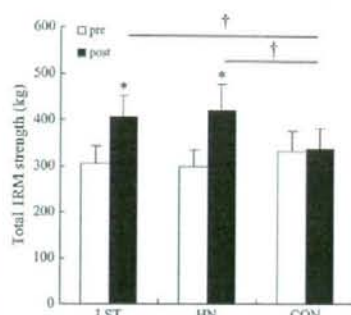


**Figure 6.** Sum of whole-body subcutaneous fat thickness of air sites before (open bars) and after (filled bars) the experimental period. Mean values  $\pm$  SD ( $n = 12$  for each group) are shown. \*Significant differences between pre- and posttraining values ( $p < 0.05$ ). †Significant differences between groups ( $p < 0.05$ ).



**Figure 7.** Sum of one-repetition maximum (1RM) strength of five exercises before (open bars) and after (filled bars) the experimental period. Mean values  $\pm$  SD ( $n = 12$  for each group) are shown. \*Significant differences between pre- and posttraining values ( $p < 0.05$ ). †Significant differences between groups ( $p < 0.05$ ).

absolute changes in LSTM were  $1.4 \pm 1.4$  kg in LST,  $1.8 \pm 1.3$  kg in HN, and  $0.6 \pm 0.7$  kg in CON. These changes in LST and in HN were significantly greater than those in CON, and there were no significant differences between the changes in LST and in HN. The LSTM increase observed in the CON group may have been attributable to weight gain associated with seasonal variations and growth. Whole-body percent body fat in the HN group decreased significantly after the experimental period. This decrease in HN was significantly greater than those in LST and CON, and there were no significant differences between the changes in LST and in CON. No significant changes occurred in body mass, fat mass, or BMD in any of the groups. All values measured by DXA before and after the experimental period are summarized in Table 4. Changes in FFM and fat mass in DXA were similar to those in MTH and SFT as determined by ultrasound imaging. Ultrasound imaging was used for direct assessment in regions involved in training, so ultrasound imaging may have higher detection sensitivity for detecting significant changes than DXA.

#### Changes in Muscular Strength

Figure 7 shows changes in total 1RM strength, defined as the sum of values for all five types of exercise used in the training regimen, in the three groups after the experimental period. No significant differences were observed among groups in 1RM strength in each type of training before the experimental period. In the LST group and the HN group, total 1RM strength increased significantly after the experimental period (Table 4), whereas there was no such change in the CON group (Figure 7). The percent changes in total 1RM strength were  $+33.0 \pm 8.8\%$  in LST,  $+41.2 \pm 7.8\%$  in HN, and

$+1.3 \pm 2.4\%$  in CON. These increases in LST and in HN after the experimental period were significantly greater than the value in CON, and there were no significant differences between the changes in LST and HN. In both LST and HN, 1RM strength in all five exercises increased significantly after the experimental period. There were no such changes in CON. The increases in LST and HN in 1RM strength in all five types of exercise were significantly larger than the values in CON, and there were no significant differences between the changes in LST and in HN except in back extension. The increase in 1RM strength on back extension in HN was significantly greater than that in LST. The values of 1RM strength in each type of exercise before and after the experimental period are summarized in Table 2.

#### DISCUSSION

The results of the present study indicate a significant increase in muscular size and concomitant increase in muscular strength after a 13-week whole-body LST training program consisting of the five following exercises: vertical squat, chest press, latissimus dorsi pull-down, abdominal bend, and back extension. The term *LST* refers to a low-intensity ( $\sim 55$ – $60\%$  1RM) resistance training program with slow movement and tonic force generation. The gains in muscular size and strength were similar to those after the same whole-body training program using a high-intensity load ( $\sim 80$ – $90\%$  1RM) with normal speed (HN). Previously, we reported that a 12-week LST training program with one type of exercise (knee extension) caused significant increases in muscular size and strength to the same degree as HN. This previous study investigated only local effects and provided no information about systemic effects of LST whole-body resistance training.

Single-joint exercises with exercise machines, such as knee extensions, are considered more appropriate for LST to achieve strict continuous force generation throughout the exercise movement than multijoint exercises. However, whole-body resistance training programs usually consist mainly of multijoint exercises. Multijoint exercises usually recruit more large muscle areas than single-joint exercises. In addition, the movements in most multijoint exercises are considered more similar to sport and daily performance movements. The significance of the present study lies in the demonstration that a whole-body LST training program consisting mainly of multijoint exercises, as a prescription program for actual training, was effective for muscular hypertrophy and strength gain as systemic effects.

In the previous study, the increase in muscular size after a 12-week knee extension LST training program tended to be higher than that after HN training. On the other hand, the increase in systemic muscular size after 13 weeks of whole-body LST training mainly consisting of multijoint exercises tended to be lower than that after HN in this study (no significant difference). The difference between the results in these two studies may be related to the fact that knee extension exercise, which is a single-joint exercise, is considered to be better suited for continuous muscle contraction in LST.

Multijoint LST exercise (vertical squat) has the following physiological characteristics: a) continuous muscle activity is kept constant throughout the entire exercise movement (Figure 1A); b) lowered peripheral muscle oxygenation level during exercise (Figure 2A); c) elevated peripheral muscle oxygenation level immediately after exercise (Figure 2B); and d) increased blood lactate concentration (Figure 3). These characteristics in multijoint LST exercise are similar to those of single-joint LST exercise with a knee extension exercise machine examined in the previous study (37). The lowered muscle oxygenation level and increased blood lactate concentration during LST exercise were likely attributable to the restriction of muscular blood flow by continuous muscle activity. It has been speculated that local accumulation of anaerobic energy metabolites, such as lactate, stimulates the hypophyseal secretion of GH (22,33) and the local secretion of growth factors, such as insulin-like growth factor 1 (28). It has also been shown that plasma GH stimulates synthesis and secretion of insulin-like growth factor 1 within muscle, which may then act on the muscle itself and promote growth (8,17). The production of ROS may play an important role in muscular hypertrophy. The activity of ROS within the muscle has been shown to be enhanced in hypoxic environments (20). A considerable amount of ROS could be produced when the muscle is kept hypoxic and subsequently exposed to reperfusion (31). Among the ROS, nitric oxide, which is the strongest vasodilator characterized to date, has also been shown to mediate the activation and proliferation of muscle satellite cells, which are muscle fiber stem cells (3). Therefore, both lowered and elevated muscle oxygenation levels during and

after exercise may cause enhanced production of ROS, thereby stimulating muscle growth. Additional recruitment of fast-twitch fibers under a hypoxic condition is likely to mediate muscle hypertrophy (30,36). Almost all of the motor units were considered to be recruited at the final repetition in all sets in LST as well as in HN exercise, because subjects in both HN and LST repeated the movement until exhaustion (27). The physiological characteristics of LST differ significantly from those of HN using a high-intensity load. However, 13 weeks of whole-body resistance training using both LST and HN caused comparable increases in muscular size and strength.

Some recent studies have indicated that low-intensity resistance training combined with moderate vascular occlusion using artificial occlusive pressure causes marked increases in muscular size and strength (2,29,34,36). These studies suggest that large mechanical stress is not indispensable for muscular hypertrophy and strength gain. They also suggest that the muscle trophic effect of resistance training involves not only large mechanical stress but also metabolic, hormonal, and neuronal factors. However, resistance training with vascular occlusion is so specialized that it should not be widely used without careful monitoring of occlusive pressure and blood flow. Its application is limited to upper-limb and lower-limb muscles, because it can be applied only to distal muscles from occlusive pressure belts. Usually, resistance training combined with moderate vascular occlusion is performed using occlusive pressure belts at the roots of the limbs. This is often associated with pain attributable to artificial occlusive pressure. The LST training, which sustains continuous force generation at >40% MVC to restrict muscle blood flow, would also be effective to make the intramuscular environment hypoxic even without artificial occlusive pressure. This can be applied not only to limb muscles but also to trunk muscles, and it is free from the pain associated with artificial occlusive pressure. Therefore, this represents a good alternative to resistance training with vascular occlusion.

