Resistance training in men is associated with increased arterial stiffness and blood pressure but does not adversely affect endothelial function as measured by arterial reactivity to the cold pressor test

Hiroshi Kawano1,2, Michiya Tanimoto1, Kenta Yamamoto2, Kiyoshi Sanada2, Yuko Gando1,2, Izumi Tabata1, Mitsuru Higuchi2 and Motohiko Miyachi1

1National Institute of Health and Nutrition Program for Health Promotion, 1-23-1 Toyama, Shinjuku 162-8636, Japan
2Wasada University, 2-579-15 Mikajima, Tokorazawa, Saitama, Japan

Resistance training is a popular mode of exercise, but may result in stiffening of the central arteries. Changes in carotid artery diameter were determined using the cold pressor test (CPT), which results in production of nitric oxide via sympathetic activation and is one of the novel methods available for assessing endothelial function in the carotid artery. To investigate the effect of resistance training on endothelial function, we designed a cross-sectional study of carotid arterial vasoreactivity to CPT in men participating in regular resistance training with increased carotid arterial stiffness compared with age-matched control subjects. Twelve resistance-trained middle-aged men (age 38.7 ± 1.7 years) and 17 age-matched control subjects (age 36.8 ± 1.2 years) were studied. The direction and magnitude of changes in carotid artery diameter were measured by B-mode ultrasonography during sympathetic stress induced by submersion of the foot in ice slush for 90 s. Carotid arterial $\beta$-stiffness index, and systolic and mean arterial blood pressure were higher (7.7 ± 0.7 versus 6.0 ± 0.4 arbitrary units, 116 ± 2 versus 131 ± 4 mmHg and 86 ± 2 versus 95 ± 2 mmHg, respectively, all $P < 0.05$) in the resistance training group compared with control subjects. There were, however, no significant differences in the amount or percentage change in carotid artery diameter in CPT between the two groups (resistance training group, 0.33 ± 0.07 mm and 5.2 ± 1.1%; control group, 0.37 ± 0.06 mm and 5.8 ± 0.9%, respectively). These findings suggest that while carotid arterial stiffening and higher blood pressure are observed in regular resistance-trained men, these are not associated with abnormalities in carotid arterial vasoreactivity to sympathetic stimulus, which implies intact endothelial function.

(Received 9 August 2007; accepted after revision 27 September 2007; first published online 2 October 2007)

Corresponding author M. Miyachi: National Institute of Health and Nutrition Program for Health Promotion, 1–23-1 Toyama, Shinjuku 162–8636, Japan. Email: miyachi@nih.go.jp

Resistance training is a popular form of exercise, and has become an integral component of exercise recommendations endorsed by a number of national health organizations (American College of Sports Medicine Position Stand, 1998; Pollock et al. 2000). Resistance training has favourable effects on the musculoskeletal system, thereby contributing to maintenance of functional capacity and prevention of sarcopenia and osteoporosis. In contrast, resistance training may be associated with reduction of compliance and increases in arterial stiffness in the central elastic artery (carotid artery; Bertovic et al. 1999; Miyachi et al. 2003, 2004; Cortez-Cooper et al. 2005; Kawano et al. 2006).

Increased arterial stiffness and reduced arterial compliance may be associated with endothelial dysfunction (Lind et al. 1999; Cheung et al. 2002; Nakamura et al. 2004). Indeed, impaired endothelial function and arterial stiffening are induced with advancing age and in the presence of cardiovascular diseases (Zeihner et al. 1989; O’Rourke, 1990; Taddei et al. 1995; Tanaka et al. 2000; Najjar et al. 2005). Therefore,
impaired endothelial function is thought to be one of the physiological mechanisms underlying the reduction in carotid arterial compliance with resistance training. In this context, we hypothesized that resistance training would cause impairment of endothelial function in the carotid artery.

