 2002.
- Takarada Y, Takazawa H, and Ishii N. Applications of vascular occlusion diminish disuse atrophy of knee extensor muscles. *Med Sci Sports Exerc* 32: 2035–2039, 2000.
- Takarada Y, Takazawa H, Sato Y, Takebayashi S, Tanaka Y, and Ishii N. Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. *J Appl Physiol* 88: 2097–2106, 2000.
- Tanimoto M, Madarame H, and Ishii N. Muscle oxygenation and plasma growth hormone concentration during and after resistance exercise: comparison between "Kaatsu" and other types of regimen. *Int J Kaatsu Training Research* 2: 53–58, 2005.
- Toji H and Kaneko M. Effect of multiple-load training on the force-velocity relationship. *J Strength Cond Res* 18: 792–795, 2004.
- Westcott WL, Winett RA, Anderson ES, Wojcik JR, Loud RL, Clegg E, and Glover S. Effects of regular and slow speed resistance training on muscle strength. *J Sports Med Phys Fitness* 41: 154–158, 2001.