The movement speed of LST in this study (3 seconds for concentric and eccentric actions) was configured so that all subjects could easily maintain continuous force generation throughout the exercise movement. In the exercise movement consisting of 2 seconds for concentric and eccentric actions, it seemed to be difficult for the subjects to maintain constant tension, whereas in the exercise movement consisting of 4 seconds for concentric and eccentric actions, the subjects could maintain constant tension easily, but it was almost impossible for them to perform several repetitions at sufficient intensity (>40% MVC) to restrict muscle blood flow. Thus, the movement speed of LST was determined based on the requirements described below.

1. Continuous force generation could be easily achieved even by beginners without previous experience of resistance training.



2. Continuous force generation throughout the exercise movement with more than 40% MVC load to restrict muscle blood flow.

The prime point of LST is slow movement to achieve tonic force generation, and not to slow movement itself. In this point, LST is different from SuperSlow (10-second lifting and 4-second lowering movement), a registered trademark of Ken Hutchins (42).

Fat mass measured by DXA decreased significantly, although not markedly, after HN training, whereas no significant decrease was observed after LST. Acute increase in plasma catecholamine concentration during exercise may be one of the reasons for fat loss in HN. We also have shown previously that LST and HN leg extension exercise immediately increased plasma norepinephrine concentration. The amount of increase in HN tended to be higher than that in LST (38). Acute increases in plasma catecholamine concentration during and immediately after exercise enhance fat oxidation for energy expenditure (12,25). In addition, the larger amount of mechanical work may cause fat loss in HN. The amount of work in HN was about 1.5 times that in LST.

Bone mass density (see Table 4) and bone mass component (BMC data not shown) were not increased after the experimental period in any groups. This result is perhaps related to the length of the experimental period. It is considered that the experimental period in this study was short, and therefore no changes were observed in BMD or BMC. Bone adapts to high mechanical stress by changing its size and density, and the heavier the magnitude of load, the greater the stimulus for bone growth (40). Thus, BMD and BMC increases from long-term resistance training would be more effective in HN than in LST.

High-intensity resistance training does not necessarily increase the risk of injury. High-intensity resistance training does not cause orthopedic or cardiovascular problems when performed or supervised appropriately (13). However, it has also been reported that approximately 20% of the elderly (aged 70–79 years) showed some symptoms of orthopedic injury after training at 1RM (26). In addition, a marked increase in systolic blood pressure (up to 250 mm Hg) has been reported to occur during high-intensity resistance training (~8RM) for large muscle groups (10). Some studies have reported large numbers of cases in which vascular events, such as aortic dissection, occurred during high-intensity resistance training (15,16). Thus, high-intensity resistance training can increase the risk of injury and vascular events during exercise. Therefore, the development of a resistance training regimen that can cause substantial gains in strength with much lower mechanical stress would be advantageous for the development of safer and effective methods of promoting muscle hypertrophy for a wider range of people, including older people and those with cardiovascular problems.

In conclusion, low-intensity whole-body resistance training with slow movement and tonic force generation consisting

mainly of multijoint exercises was as effective for increasing muscular size and strength as high-intensity resistance training. This training method was not associated with the generation of large force or with any considerable elevation of blood pressure. Therefore, it would be useful for promoting muscular hypertrophy and strength increases in a larger population, including the elderly and those at higher risk of cardiovascular adverse events. In this regard, however, LST is anything but easy for subjects to carry out despite the use of a relatively low-intensity load. Subjects repeat movement until exhaustion in LST as in HN.

#### PRACTICAL APPLICATIONS

The guideline of "load and repetition assignments based on the training goal" based on Fleck and Kraemer's systematic review of resistance training (11) and other studies (39) has been widely used in the field of physical fitness. This guideline recommends resistance training with 6–12 repetitions using a 67–85% 1RM load for muscle hypertrophy. This guideline seems like an appropriate assignment in voluntary movement, but it does not include the concept of enhancing exercise movement variation. When exercise movement is devised to place muscles under continuous tension throughout the exercise movement as in the LST method, resistance training, even with low-intensity loads of less than 65% 1RM, can cause muscular hypertrophy and increase strength. The results of this study indicate that whole-body LST training is an effective method for gaining muscular size and strength in actual training. A regimen of LST training with a relatively low-intensity load can be chosen as a safe resistance training method with relatively low risk for orthopedic injury and cardiac event during exercise. The LST training should be performed with a speed that easily enables continuous force generation throughout the exercise movement. In actual training, LST does not have to be performed with the speed used in this study (3 seconds for concentric and eccentric actions). However, if the movement is too slow (e.g., more than 5 seconds for concentric and eccentric actions), it may be difficult to perform several repetitions at an intensity sufficient to restrict muscle blood (>40% MVC). Also, the mechanical work may not be sufficient to enhance local accumulation of metabolic byproducts such as lactate and proton. We recommend that the movement speed should be as fast as possible within the limits in which continuous force generation can be maintained. We regard tonic force generation rather than slow movement to be the primary point of LST training.

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## Pulse Wave Velocity for Assessment of Arterial Stiffness Among People With Spinal Cord Injury: A Pilot Study

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### Abstract

**Background/Objective:** The most significant complication and leading cause of death for people with spinal cord injury (SCI) is coronary artery disease (CAD). It has been confirmed that aortic pulse wave velocity (PWV) is an emerging CAD predictor among able-bodied individuals. No prior study has described PWV values among people with SCI. The objective of this study was to compare aortic (the common carotid to femoral artery) PWV, arm (the brachial to radial artery) PWV, and leg (the femoral to posterior tibial artery) PWV in people with SCI (SCI group) to able-bodied controls (non-SCI group).

**Methods:** Participants included 12 men with SCI and 9 non-SCI controls matched for age, sex, height, and weight. Participants with a history of CAD or current metabolic syndrome were excluded. Aortic, arm, and leg PWV was measured using the echo Doppler method.

**Results:** Aortic PWV (mean  $\pm$  SD) in the SCI group ( $1,274 \pm 369$  cm/s) was significantly higher ( $P < 0.05$ ) than in the non-SCI group ( $948 \pm 110$  cm/s). There were no significant between-group differences in mean arm PWV (SCI:  $1,152 \pm 193$  cm/s, non-SCI:  $1,237 \pm 193$  cm/s) or mean leg PWV (SCI:  $1,096 \pm 173$  cm/s, non-SCI:  $994 \pm 178$  cm/s) values.

**Conclusions:** Aortic PWV was higher among the SCI group compared with the non-SCI group. The higher mean aortic PWV values among the SCI group compared with the non-SCI group indicated a higher risk of CAD among people with SCI in the absence of metabolic syndrome.

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**Key Words:** Arterial stiffness; Pulse wave velocity; Spinal cord injuries; Doppler ultrasound; Coronary artery disease; Risk factors

### INTRODUCTION

Coronary artery disease (CAD) is the most significant complication and leading cause of mortality after spinal cord injury (SCI) (1). Individuals with chronic SCI have higher cardiovascular mortality rates and cardiovascular mortality occurs at earlier ages compared with the able-bodied population (2-4). Stiffening of the central or cardiothoracic arteries is a significant independent risk factor for CAD in able-bodied people (5-7). Decreases in the elastic properties of arteries reduce their buffering

capacity, leading to increased pulse pressure, aortic impedance, and left ventricular wall tension, all of which augment the workload of the heart, thereby increasing CAD risk. Several indices have been used to quantify the stiffness of the peripheral and cardiothoracic arteries. These include (a) measuring pulse wave velocity (PWV); (b) relating changes in arterial diameter to distending pressure; and (c) assessing arterial pressure wave forms. Of the above indirect methods for measuring arterial stiffness, PWV is the most widely accepted technique (8). PWV has been a useful noninvasive measure to assess arterial stiffness and severity of CAD among able-bodied people in a number of previous studies (9-11).