Local endothelial function in humans can be estimated by flow-mediated dilatation (Corretti et al. 2002) and/or vasoreactivity in response to medication with acetylcholine, etc. (Ludmer et al. 1986). Since it is difficult to determine endothelial function of the carotid artery in healthy humans using these methods, the cold pressor test (CPT), which results in production of nitric oxide (NO) via sympathetic activation (Nase & Boegehold, 1996; Tousoulis et al. 1997) is one of the novel methods (Rubenfire et al. 2000; Lavi et al. 2006) available for assessing endothelial function in the carotid artery.

To evaluate our hypothesis, we designed a cross-sectional study in which carotid arterial vasoreactivity to receptor-mediated sympathetic cold stimulus in regular resistance-trained men with reduced carotid arterial compliance was compared with age-matched sedentary control subjects.

### Methods

#### Subjects

A total of 29 healthy men, 28–49 years of age, participated in the present study (Table 1). The sedentary subjects were recruited through various forms of advertisement and had not participated in a regular exercise programme for at least the previous 2 years. The resistance-trained men were recruited from various fitness clubs and had been performing vigorous resistance training for >10 years. All resistance-trained men had been performing moderate-to high-intensity ‘full-body’ resistance exercise involving large muscle groups. To better isolate the effects of resistance exercise training, those who had been concurrently performing regular aerobic exercise (i.e. ‘cross-training’) were excluded from the study. All subjects were normotensive (<140/90 mmHg), non-obese and free of overt chronic diseases as assessed by medical history, physical examination and complete blood chemistry and haematological evaluation. Candidates who smoked in the past 4 years, were taking medications, had ever used anabolic steroids or other performance-enhancing drugs, or who had significant femoral intima–media thickening (<1.1 mm), plaque formation and/or other characteristics of atherosclerosis [ankle–brachial index (ABI) < 0.9] were excluded. All subjects gave their written, informed consent to participation in this study. All procedures were reviewed and approved by the Human Research Committee of the National Institute of Health and Nutrition.

#### Measurements

Before testing, subjects abstained from caffeine and fasted for at least 4 h (a 12 h overnight fast was used for determination of metabolic risk factors). All measurements were performed under comfortable laboratory conditions in the morning. Tests of resistance-trained men were conducted 20–24 h after their last exercise training session to avoid the immediate (acute) effects of exercise, but they were still considered to be in their normal (i.e. habitually exercising) physiological state.

#### Body composition

Body composition was determined using dual-energy X-ray absorptiometry (DEXA; model DPX-IQ, Lunar

### Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Subject characteristics</th>
<th>Control</th>
<th>Resistance trained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Age (years)</td>
<td>36.8 ± 1.2</td>
<td>38.7 ± 1.7</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>171.0 ± 1.2</td>
<td>171.0 ± 1.8</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>71.9 ± 1.9</td>
<td>74.9 ± 2.1</td>
</tr>
<tr>
<td>Percentage body fat (%)</td>
<td>19.4 ± 1.2</td>
<td>12.3 ± 0.9*</td>
</tr>
<tr>
<td>Total cholesterol (mmol l⁻¹)</td>
<td>5.0 ± 0.2</td>
<td>4.7 ± 0.2</td>
</tr>
<tr>
<td>HDL cholesterol (mmol l⁻¹)</td>
<td>1.3 ± 0.1</td>
<td>1.6 ± 0.1*</td>
</tr>
<tr>
<td>Plasma glucose (mmol l⁻¹)</td>
<td>5.0 ± 0.1</td>
<td>5.1 ± 0.1</td>
</tr>
<tr>
<td>Triglycerides (mmol l⁻¹)</td>
<td>1.5 ± 0.3</td>
<td>0.9 ± 0.1</td>
</tr>
<tr>
<td>Resting heart rate (beats min⁻¹)</td>
<td>58 ± 2</td>
<td>56 ± 2</td>
</tr>
<tr>
<td>Maximal heart rate (beats min⁻¹)</td>
<td>186 ± 3</td>
<td>183 ± 4</td>
</tr>
<tr>
<td>( \dot{V}<em>O_2</em>{max} ) (l min⁻¹)</td>
<td>2.7 ± 0.1</td>
<td>2.8 ± 0.1</td>
</tr>
<tr>
<td>( \dot{V}<em>O_2</em>{max}/body weight ) (ml kg⁻¹ min⁻¹)</td>
<td>37.7 ± 1.4</td>
<td>36.9 ± 1.3</td>
</tr>
<tr>
<td>Leg extension power (W)</td>
<td>1719 ± 91</td>
<td>2293 ± 155*</td>
</tr>
<tr>
<td>Handgrip (kg)</td>
<td>45.6 ± 1.6</td>
<td>51.0 ± 2.0*</td>
</tr>
</tbody>
</table>

