In this study, we evaluated the link between a reduction of waist circumference and metabolic syndrome in obese Japanese subjects with a 1-year follow-up.

2. Subjects and methods

2.1. *Subjects*

We used data of 105 obese Japanese men (body mass index (BMI) ≧25 kg/m^2), aged 45.4 ± 8.4 years, retrospectively from a database of 14,345 subjects who met the following criteria: (1) received an annual health check-up at baseline from June 1997 to March 2006, (2) received an annual health check-up every year with a follow-up duration of 1 year, (3) received anthropometric measurements, fasting blood examination and blood pressure measurements as part of the annual health check-up, (4) received no medications for diabetes, hypertension, and/or dyslipidemia, and (5) provided written informed consent (Table 1).

At the first annual health check-up, all subjects were given instructions by well-trained medical staff on how to change their lifestyle.

Ethical approval for the study was obtained from the Ethical Committee of Okayama Health Foundation.

2.2. *Anthropometric and body composition measurements*

The anthropometric and body compositions were evaluated based on the following parameters: height, body weight, waist circumference, hip circumference and body fat percentage. Body mass index (BMI) was calculated by weight/[height]^2 (kg/m^2) and obesity was defined by body mass index (BMI) ≧25 kg/m^2 [6]. The waist circumference was measured at the umbilical level, and the hip was measured at the widest circumferences over the trochanter in standing subjects after normal expiration. Body fat percentage was measured by an air displacement plethysmograph called the BOD POD Body Composition System (Life Measurement Instruments, Concord, CA, USA) [7,8].

2.3. *Blood pressure measurements at rest*

Resting systolic blood pressure and diastolic blood pressure were measured indirectly using a mercury sphyngmomanometer placed on the right arm of the seated participant after at least 15 min of rest.

2.4. *Blood sampling and assays*

Overnight fasting serum levels of high-density lipoprotein (HDL) cholesterol, triglycerides (L Type Wako Triglyceride-H, Wako Chemical, Osaka) and plasma glucose were measured.

2.5. *Definition of metabolic syndrome*

Men with a waist circumference in excess of 85 cm were defined as having metabolic syndrome if they also had two or more of the following components: (1) dyslipidemia: triglycerides ≧150 mg/dl and/or HDL cholesterol <40 mg/dl, (2) high blood pressure: blood pressure ≧130/85 mmHg, (3) impaired glucose tolerance: fasting plasma glucose ≧110 mg/dl [9].

2.6. *Statistical analysis*

All data are expressed as mean ± standard deviation (S.D.) values. A statistical analysis was performed using a paired t test, an unpaired t test and χ^2 test: $p < 0.05$ was considered to be statistically significant.

3. Results

The clinical parameters at the baseline and the 1-year follow-up are summarized in Table 1. Anthropometric and body composition parameters such as body weight, body mass index, body fat percentage, waist circumference and hip circumference were significantly reduced after 1 year. Systolic blood pressure, diastolic blood pressure and triglyceride levels were also significantly reduced and HDL cholesterol significantly increased.

We investigated the changes in the number of subjects with metabolic syndrome as classified into different levels of

Table 1 – Clinical parameters at baseline and 1-year follow-up in obese Japanese men

	Mean ± S.D.		*p*
	Baseline	Follow-up	
Number of subjects	105		
Height (cm)	169.2 ± 5.2		
Body weight (kg)	80.9 ± 8.8	78.7 ± 8.9	<0.0001
Body mass index (kg/m^2)	28.2 ± 2.6	27.5 ± 2.7	<0.0001
Body fat percentage (%)	28.7 ± 4.8	26.9 ± 6	<0.0001
Waist circumference (cm)	93.3 ± 7.2	90.5 ± 8.1	<0.0001
Hip circumference (cm)	99.6 ± 4.5	98.3 ± 4.6	<0.0001
Systolic blood pressure (mmHg)	133.5 ± 15.4	124.3 ± 12.2	<0.0001
Diastolic blood pressure (mmHg)	83.0 ± 12.0	77.8 ± 9.5	<0.0001
Triglyceride (mg/dl)	167.2 ± 101.7	125.2 ± 70.4	<0.0001
HDL cholesterol (mg/dl)	51.0 ± 11.5	53.5 ± 13.6	0.0091
Blood sugar (mg/dl)	105.8 ± 21.3	106.1 ± 29.7	0.8773

Table 2 – Changes in the number of subjects with metabolic syndrome as classified into different levels of waist circumference and body weight reduction

		Number of subjects		Change rate (%)
		Baseline	Follow-up	
Delta waist circumference (cm)				
−1<		12	15	25.0
−2<	≦−1	8	4	−50.0
−3<	≦−2	6	3	−50.0
−4<	≦−3	5	2	−60.0
−5<	≦−4	5	1	−80.0
	≦−5	10	3	−70.0
Delta body weight (kg)				
−1<		15	13	−13.3
−2<	≦−1	8	5	−37.5
−3<	≦−2	6	2	−66.6
−4<	≦−3	7	3	−57.1
−5<	≦−4	3	4	33.3
	≦−5	7	1	−85.7

Table 3 – Number of subjects with and without metabolic syndrome at baseline and follow-up

	Baseline	Follow-up		
		Group R	Group C	Total
Metabolic syndrome (+)	46	6	22	28
Metabolic syndrome (−)	59	36	41	77
p		0.0007	0.2558	0.0093

p: compared with baseline by χ^2 test. Group R: Delta waist circumference ≦−3 cm. Group C: Delta waist circumference > −3 cm.

waist circumference and body weight reduction (Table 2). Change rate was under the level of −50% in subjects by at least 3 cm of waist circumference reduction. However, clear relation between body weight reduction and metabolic syndrome and the threshold of body weight reduction were not noted.