PWV is the velocity of the blood pressure wave as it travels a known distance between 2 anatomic sites within the arterial system; it is determined by the elasticity and other properties of the artery (12). PWV values positively

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correlate with arterial distensibility and stiffness. Three locations for the measurement of PWV have been proposed: (a) trunk (aortic PWV); (b) arm (arm PWV); and (c) leg (leg PWV). Aortic PWV is the established index for measuring arterial stiffness.

Aortic PWV values have been directly linked with cardiovascular mortality, fatal and nonfatal coronary events, and fatal strokes in patients with low and high levels of traditional CAD risk factors (9-11,13-15). For example, aortic PWV values of at least 1,300 cm/s are a strong predictor of cardiac mortality among patients with hypertension (13). Among people with hypertension, a 500-cm/s increment in aortic PWV is an independent predictor of both cardiovascular mortality (odds ratio = 1.34) and all-cause mortality (odds ratio = 1.51) (14). Although leg PWV and arm PWV have not been studied to the same extent, it has been suggested that these peripheral PWV measures are insensitive to physical activity levels and/or aging compared with aortic PWV in able-bodied people (16,17).

Several CAD risk factors have been identified as determinants of PWV in the able-bodied population including obesity (18-20), diabetes mellitus (21,22), hypercholesterolemia (23) and hypertension (9,24), poor cardiorespiratory fitness (25,26), and low physical activity (27). These same CAD risk factors are common among people with SCI (28-32). In addition, people with SCI above the splanchnic outflow (T6) have autonomic dysfunction, which may contribute to disordered cardiac regulation and abnormalities of the vascular system. Thus, it was hypothesized that people with chronic SCI will have an increased risk of adverse vascular health and increased arterial stiffness as measured by PWV.

The purpose of this study was to compare aortic PWV in people with chronic SCI (SCI group) to that of age-, sex-, height-, and weight-matched able-bodied controls (non-SCI group) and to compare arm PWV and leg PWV in these same groups to determine whether differences exist in the values obtained.

## METHODS

The SCI group was made up of 15 individuals with SCI (C3-T10, ASIA A, B, and C). The non-SCI group was made up of 11 sedentary able-bodied controls matched for age, height, and weight. Individuals with SCI were recruited by a poster campaign from Toronto Rehab's Lyndhurst Centre. Non-SCI participants were recruited from the staff and friends of the authors affiliated with the Lyndhurst Centre. Participants in this study did not participate in any regular exercise or endurance-type wheelchair exercise beyond their normal activities of daily living for 6 months before enrollment. All participants were nonsmokers for at least 1 year before the study. No participants reported a prior history of CAD, pulmonary disease, diabetes mellitus, or metabolic syndrome. Each participant's current medications were recorded. No

participants were taking medications known to interfere with the cardiovascular system.

A 12-lead ECG was done to screen for signs of arrhythmia or prior myocardial infarction. Fasting serum blood sugar, glycosylated hemoglobin (HbA1C), total cholesterol (TC), high-density lipoproteins (HDL), low-density lipoproteins (LDL), triglycerides (TG), C-reactive protein (CRP), and apolipoprotein (A and B) levels, resting blood pressure (BP), and waist circumference were measured to screen for metabolic syndrome. Heart rate and BP were recorded from the right antecubital fossa using a stethoscope and hand-held dynamometer. Metabolic syndrome was defined as per the American Heart Association Guidelines as at least 3 or more of the following criteria: abdominal obesity (waist circumference  $\geq 102$  cm for men); dyslipidemia (TC/HDL  $> 4$  or LDL  $> 2.5$ ); glucose intolerance (fasting blood sugar  $> 7$  mmol/L); elevated CRP ( $> 3$  mg/dL); or hypertension (BP  $> 140/90$  mmHg).

Fifteen people with SCI and 11 people without SCI were screened for enrollment in the study. Five individuals' data were excluded from the analysis; 3 individuals had metabolic syndrome; 1 individual had an arrhythmia (atrial fibrillation) that interfered with PWV measurement; and 1 individual had an incomplete assessment. In total, 12 individuals with SCI and 9 controls were included in the study. The study protocol was approved by the Toronto Rehab Research Ethics Board.

PWV was measured from the foot; blood flow waves were recorded at 2 points along the path of the arterial pulse wave. PWV was calculated from the measured wave latency and the distance traveled between the 2 arterial recording sites (Figure 1) (10,15,17,33,34). Two identical transcutaneous Doppler flowmeters (Smartdop50, Hade-co, Kanagawa, Japan) were used to obtain the PWV values at 3 locations: (a) between the carotid and the femoral arteries (aortic PWV); (b) between the femoral and posterior tibial arteries (leg PWV); and (c) between the brachial and radial arteries (arm PWV; Figure 1B). Distance traveled by the pulse was measured over the surface of the body with a tape measure as the distance (D) between recording sites (cm). A minimum of 20 sequentially recorded wave forms were analyzed and averaged. All PWV data were obtained by 2 trained technicians between 10:00 AM and 1:00 PM to avoid circadian changes in PWV values. Measurement of PWV was conducted after abstinence from caffeine and an overnight fast of at least 8 hours. Flow measurements were obtained sequentially in the arm, aorta, and leg over a 40-minute period. Arterial pulse waves were digitized for off-line analysis with signal-processing software (Chart 5.5.5, AD Instruments, New South Wales, Australia). PWV was determined over the 3 arterial segments as  $PWV = D/\Delta t$  (cm/s), where  $\Delta t$  was determined from time delay between the proximal and the distal foot of the wave form (Figure 1A). The foot of the wave was identified as the start of the sharp systolic

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**Table 1.** Participant Characteristics

	SCI Group	Non-SCI Group
N	12	9
Age (y)	45.9 ± 7.8	44.1 ± 10.9
Height (cm)	177.6 ± 7.0	174.5 ± 8.2
Weight (kg)	81.1 ± 20.6	73.7 ± 11.5
Body mass index (kg/m <sup>2</sup> )	25.5 ± 5.7	24.1 ± 1.9
Systolic blood pressure (mmHg)	121.0 ± 9.5	116.2 ± 11.4
Diastolic blood pressure (mmHg)	74.8 ± 9.3	71.2 ± 6.5
Heart rate (beats/min)	64.3 ± 10.5	65.4 ± 8.0

Data are means ± SD.

upstroke. All analyses were performed by a trained technician blinded to the participant's group assignment (SCI or non-SCI).

The test-retest variability of PWV measures in our laboratory was established by sequential measurement of 9 able-bodied men (21–39 years) on 2 separate days. The intraclass correlation coefficients for test-retest reliability were 0.730 to 0.972 for each PWV value. The mean PWV combined for the 3 sites was 1,095 ± 238 vs 1,057 ± 210 cm/s for Trial 1 vs Trial 2 (not significant).

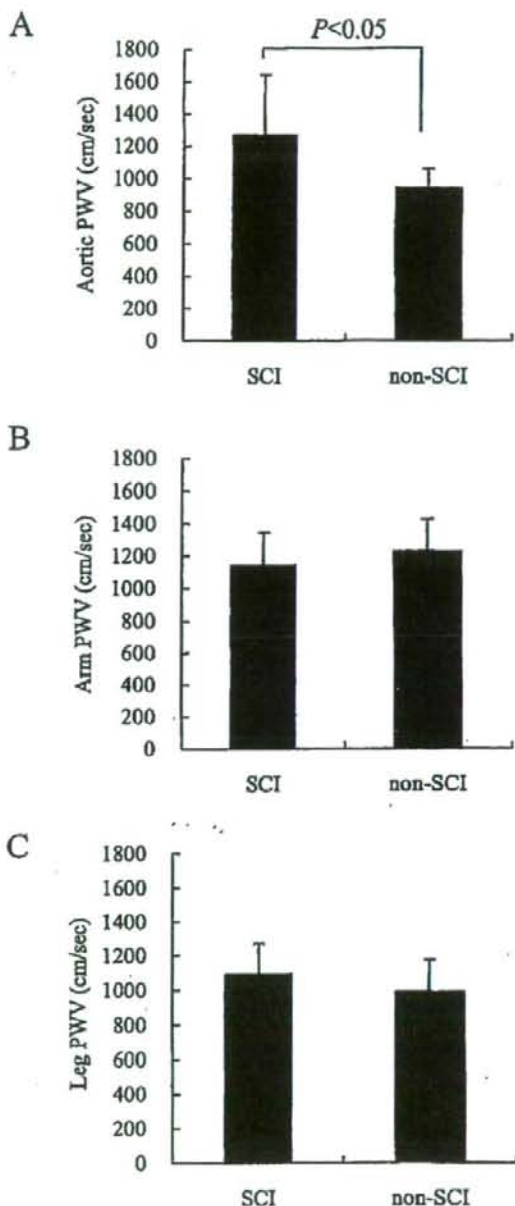
Statistical analyses were performed using StatView (Version 5.0) software. Demographic, anthropometric, and PWV data are expressed as mean ± SD. Participants with and without SCI were compared by the nonparametric Mann-Whitney *U* test because of the small group size. A 2-sided *P* < 0.05 was considered significant.