Data are means ± s.e.m.; \( \dot{V}_O_2_{max} \), maximal oxygen consumption. *P < 0.05 versus control subjects.
Radiation) with subjects in the supine position. Measurement of fat mass using DEXA has been well validated against other standards (Haarbo et al. 1991).

**Carotid arterial intima–media thickness (IMT)**

Carotid artery IMT was measured from the images obtained using a SonoSite 180 PLUS ultrasound system (SonoSite, Bothell, WA, USA) equipped with a high-resolution linear-array broad-band transducer as previously described (Miyachi et al. 2004). Ultrasound images were analysed using image analysis software (NIH Image 1.63, Bethesda, MD, USA). At least 10 measurements of IMT were taken at each segment, and the mean values were used for analysis. This technique has excellent day-to-day reproducibility (coefficient of variation, 3 ± 1%) for the carotid IMT.

**Carotid arterial compliance**

A combination of ultrasound imaging of the pulsatile common carotid artery with simultaneous applanation of tonometrically obtained arterial pressure from the contralateral carotid artery permits non-invasive determination of arterial compliance (Tanaka et al. 2000). The carotid artery diameter was measured from images obtained using an ultrasound system (Sonosite, Bothell, WA, USA) equipped with a high-resolution linear-array transducer. A longitudinal image of the cephalic portion of the common carotid artery was acquired 1–2 cm proximal to the carotid bulb. All image analyses were performed by the same investigator who was blinded to the group assignments.

Pressure waveforms and amplitudes were obtained from the common carotid artery with a pencil-type probe incorporating a high-fidelity strain-gauge transducer (SPT-301; Millar Instruments, Houston, TX, USA; Kelly et al. 1989; Tanaka et al. 2000). Since baseline levels of blood pressure are subjected to hold-down force, the pressure signal obtained by tonometry was calibrated by equating the carotid mean arterial and diastolic BP to the brachial artery value (Tanaka et al. 2000; Miyachi et al. 2004). In addition to arterial compliance (Van Merode et al. 1988), we also calculated the β-stiffness index, which provides an index of arterial compliance adjusted for distending pressure (Hirai et al. 1989). The arterial compliance and the β-stiffness index were calculated using the following equations:

\[
\text{arterial compliance} = \frac{[(D_1 - D_0)/D_0]}{2(P_1 - P_0)} \times \pi \times D_0^2
\]

and

\[
\beta - \text{Stiffness index} = \frac{\ln(P_1/P_0)}{[(D_1 - D_0)/D_0]}
\]

where \(D_1\) and \(D_0\) are the maximal and minimal diameters, and \(P_1\) and \(P_0\) are the highest and lowest blood pressures, respectively. The day-to-day coefficients of variation were 2 ± 1, 7 ± 3 and 5 ± 2% for the carotid artery diameter, pulse pressure and arterial compliance, respectively.

**Cold pressor test**

The CPT was performed by submersion of the right foot up to the ankle in ice slush for 90 s, a modification of the method published previously (Corretti et al. 1995b; Rubenfire et al. 2000). The foot was chosen to maximize the haemodynamic and sympathetic responses (Seals, 1990). Subjects were instructed to avoid breath-holding, muscle contractions and Valsalva’s manoeuvre. Measurements of carotid arterial geometry were obtained before (baseline) and for 10 s during CPT. The day-to-day coefficient of variation for the change in carotid arterial diameter response to CPT was 4 ± 1%.