## RESULTS

There were no significant differences between groups in the baseline demographic or anthropometric parameters including age, height, weight, heart rate, and BP (Table 1). The mean duration of injury of the participants with SCI was 20 ± 13 years (SD). Mean aortic PWV in the SCI group (1,274 ± 369 cm/s) was significantly higher (*P* < 0.05) than that of the non-SCI group (948 ± 110 cm/s; Figure 2A). There were no statistically significant differences between the SCI group and the non-SCI group (Figure 2B and C) in either arm PWV (SCI: 1,152 ± 193 cm/s, non-SCI: 1,237 ± 193 cm/s; *P* = 0.434) or leg PWV (SCI: 1,096 ± 173 cm/s, non-SCI: 994 ± 178 cm/s) values (*P* = 0.145).

## DISCUSSION

Aortic PWV values in the SCI group were higher than those of able-bodied controls (non-SCI group), whereas there were no significant differences between the SCI and non-SCI groups in arm PWV and leg PWV values. Recently reported aortic PWV values in healthy able-bodied individuals 24 to 62 years of age ranged from 600 to 1,000 cm/s (8). Among hypertensive study participants, aortic PWV values ranged from 1,100 to 1,500 cm/s (8).



**Figure 2.** Aortic PWV (A), arm PWV (B), and leg PWV (C) in participants with SCI and able-bodied controls (non-SCI).

Arm and leg PWV values in healthy able-bodied individuals ranged from 840 to 1,200 and from 920 to 1,050 cm/s, respectively (8). The values for PWV documented herein are comparable with those previous-

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ly reported for able-bodied individuals within the same age range.

Additionally, we found that aortic PWV values among healthy SCI participants were higher than those of the age-matched non-SCI participants. Aortic PWV values in the SCI group were equally high compared with the values ( $>1,300$  cm/s) associated with an increased risk of developing CAD in the report of Blacher et al (13). These results suggest that the SCI group has a high risk of CAD. Screening protocols to diagnose and prevent CAD related mortality are urgently needed.

In contrast to the aortic PWV result, there were no significant differences between the SCI and non-SCI groups in either arm PWV or leg PWV. These results concur with a prior study reporting that aortic PWV is sensitive to daily activity and aging, whereas leg and arm PWV values are not (16,17). This sensitivity of the PWV of central vs peripheral arteries may be related to their distinct roles in hemodynamic regulation. Compared with the central arteries whose cushioning function damps fluctuations in flow, the peripheral arteries do not exhibit the same extent of pulsatile changes in diameter (35) and, as such, may not undergo the adaptations leading to a loss of elasticity. However, previous studies, which investigated femoral arterial stiffness by augmentation index (AI) (36) and arterial compliance (37,38) among people with SCI, showed that stiffness of the femoral artery in people with SCI was higher than that of able-bodied people. The reasons for this discrepancy is not clear; however, the use of the PWV methodology as opposed to the AI and arterial compliance to assess arterial stiffness may in part explain the discrepancy between our finding of normal leg PWV values and prior publications reporting elevated femoral AI and decreased arterial compliance values among patients with SCI. The PWV method measures pulse wave latency over the femoral and posterior tibial arteries as opposed to the femoral artery alone when assessing AI or arterial compliance.

Although there are no prior studies determining PWV in people with SCI, 3 previous studies investigated arterial stiffness using other measures of arterial stiffness: the AI (36) and arterial compliance (37,38) and compared them with those of able-bodied controls. de Groot et al (37) and Schmidt-Trucksass et al (38) reported that arterial compliance of the superficial femoral and carotid artery were significantly lower in people with SCI compared with people without SCI. Wecht et al (36) reported that arterial stiffness evaluated by AI was high in a group of people with paraplegia compared with an able-bodied group. Moreover, premature and advanced coronary atherosclerosis was found in persons with SCI compared with able-bodied people using electron beam tomography (39). Our observation of increased aortic arterial stiffness supports prior reports of premature CAD in the SCI population.

Mechanisms that may potentially account for higher aortic PWV among people with SCI include (a) structural changes in the vessel as a result of long-term sympathectomy and increased collagen content in the vascular wall (40) or (b) functional changes in the endothelium caused by decreased regional blood flow. Decreased regional blood flow as a result of inactivity impedes endothelium function and subsequently inhibits NO production, which is a mediator of endothelium dilatation (38). Although the relative importance of structural and functional changes in vascular tone is unknown, these may relate to both disordered cardiac regulation and inactive lifestyles after SCI. The mechanism(s) that account for these results are unknown.

This study has limitations that require caution when interpreting and generalizing the findings reported herein. First, the reliability of PWV values for people with SCI has not been reported. Second, this pilot study had a small sample size. Third, adjustments for confounding variables including the participant's injury level, duration of injury, and physical activity levels, which impact CAD risk, were not done. Future studies may want to use validated measures such as the Physical Activity Recall Assessment for People with SCI (PARA-SCI) (31) to quantify activity and explore the relationship between PWV and activity. Last, it is uncertain if the high PWV values reported reflect the presence of CAD among the subjects' in this study. Further studies with larger representative samples of participants with SCI are needed to determine the relationship between the increased arterial stiffness and the development/onset of atherosclerotic and asymptomatic CAD among people with SCI.

#### CONCLUSION

To our knowledge, this is the first study describing aortic PWV in people with SCI. High aortic PWV values were found in study participants with SCI compared to age-, sex-, height-, and weight-matched able-bodied participants, indicating a higher risk of CAD among individuals with SCI. Arm PWV and Leg PWV were found to be insensitive to the differences between the 2 groups. PWV is potentially a good screening test to assess CAD risk among people with chronic SCI. However, this pilot study merely measured PWV among people with SCI. Further study is needed to confirm the reproducibility of PWV measures among people with SCI. Further study of the PWV method's reliability, validity, and responsiveness while considering the potential confounding effects of: age, duration of injury, impairment, and physical activity on PWV among individuals with SCI are needed.

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# Low-intensity resistance training with slow movement and tonic force generation increases basal limb blood flow

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## Summary

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Metabolic syndrome is associated with reductions in basal limb blood flow. Resistance training increasing muscle mass and strength increases basal limb blood flow. Low-intensity resistance exercise with slow movement and tonic force generation (LST) has been proposed as one of the effective methods of resistance training increasing muscle mass and strength. The hypothesis that LST training increases basal femoral blood flow as well as traditional high-intensity resistance training at normal speed (HN) was examined. Thirty-six healthy young men without a history of regular resistance training were randomly assigned to the LST [ $\sim 55$ – $60\%$  one repetition maximum (1RM) load, 3 s lifting and 3 s lowering with no relaxation phase,  $n = 12$ ], HN ( $\sim 85$ – $90\%$  1RM, 1 s lifting and 1 s lowering with 1 s relaxation,  $n = 12$ ) or sedentary control (CON,  $n = 12$ ) groups. Participants in the training groups underwent two whole-body training sessions per week for 13 weeks. Basal femoral blood flow increased significantly by +18% in LST and +35% in HN (both  $P < 0.05$ ), while there was no such change in CON. There were no significant differences between these increases induced by LST and HN, although the increase in LST corresponded to about half that in HN. In conclusion, not only resistance training in HN but in LST as well, were effective for increasing basal limb blood flow, and that this effect was evident even in healthy young men.

## Introduction

Basal limb blood flow decreases with advancing age in healthy men and women (Dinenno *et al.*, 2001a,b; Moreau *et al.*, 2003; Miyachi *et al.*, 2005), which is related to corresponding reductions in leg fat-free mass and estimated leg oxygen demand (Dinenno *et al.*, 2001a,b). Reductions in peripheral blood flow have been suggested to be mechanistically involved in metabolic syndrome, a cluster of disease states including hyperinsulinemia, dyslipidaemia and hypertension (Lind & Lithell, 1993). Accordingly, the prevention and treatment of age-related reductions in basal femoral blood flow may be of clinical importance.

Habitual aerobic exercise is regarded as an important component of preventing and treating cardiovascular disease and functional disability (Pate *et al.*, 1995). However, habitual aerobic exercise does not appear to modulate the age-related reductions in basal limb blood flow (Dinenno *et al.*, 2001a,b). Several recent studies showed that resistance training, which

increases muscle mass and strength (MacDougall *et al.*, 1977; Staron *et al.*, 1984), is associated with increased basal femoral blood flow in middle-aged men and women (Miyachi *et al.*, 2005; Anton *et al.*, 2006). Resistance training is known to have some additional favourable health promoting effects aside from muscular hypertrophy and strength gain, such as improving insulin sensitivity (Dela & Kjaer, 2006). Increasing basal femoral blood flow by resistance training is considered one such favourable effect.

In general, traditional high-intensity ( $\sim 80\%$  1RM) resistance training has been regarded as optimal for gaining muscle size and strength (McDonagh & Davies, 1984). However, such strenuous exercise may be associated with a risk of orthopaedic injury. In addition, a marked increase in systolic blood pressure (over 300 mmHg) has been reported to occur during high-intensity resistance exercise ( $\sim 8$ RM) involving large muscle groups (MacDougall *et al.*, 1985; Fleck, 1988). These problems must be considered in high-intensity resistance exercise regimens especially for high-risk populations.

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Relatively low-intensity (~50–60% 1RM) resistance training with slow movement and tonic force generation (LST) is another method of resistance exercise. Previously, we reported that LST training resulted in a significant increase in muscular size and strength as high-intensity (~80–90% 1RM) resistance training with normal speed (HN) in knee extension training (Tanimoto & Ishii, 2006) and in a whole-body training regimen (Tanimoto et al., 2008), and LST was not associated with either generation of large force or marked elevation of blood pressure (Tanimoto & Ishii, 2006). Therefore, LST would be one of the useful methods of resistance training for promoting muscular hypertrophy and strength gain, which is relatively safe for a larger population.

With regard to the hypothesis of the effects of LST in promoting muscle hypertrophy, LST exercise movement was configured to achieve continuous force generation throughout the exercise movement. Continuous force generation at >40% maximum voluntary contraction has been shown to suppress both blood inflow to and outflow from the muscle due to an increase in intramuscular pressure (Bonde-Petersen et al., 1975). Resistance training regimens with restricted muscular blood flow were considered to induce increases in muscular size and strength mediated by the following processes due to oxygen insufficiency in muscle: (i) stimulated secretion of growth hormone by intramuscular accumulation of metabolic by-products, such as lactate (Takarada et al., 2000a); (ii) moderate production of reactive oxygen species promoting tissue growth (Takarada et al., 2000b); and (iii) additional recruitment of fast-twitch fibres under hypoxic conditions (Shinohara & Moritani, 1992).

The present study was performed to investigate whether resistance training even in LST also increases basal femoral blood flow as well as in HN, and whether resistance training in LST and HN increase basal femoral blood flow even in healthy young men.

The present study examined whether LST training can safely increase basal limb blood flow in healthy young people as a

preventive effect, before such investigations are carried out in patients with metabolic syndrome or others and in older people as a curative effect.

## Methods

### Subjects

Thirty-six healthy young men without a history of regular exercise training volunteered as subjects in the present study. All subjects were non-smokers, normotensive (blood pressure <140/90 mmHg), non-obese (body mass index <30 kg m<sup>-2</sup>) and free of overt chronic diseases as assessed by medical history, physical examination and complete blood chemistry and haematological evaluation. Candidates showing signs of peripheral artery disease [ankle-brachial index (ABI) <0.90] were excluded. The subjects were assigned at random into three experimental groups (*n* = 12 for each group: LST, HN, CON defined below). Groups were matched for physical parameters, such as height, weight and age (Table 1). All subjects were fully informed about the experimental procedures as well as the purpose of the study, and each subject provided written informed consent before participating in the study. The study protocol was approved by the Ethics Committee for Human Experiments, National Institute of Health and Nutrition.

### Regimens for exercise training

The subjects in each training group performed whole-body resistance training regimens consisting of five types of exercise: vertical squat, chest press, latissimus dorsi pull-down, abdominal bend and back extension, as described previously (Tanimoto et al., 2008). The subjects performed the following training regimens.

LST group: low-intensity (55~60% of 1RM) training with slow movement and tonic force generation [3 s for concentric

**Table 1** Characteristics of the subjects

	LST		HN		CON	
	Pretraining	Post-training	Pretraining	Post-training	Pretraining	Post-training
Age, year	19.0 ± 0.2		19.5 ± 0.1		19.8 ± 0.2	
Height, cm	174.1 ± 1.6		174.8 ± 1.2		174.3 ± 2.1	
Body mass, kg	62.5 ± 1.4	64.1 ± 1.5	63.8 ± 1.2	65.3 ± 1.2	64.2 ± 1.2	64.7 ± 1.1
ISTM, kg	53.9 ± 3.9	55.2 ± 3.7 <sup>a,b</sup>	53.7 ± 3.0	55.6 ± 3.4 <sup>a,c</sup>	54.6 ± 2.7	55.2 ± 2.6 <sup>c</sup>
%Fat, %	13.7 ± 3.6	13.7 ± 3.8	15.7 ± 3.2	14.8 ± 2.9 <sup>b</sup>	14.8 ± 3.6	14.6 ± 3.5
Left leg muscle mass, kg	8.82 ± 0.21	9.07 ± 0.19 <sup>a,b</sup>	8.80 ± 0.19	9.19 ± 0.21 <sup>a,c</sup>	8.89 ± 0.18	8.98 ± 0.18

Values are means ± SE; *n* = 12 for each group.

LST, low-intensity exercise with slow movement and tonic force generation; HN, high-intensity exercise with normal speed; CON, sedentary control; ISTM, lean soft tissue mass.

<sup>a</sup>Significant difference (*P* < 0.05) between pretraining and post training.

<sup>b</sup>Increase in LST was significantly higher (*P* < 0.05) than that in CON.

<sup>c</sup>Increase in HN was significantly higher (*P* < 0.05) than that in CON.

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(lifting phase) and eccentric (lowering phase) actions, and no relaxation phase; LST].

HN group: high-intensity (85–90% 1RM) training with normal speed (1 s for concentric and eccentric actions and 1 s for relaxation; HN). CON group: sedentary controls.

The training intensity was determined at 8RM in both LST and HN. 8RM means the load which person is only able to perform 8 correct form repetitions with. Subjects performed each type of training with 8RM intensity. Exercise intensities of LST and HN were adjusted to the same RM (8RM). Mechanical load in LST training was much lower than that in HN training (~55–60% 1RM in LST versus ~80–90% 1RM in HN). The difference in mechanical load under the same 8RM intensity between the two groups may have been due to differences in the type of movement. Subjects performed one warm-up set and three regular sets with an interest rest period of 60 s for each type of exercise. A 3-min rest was taken between exercise events. Training sessions were performed twice a week for 13 weeks.