**Maximal oxygen uptake**

We measured maximal oxygen consumption (\(\dot{V}_{O_2,\text{max}}\)) during incremental cycle ergometer exercise (Miyachi et al. 2001). Oxygen consumption (coefficient of variation, 4 ± 1%), heart rate and ratings of perceived exertion were measured throughout the protocol (Miyachi et al. 2001).

**Metabolic risk factors for coronary heart disease**

To screen for the presence of coronary heart disease, concentrations of fasting serum lipids and plasma glucose were determined with enzymatic techniques (Tanaka et al. 2000).

**Arterial blood pressure at rest**

Chronic levels of arterial blood pressure at rest were measured with a semi-automated device (Form PWV/ABI; Colin Medical, Komaki, Japan) over the brachial and dorsalis pedis arteries. Recordings were made in triplicate with subjects in the supine position (Miyachi et al. 2005).

**Muscle strength**

Leg extension power was determined using a dynamometer (Anaero Press 3500; Combi Wellness, Tokyo, Japan) in the sitting position. The subjects were fastened with a seat belt to a chair. In the starting position, the feet were placed on a sliding plate with the knee angle adjusted to 90 deg. Subjects were advised to vigorously extend their legs. Five trials were performed at 15 s intervals and the average of the two highest recorded power outputs (in W) was taken as the definitive measurement (Yoshiga et al. 2002).
Table 2. Cardiovascular measures

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Resistance trained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachial systolic BP (mmHg)</td>
<td>116 ± 2</td>
<td>131 ± 4*</td>
</tr>
<tr>
<td>Brachial mean BP (mmHg)</td>
<td>86 ± 2</td>
<td>95 ± 3*</td>
</tr>
<tr>
<td>Brachial diastolic BP (mmHg)</td>
<td>71 ± 2</td>
<td>74 ± 3</td>
</tr>
<tr>
<td>Brachial PP (mmHg)</td>
<td>45 ± 1</td>
<td>57 ± 2*</td>
</tr>
<tr>
<td>Carotid systolic BP (mmHg)</td>
<td>104 ± 2</td>
<td>123 ± 5*</td>
</tr>
<tr>
<td>Carotid PP (mmHg)</td>
<td>33 ± 2</td>
<td>48 ± 4*</td>
</tr>
<tr>
<td>Carotid artery diameter (mm)</td>
<td>6.4 ± 0.1</td>
<td>6.2 ± 0.1</td>
</tr>
<tr>
<td>Carotid artery IMT (mm)</td>
<td>0.64 ± 0.02</td>
<td>0.65 ± 0.03</td>
</tr>
</tbody>
</table>

Data are means ± S.E.M.; BP, blood pressure; PP, pulse pressure; IMT, intima–media thickness. *P < 0.05 versus control subjects.

Handgrip strength of the right arm was measured with a hand-held dynamometer, with the subject standing and the arms extended by their sides. The subjects then gripped the dynamometer as strongly as possible for 3 s without pressing the instrument against their body or bending at the elbow, and values (in kg) were recorded as the averages of two trials.

Statistics

Statistical analyses were performed using statistical software (StatView, SAS, Cary, NC, USA). All data are presented as means ± S.E.M. Mean differences between resistance-trained and control men were examined using Student’s unpaired t test. Analysis of covariance (ANCOVA) was used to test for differences in carotid arterial compliance and β-stiffness index between resistance-trained men and control subjects, with mean arterial blood pressure as a covariate.

Statistical significance was set a priori at P < 0.05 for all comparisons.

Results

Subject characteristics are presented in Table 1. Body fat was lower in the resistance-trained men compared with the control subjects. Although all metabolic risk factors were well within clinically normal levels in both groups, high-density lipoprotein (HDL) cholesterol levels were higher in resistance-trained men compared with control subjects. Muscle strength, assessed by leg extension power and handgrip strength, was higher in resistance-trained men than in the control subjects. There were no significant differences in other parameters between the two groups.