All subjects were advised to maintain their usual physical activity and dietary habits to avoid any influence of physical activity outside the training session and nutritional influence.

### Measurements

Before they were tested, subjects abstained from caffeine and alcohol, and fasted for 12 h overnight. All testing, except muscular strength testing, was conducted under comfortable laboratory conditions early in the morning. Subjects were studied 4 or 5 days after their last exercise session to avoid any acute effects of exercise.

### Arterial blood flow

A duplex ultrasound machine (model 180 Plus; Sonosite, Bothell, WA, USA) equipped with a high-resolution (5–10 MHz) linear-array transducer was used to measure vessel diameter and blood velocity on the left common femoral artery and right common carotid artery, as described previously (Dinno et al., 1999, 2001a,b; Ozdemir et al., 2006). Mean blood velocity measurements were performed with an insonation angle <60°. The mean diameter [ $D = D(\text{systole}/3) + D(\text{diastole } 2/3)$ ] based on the relative time periods of the systolic (1/3) and diastolic (2/3) blood pressure phases was used to represent the cross-sectional area. Femoral blood flow was calculated as: mean blood velocity (MBV)  $\times \pi \times (\text{femoral arterial radius})^2 \times 60$ . The data reported were time averages of 10 measurements for all variables and were analysed by the same investigator, who was blinded to the identity of the subject. Vascular conductance and resistance were calculated as arterial blood flow/mean blood pressure and mean blood pressure/arterial blood flow, respectively. In our laboratory, the day-to-day reproducibility of the measurements for arterial diameter, mean blood velocity and absolute blood flow were  $3 \pm 1$ ,  $7 \pm 2$  and  $6 \pm 2\%$  (average  $\pm$  SD), respectively.

### Arterial blood pressure at rest

Arterial blood pressure at rest was measured with a semiautomated device (Form PWV/ABI; Colin Medical Technology, Komaki, Japan) over the brachial and dorsalis pedis arteries. Recordings were made in triplicate with subjects in the supine position. ABI was then calculated and used as a measure of atherosclerosis in leg arteries.

### Left ventricular function

Echocardiography was used to measure left ventricular (LV) function, according to established guidelines (Sahn et al., 1978; Cheitlin et al., 2003). Stroke volume (SV) was measured from LV end-diastolic and end-systolic volumes calculated from LV internal dimensions (Miyachi et al., 2004). Cardiac output was calculated as SV  $\times$  heart rate. Systemic vascular resistance was calculated by the following formula: brachial mean blood pressure/cardiac output. All image acquisition and image analyses were performed by the same investigator, who was blinded to the group assignment of subjects. At least 10 measurements of cardiac output were taken and the mean values were used for analysis.

### Muscle thickness by B-mode ultrasound imaging

The muscle thickness (MT) was measured by B-mode ultrasound (5 MHz scanning head) at six sites from the anterior and posterior surfaces of the body, in principle following the standard method described by Abe et al. (Abe et al., 1994). The sites were: chest, anterior and posterior upper arm, abdomen, subscapula and anterior and posterior thigh. Six anatomical landmarks for the sites were noted in our previous study (Tanimoto et al., 2008).

Muscle thickness was scanned using a real-time linear electronic scanner with a 5 MHz scanning head (SSD-500; Aloka, Tokyo, Japan). The scanning head was prepared with water-soluble transmission gel that provided acoustic contact without depression of the skin surface. The scanner was placed perpendicular to the tissue interface at the marked sites.

### Body composition determined by dual energy X-ray absorptiometry scan

Lean soft tissue mass (LSTM: body mass minus bone and fat mass) and fat mass were determined for the whole body using dual energy X-ray absorptiometry (DXA) (Hologic QDR-4500A scanner; Hologic, Waltham, MA, USA). Subjects were positioned for whole-body scans according to the manufacturer's protocol. Participants lay in the supine position on the DXA table with the limbs close to the body. To minimize interobserver variation, all scans and analyses were carried out by the same investigator. The whole body was divided into several regions, i.e. arms, legs, trunk and head. The body compositions were analysed using manual DXA analysis software (version 11.2.3; Waltham, MA, USA). The arm region was defined as the region extending from the head of the humerus to the distal tip of the fingers. The reference point

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between the head of the humerus and the scapula was positioned at the glenoid fossa. The leg region was defined as the region extending from the inferior border of the ischial tuberosity to the distal tip of the toes. The whole body was defined as the region extending from the shoulders to the distal tip of the toes. A reference point that could be visualized clearly on the DXA system terminal was selected.

### Muscular strength

Maximal muscular strength was tested with the five types of exercise used in the training regimen. Values were obtained for 1RM according to the established guidelines (Baechle et al. 2000).

### Metabolic risk factors for coronary heart disease

To screen for the presence of coronary heart disease, fasting plasma concentrations of total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides and glucose were determined with enzymatic techniques (Tanaka et al., 2000).

### Statistical analyses

All values are expressed as means  $\pm$  SE. One-way analysis of variance (ANOVA) with Fisher's protected least significant difference (PLSD) was used to determine the significance of any differences among the initial parameters of the three groups. Two-way ANOVA repeated measures (group  $\times$  period) with Newman-Keuls method was used to examine differences in changes in any parameters between groups. For all statistical tests,  $P < 0.05$  was considered significant.

## Results

Before the intervention period, there were no significant differences in any of the variables among the three groups.

### Changes in muscle mass and strength

The percent changes in total MT in ultrasound imaging, defined as the sum of the values for all six measurement sites, after the

experimental period were  $+6.8 \pm 3.4\%$  in LST,  $+9.1 \pm 4.2\%$  in HN and  $+1.3 \pm 2.2\%$  in CON. The absolute changes in LSTM (body mass minus fat and bone mass) in DXA were  $1.4 \pm 0.4$  kg in LST,  $1.8 \pm 0.4$  kg in HN and  $0.6 \pm 0.2$  kg in CON. The percent changes in left leg LSTM, defined as leg muscle mass, were  $3.0 \pm 1.0\%$  in LST,  $4.4 \pm 1.0\%$  in HN and  $1.1 \pm 0.8\%$  in CON. On measurement of muscular strength, the percent changes in total 1RM strength, defined as the sum of values for all five types of exercise used in the training regimen, were  $+33.0 \pm 8.8\%$  in LST,  $+41.2 \pm 7.8\%$  in HN and  $+1.3 \pm 2.4\%$  in CON. For all changes in muscle mass and strength shown above, increases in the LST and HN groups after the experimental period were significantly greater than those in CON, and there were no significant differences between the changes in LST and HN. Our previous study provided detailed data regarding changes in muscle mass and muscular strength (Tanimoto et al., 2008).

### Metabolic risk factors for coronary heart disease

There were no significant changes in fasting plasma concentrations of total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, fasting glucose or ABI (Table 2). All metabolic risk factors were well within clinically normal levels in all subjects. Brachial blood pressure, cardiac output and systemic vascular resistance (total peripheral resistance: TPR) did not change in any group (Table 3).

### Changes in arterial blood flow

Figure 1 shows basal femoral (top) and carotid (bottom) blood flow and basal femoral blood flow per unit volume of leg muscle mass (middle) in the three groups before and after the experimental period. Figure 2 shows femoral and carotid vascular conductance (upper) and both femoral and carotid vascular resistance (lower).

In the LST and HN groups, basal femoral blood flow increased significantly after the experimental period, while there was no such change in CON. The percent changes in basal femoral blood flow were  $+18.0 \pm 4.7\%$  in LST and  $+34.8 \pm 8.3\%$  in HN. There were no significant differences between these changes induced by LST and HN, although the increase in basal

Table 2 Metabolic risk factors.