Table 2 shows cardiovascular measures. With the exception of diastolic blood pressure in the brachial artery, blood pressure parameters of brachial and carotid arteries were higher in resistance-trained men compared with control subjects. Ankle–brachial index was lower in resistance-trained men than control subjects. There were no significant differences in the diameter or IMT in the carotid artery between the two groups.

Figure 1. Carotid arterial β-stiffness index (A), carotid arterial (CA) compliance (B), and amount (C) and percentage change (D) in carotid artery diameter in response to CPT in resistance-trained men and control subjects

Values are means ± S.E.M. *P < 0.05 versus control subjects.
Carotid arterial $\beta$-stiffness (Fig. 1A) was higher and compliance (Fig. 1B) was lower in resistance-trained men compared with control subjects. There were no significant differences in the amount (Fig. 1C) or percentage change (Fig. 1D) of carotid arterial diameter in response to CPT between resistance-trained men and control subjects. The differences in carotid arterial compliance and $\beta$-stiffness index between resistance-trained men and control subjects disappeared after normalizing carotid arterial compliance and $\beta$-stiffness index relative to mean arterial blood pressure (ANCOVA; $P = 0.081$ and $P = 0.101$, respectively).

**Discussion**

The results of the present study indicated that, although the carotid arterial compliance was lower in resistance-trained men compared with age-matched control subjects, there were no significant differences in the amount or percentage change of carotid arterial diameter in CPT between resistance training and control groups. In contrast to our original hypothesis, these findings suggest that while regular resistance training can increase carotid arterial stiffness, this is not associated with abnormalities of carotid arterial vasoreactivity to sympathetic physiological stress induced by cold.

The endothelial function of conduit arteries is one of the vascular functions, and has been identified as a primary target of injury from mechanical forces and processes that increase cardiovascular risk, such as hypertension (Moyna & Thompson, 2004). Owing to the clinical and functional importance of health of the endothelium, we examined the impact of resistance training on endothelial function. As a primary approach to resolve this issue, we performed a cross-sectional study. To isolate the effects of resistance training as much as possible, resistance-trained men and control subjects were carefully matched for age, height, body weight, aerobic capacity and metabolic risk factors. Although subjects were recruited carefully, as described in the Methods, blood pressure in resistance-trained men was higher than that in the control subjects. As a result, we found a 30% reduction in central arterial compliance in resistance-trained men compared with control subjects. These results are consistent with those of a previous cross-sectional study (Bertovic et al. 1999). Differences in carotid arterial compliance and $\beta$-stiffness index between resistance-trained men and control subjects were affected after normalizing carotid arterial compliance and $\beta$-stiffness index relative to mean arterial blood pressure. Given this association between blood pressure and arterial compliance, higher blood pressure may lead to lower arterial compliance in resistance-trained men than in control subjects due to equation using arterial distensibility and blood pressure. However, we feel that the higher blood pressure in resistance-trained men may be induced by greater arterial stiffening associated with the resistance training. Nevertheless, despite the higher arterial stiffness and blood pressure in resistance-trained men than in control subjects, there was no difference in carotid arterial vasoreactivity to CPT between the two groups.