	LST		HN		CON	
	Pretraining	Post-training	Pretraining	Post-training	Pretraining	Post-training
Total cholesterol, mg dl <sup>-1</sup>	185.9 $\pm$ 7.2	182.3 $\pm$ 9.8	164.4 $\pm$ 6.3	162.4 $\pm$ 5.4	162.6 $\pm$ 7.4	153.1 $\pm$ 7.4
HDL cholesterol, mg dl <sup>-1</sup>	63.2 $\pm$ 2.3	62.3 $\pm$ 3.7	61.4 $\pm$ 5.3	63.1 $\pm$ 4.1	56.3 $\pm$ 3.0	56.3 $\pm$ 3.7
LDL cholesterol, mg dl <sup>-1</sup>	106.8 $\pm$ 5.4	104.2 $\pm$ 5.8	90.2 $\pm$ 5.5	88.0 $\pm$ 5.1	93.5 $\pm$ 6.0	84.9 $\pm$ 5.1
Triglycerides, mg dl <sup>-1</sup>	79.6 $\pm$ 6.5	79.6 $\pm$ 9.9	64.0 $\pm$ 7.4	56.9 $\pm$ 6.3	63.9 $\pm$ 7.6	59.8 $\pm$ 5.1
Fasting glucose, mg dl <sup>-1</sup>	88.1 $\pm$ 1.7	87.4 $\pm$ 1.4	90.1 $\pm$ 1.5	89.0 $\pm$ 1.8	87.2 $\pm$ 1.3	84.8 $\pm$ 1.1

Values are means  $\pm$  SE; n = 12 for each group

LST, low-intensity exercise with slow movement and tonic force generation; HN, high-intensity exercise with normal speed; CON, sedentary control.

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Table 3 Hemodynamic characteristics.

	LST		HN		CON	
	Pretraining	Post-training	Pretraining	Post-training	Pretraining	Post-training
Brachial systolic BP, mmHg	111.3 ± 1.6	111.4 ± 2.8	108.3 ± 1.8	110.3 ± 1.3	108.4 ± 2.1	107.6 ± 2.6
Brachial mean BP, mmHg	80.3 ± 1.6	80.0 ± 2.2	77.8 ± 0.9	81.3 ± 1.4	77.8 ± 1.9	77.9 ± 2.0
Brachial diastolic BP, mmHg	60.7 ± 1.5	60.3 ± 2.4	59.4 ± 1.7	61.8 ± 1.9	59.3 ± 1.7	60.0 ± 1.5
Femoral artery lumen diameter, mm	8.5 ± 0.2	8.7 ± 0.2	8.4 ± 0.1	8.6 ± 0.2	8.3 ± 0.2	8.5 ± 0.2
Femoral artery IMT, mm	5.4 ± 0.8	5.6 ± 0.8	5.4 ± 0.7	5.4 ± 0.8	5.2 ± 0.7	5.3 ± 0.5
Femoral artery MBV, cm s <sup>-1</sup>	13.9 ± 0.8	15.2 ± 0.7 <sup>h</sup>	12.2 ± 0.8	15.7 ± 1.4 <sup>h</sup>	15.3 ± 1.5	14.7 ± 0.8
Carotid artery lumen diameter, mm	6.1 ± 0.1	6.1 ± 0.1	6.2 ± 0.1	6.1 ± 0.1	6.1 ± 0.1	6.2 ± 0.1
Carotid artery IMT, mm	4.8 ± 0.5	4.9 ± 0.3	4.7 ± 0.4	4.9 ± 0.5	4.7 ± 0.4	4.7 ± 0.5
Carotid artery MBV, cm s <sup>-1</sup>	31.0 ± 1.3	32.5 ± 1.0	29.3 ± 1.1	32.1 ± 1.1	31.0 ± 1.2	31.3 ± 1.3
Cardiac output, l min <sup>-1</sup>	3.7 ± 0.6	3.8 ± 0.6	3.9 ± 0.7	4.1 ± 0.9	4.2 ± 0.8	3.9 ± 0.7
systemic vascular resistance, U	22.4 ± 3.4	21.4 ± 4.4	20.8 ± 1.1	21.0 ± 1.7	19.4 ± 1.4	20.4 ± 0.8

Values are means ± SE; n = 12 for each group.

LST, low-intensity exercise with slow movement and tonic force generation; HN, high-intensity exercise with normal speed; CON, sedentary control; MBV, mean blood velocity; IMT, intima-media thickness.

<sup>a</sup>Significant difference (P < 0.05) between pretraining and post-training.

<sup>b</sup>Increase in LST was significantly higher (P < 0.05) than that in CON.

<sup>h</sup>Increase in HN was significantly higher (P < 0.05) than that in CON.

femoral blood flow in LST corresponded to about half that in HN.

Basal femoral blood flow per unit volume of leg muscle mass changed after the experimental period in a manner similar to the basal femoral blood flow changes described above. The percent changes in basal femoral blood flow per unit volume of leg muscle mass were +15.0 ± 4.8% in LST and +29.1 ± 8.2% in HN. Percent changes in leg muscle mass after the experimental period were not related to those in basal leg blood flow in either training group (LST and HN; Fig. 3). Furthermore, percent changes in cardiac output after the experimental period were not related to those in basal leg blood flow in either training group (LST and HN; Fig. 4).

These changes were associated with a significant increase in femoral vascular conductance and a significant reduction in femoral vascular resistance in the LST and HN groups, respectively. The increases in femoral blood flow in the LST and HN group were primarily dependent on an increase in mean blood velocity, not on artery lumen diameter (see Table 3). There were no significant changes in any carotid parameter (blood flow, vascular conductance or vascular resistance) after the experimental period in any of the three groups.

## Discussion

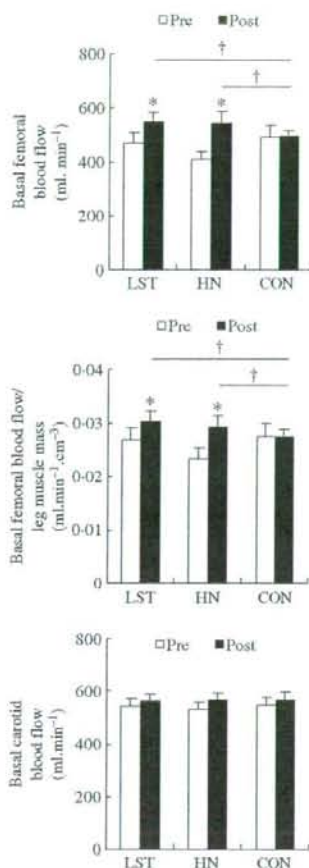
The present randomized-control intervention study is the first to document the effect of low-intensity (~50–60% 1RM) resistance training with slow movement and tonic force generation (LST) on basal femoral blood flow and vascular conductance. The salient findings of the present study were that basal femoral blood flow and vascular conductance significantly increased even after 13 weeks of LST training, as well as after 13 weeks of traditional high-intensity (~85–90% 1RM) resistance training with normal speed (HN) in young men.

In addition, LST resulted in increases in muscular size and strength comparable to those associated with HN (Tanimoto et al., 2008). LST met the requirement of the primary purpose of resistance training, which is to be effective for gaining muscular size and strength. Meeting this requirement is essential for any study investigating the additional effects of resistance training methods.

These findings extend our understanding of the relation between resistance training and basal limb blood flow in at least two additional ways. First, by establishing that traditional high-intensity resistance training is effective for increasing basal femoral blood flow (Miyachi et al., 2005; Anton et al., 2006), the findings presented here indicate that resistance training even in LST, which used a relatively low mechanical load, is effective for increasing basal femoral blood flow. However, we should emphasize that although not significantly different, the change in basal femoral blood flow in LST corresponded to about half that in HN. Second, by establishing that resistance training increases basal femoral blood flow in middle-aged men and women whose basal femoral blood flow decreases with the advancing age (Dinenna et al., 2001a,b; Moreau et al., 2003), the findings of the present study indicated that in both the LST and HN groups, resistance training increases basal femoral blood flow even in young men. With regard to the intergenerational differences in basal femoral blood flow changes, changes in basal femoral blood flow in young men caused by resistance training in the present study (15% in LST and 29% in HN) were lower than those in middle-aged men and women in the previous study (over 50%). This age-related difference would be due to differences in the baselines of basal femoral blood flow before the training intervention period. These findings suggest that LST training may be one of the effective strategies for increasing basal limb perfusion, and that regular resistance training from a

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**Figure 1** Basal femoral and carotid blood flow before and after the intervention period. Means  $\pm$  SE ( $n = 12$  for each group) in basal femoral blood flow (top), femoral blood flow/leg muscle mass (middle) and basal carotid blood flow (bottom). \*Significant difference ( $P < 0.05$ ) between pretraining and post-training values. #Significant differences ( $P < 0.05$ ) between groups. Absolute basal femoral blood flow and that per unit volume of leg muscle mass in both training groups (LST and HN) increased significantly after experimental period.

young age may contribute to preservation of basal limb blood flow.

#### Potential mechanisms

What are the physiological mechanisms that would explain the increases in basal limb blood flow following resistance training? A previous study indicated that leg oxygen demand and leg muscle mass are associated with basal femoral blood flow (Dinenno et al., 2001a,b). Therefore, it was initially hypothesized that resistance training, which promotes muscular hypertrophy, increases basal femoral blood flow because muscle mass is strongly related to

energy consumption (Evans & Cyr-Campbell, 1997). However, in the present study, increases in leg muscular size (3.0% in LST, 4.4% in HN) were much lower than the increases in basal femoral blood flow (18% in LST, 35% in HN), and percent changes in leg muscle mass after the experimental period were not related to those in whole-leg basal blood flow in the two training groups (LST and HN,  $r = -0.05$ ; Fig. 3). Moreover, increases in the relative blood flow to leg muscle mass in the two training groups were quantitatively the same as increases in whole-leg blood flow (Fig. 1). These findings suggest that qualitative changes in leg muscles by resistance training (LST and HN) have a more immediate and/or potent influence than quantitative changes (gain in muscle mass).

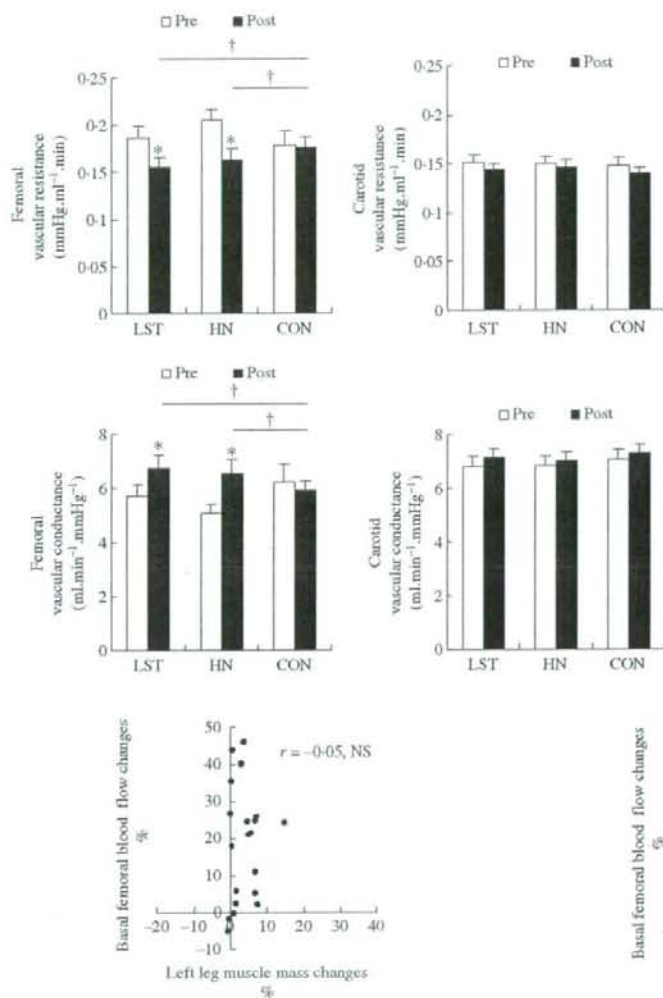
The muscle metabolic rate and capillary density may be qualitative factors contributing to increased basal femoral blood flow. Resistance training is known to be a strong stimulus that increases skeletal muscle turnover (syntheses and degradation) (Hasten et al., 2000) and basal metabolic demands (Ades et al., 2005), which may have acted to increase blood flow independent of muscle mass. Muscular metabolic rate was not measured, while basal metabolic rate (BMR) was measured. BMR increased after the experimental period in HN ( $P < 0.01$ ) and in LST ( $P < 0.1$ ) (data not shown).

An additional possible cause of the changes in leg blood flow is that peripheral blood flow may be a simple reflection of changes in systemic blood flow (cardiac output) (Leithe et al., 1984). However, there were no obvious changes in cardiac output or TPR after the intervention period, and there was no significant relation between percent changes in cardiac output and those in basal whole-leg blood flow in either training group (LST and HN,  $r = 0.19$ ; Fig. 4). Furthermore, basal carotid blood flow did not increase after LST and HN training. These findings suggest that the increase in basal femoral blood flow after both types of resistance training was affected not by systemic cardiovascular changes but by peripheral vascular and metabolic adaptations.

#### Physiological and practical implications

The present findings have potentially important physiological and practical implications. Traditional high-intensity resistance training increases muscle mass and strength. It is widely accepted that such training also facilitates performance of daily tasks, and promotes spontaneous physical activity especially in the elderly and in subjects with low physical capacity (Borst, 2004; Hunter et al., 2004). Several recent studies showed the beneficial influence of high-intensity resistance training on vascular function, contributing to increases in basal whole leg blood flow (Miyachi et al., 2005; Anton et al., 2006). The present study in healthy young men suggested that the resistance training program in the LST group promoted muscular hypertrophy without high mechanical load and increased basal femoral blood flow as efficiently as the regimen performed by the HN group. The LST regimen was not associated with either the generation of large force or marked elevation of blood





**Figure 3** Relations between leg muscle mass changes and basal femoral blood flow changes in the two trained groups ( $n = 24$ ). Left leg LSTM (lean soft tissue mass) is defined as left leg muscle mass. Change in leg muscle mass was not related to that in femoral leg blood flow ( $r = -0.05$ ).

pressure (Tanimoto & Ishii, 2006), and so it would be a safe and useful method of exercise for increasing peripheral blood flow. The reduction in leg blood flow may limit peripheral glucose uptake and contribute to glucose intolerance and hyperinsulinemia (Lind & Lithell, 1993). In addition, it may also impair the clearance of atherogenic lipids and contribute to chronic dyslipidaemia (Baron et al., 1990). Regular resistance training in the LST group may contribute to a lower incidence of cardiovascular disease through its influence on basal femoral blood flow.

**Figure 2** Femoral and carotid vascular resistance and conductance before and after the intervention period. Means  $\pm$  SE ( $n = 12$  for each group) in femoral and carotid vascular conductance (upper), femoral and carotid vascular resistance (lower) in the three experimental groups. \*Significant difference ( $P < 0.05$ ) between pretraining and post-training values. †Significant differences ( $P < 0.05$ ) between groups. Femoral carotid resistance in both training groups (LST and HN) decreased, and femoral carotid conductance in both training groups (LST and HN) increased significantly after experimental period.

**Figure 4** Relations between cardiac output changes and basal femoral blood flow changes in trained group subjects ( $n = 24$ ). Change in cardiac output was not related to that in basal femoral blood flow ( $r = 0.19$ ).

## Conclusion

The results of the present study indicated that resistance training, even in LST, increased basal femoral blood flow and vascular conductance as in HN, and that regular resistance training from a young age may contribute to preservation of basal limb blood flow. LST promotes muscular hypertrophy and strength gain comparable to those in HN without high mechanical load. LST is proposed as a safe and useful exercise method not only for muscular hypertrophy and strength gain, but also for increasing peripheral blood flow and vascular conductance as an additional

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effect. This study investigated preventive effects for healthy people, not curative effects for patients with metabolic syndrome or other diseases. Expanding this study to cover investigation in patient groups is an issue for future consideration.

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