The response of conduit arteries to systemic cold may be the result of the balance between adrenergic vasoconstriction and vasodilatation, with the latter being mediated by endothelial function (Nabel et al. 1988; Zeiher et al. 1989; Vita et al. 1992; Corretti et al. 1995a). The normal coronary vasodilator response to CPT can be blocked by competitive inhibition of $l$-arginine, a substrate for NO synthase (Tousoulis et al. 1997), and $l$-arginine can normalize the vasoconstrictor response to CPT in coronary artery disease (Gellman et al. 1996). In addition, both endogenous NO and exogenously administered NO donors suppress sympathetic outflow at the prejunctional level, and NO may exert a tonic influence on the discharge of sympathetic efferents (Zanzinger et al. 1994; Nase & Boegehold, 1996). Therefore, the endothelial function, via NO, may play an important role in changing the conduit artery diameter response to sympathetic stimulation by the CPT. We first examined the impact of resistance training with arterial stiffening on endothelial function of the carotid artery using CPT, and found that there were no significant differences in the amount or percentage change in carotid arterial diameter in response to CPT between resistance-trained men and control subjects. Our results were consistent with those of a previous study, which demonstrated that resistance training did not affect endothelial function in the peripheral muscular artery evaluated by flow-mediated dilation (FMD) (Rakobowchuk et al. 2005). These findings are consistent with the posit that regular resistance training may protect against the adverse effects of resistance load associated hypertension by preserving arterial endothelial function (Jurva et al. 2006).

The results of the present study indicated that carotid arterial compliance in resistance-trained men was lower than that in control subjects, and blood pressure was significantly higher in resistance-trained men compared with control men. In contrast, HDL cholesterol level was significantly higher in resistance-trained men than in control subjects, and there were no differences in other lipid profiles or IMT between the two groups. Considering the relationships between reduction in arterial compliance and impaired endothelial function, hypertrophied IMT or abnormal lipid profile with advancing age and/or the presence of cardiovascular disease (Zeiher et al. 1989; O’Rourke, 1990; Taddei et al. 1995; Tanaka et al. 2000; Najjar et al. 2005), the decrease in carotid arterial compliance induced by resistance training may be different from vascular alterations seen in ageing or in the presence of...
cardiovascular disease. Arterial compliance is affected by endothelial function as well as by sympathetic vascular tone, arterial calcification, elastin-to-collagen ratio and IMT, and correlates with clinical parameters, such as aerobic capacity, age, blood pressure, body fat, waist circumference and lipids (Nichols & O’Rourke, 1998; Tanaka et al. 2000). The degree to which these other factors affect the relationship between training-associated decrease in arterial compliance independent of endothelial function will require further studies in a larger cohort.

Rubenfire et al. (2000) reported that the direction and magnitude of the change in carotid artery diameter in response to CPT are altered based on the presence of risk factors and coronary disease independent of IMT. The carotid artery vasoreactivity to CPT may have a valuable role in coronary risk assessment and in predicting response to therapy. The present study revealed that there were no significant differences in carotid arterial vasoreactivity to CPT and IMT between resistance-trained men and control subjects, suggesting that regular resistance training may not affect at least two of the cardiovascular disease risk factors. In addition, HDL cholesterol, leg extension power and handgrip strength were higher in resistance-trained men than in control subjects. Given these functional and physiological benefits of resistance training, we should emphasize that the practice of resistance training should not be discouraged.

Limitations

Endothelial function assessed by FMD should optimally be adjusted by shear stress, shear rate or blood flow velocity (Pyke & Tschakovsky, 2005; Rakowchuk et al. 2005). However, it is technically difficult to determine the blood velocity or shear stress during the relatively short period (90 s) of CPT used in our study. Further, in contrast to the occlusion release technique for assessing brachial endothelial function, the carotid artery vasoreactivity to CPT is a complex interaction between clinical, adrenergic nerve and hormonal responses and endothelial function.

Conclusion

The results of the present study showed that regular resistance training is associated with reduction of central arterial compliance as measured using a combination of ultrasound images and applanation tonometry. However, there were no differences in carotid arterial vasoreactivity to CPT between resistance-trained men and sedentary control subjects. These findings suggest that while carotid arterial stiffening and higher blood pressure are observed in regular resistance-trained men, they are not associated with impaired vasoactivity to sympathetic stimulus, which implies intact endothelial function. Nevertheless, the results of the present cross-sectional study must be confirmed in future prospective exercise intervention studies.

References


Acknowledgements

This work was supported by Grant-in-Aid for Scientific Research 13780041 (to M. Miyachi) from Japan Society for the Promotion of Science and by the Sasagawa Scientific Research Grant (to H. Kawano) from the Japan Science Society.