Forty-two men reduced their waist circumference by at least 3 cm by the time of the 1-year follow-up. We investigated the changes in the prevalence of metabolic syndrome amongst men who had different levels of waist circumference reduction [Group R: Delta (delta represents positive changes in parameters) waist circumference ≦−3 cm, Group C: Delta waist circumference > −3 cm] (Table 3). The prevalence of metabolic syndrome at baseline was 43.8% (Group R: 20 men, Group C: 26 men, total: 46 men). This was significantly reduced in both Group R (6 men, change rate: −70.0%) and total subjects (28 men, change rate: −39.1%) supporting the recommendation of the Japan society for the study of obesity. However, for Group C (22 men, change rate: −15.4%) the prevalence of metabolic syndrome was similar to baseline levels and the change rate was significantly lower compared with that in Group R.

We further analyzed changes in each component of metabolic syndrome at baseline and follow-up (Table 4). The prevalence of abdominal obesity diagnosed by waist circumference, hypertension and dyslipidemia was remarkably reduced in Group R and total subjects. Only the prevalence of hypertension was significantly reduced in Group C.

Finally, we compared the delta parameters between Group G and Group C (Table 5). Significant differences were noted in delta triglyceride and delta HDL cholesterol between Group R and Group C. However, delta systolic blood pressure, delta diastolic blood pressure and delta blood sugar in Group R were similar to those in Group C.

4. Discussion

We explored, using Japanese criterion, whether at least 3 cm of waist circumference reduction can improve metabolic syndrome in obese Japanese men.

In some literature, a reduction in waist circumferences is closely linked to an improvement of metabolic risk factors through life style modification [10,11]. Villareal et al. reported

Table 4 – Number of subjects with and without each component of metabolic syndrome at baseline and follow-up

	Baseline	Follow-up		
		Group R	Group C	Total
Abdominal obesity (+)	95	26	58	84
Abdominal obesity (−)	10	16	5	21
p		0.0001	0.7269	0.0324
Hypertension (+)	69	14	29	43
Hypertension (−)	36	28	34	62
p		0.0003	0.0122	0.0003
Dyslipidemia (+)	54	8	24	32
Dyslipidemia (−)	51	34	39	73
p		0.0003	0.0934	0.0020
Impaired glucose tolerance (+)	28	7	14	21
Impaired glucose tolerance (−)	77	35	49	84
p		0.1984	0.5195	0.2534

p: compared with baseline by χ^2 test. Group R: Delta waist circumference ≦−3 cm. Group C: Delta waist circumference >−3 cm. Abdominal obesity (+): waist circumference ≧85 cm.

Table 5 – Comparison of delta clinical parameters between group R and C

	Group R	Group C	p
Number of subjects	42	63	
Delta systolic blood pressure (mmHg)	−11.3 ± 14.7	−7.7 ± 11.2	0.1503
Delta diastolic blood pressure (mmHg)	−7.0 ± 11.6	−4.1 ± 11.6	0.2054
Delta triglyceride (mg/dl)	−76.3 ± 109.9	−19.1 ± 61.1	0.0009
Delta HDL cholesterol (mg/dl)	5.4 ± 11.7	0.6 ± 7.6	0.0127
Delta blood sugar (mg/dl)	−0.3 ± 24.4	0.7 ± 14.3	0.8099

Mean ± S.D. Group R: Delta waist circumference ≤ -3 cm. Group C: Delta waist circumference > -3 cm.

that in obese older adults after a 6-months trial, 10 cm of waist reduction through diet and exercise was associated with improvements in glucose (−4 mg/dl), systolic blood pressure (−10 mmHg), diastolic blood pressure (−8 mmHg), serum free fatty acids (−99 micromol/l) and the number of subjects with metabolic syndrome (59%) [10]. Kuller et al. also reported that 508 postmenopausal women through exercise and diet change could reduce their waist size by 10 cm. This also improved low-density lipoprotein cholesterol, insulin and glucose levels in an 18-months follow-up [11]. One common factor in both these interventions is a 10 cm waist circumference reduction.

In the present study, with a 1-year follow-up, approximately 3 cm of waist circumference reduction was noted and all the parameters of metabolic risk factors, except blood sugar, improved. The prevalence of metabolic syndrome was significantly reduced in Group R and total subjects, and we can conclude that at least 3 cm of waist reduction was beneficial for improving metabolic syndrome. However, the prevalence of metabolic syndrome did not change in Group C. In addition, although the prevalence of abdominal obesity which was diagnosed by waist circumference measurements, hypertension and dyslipidemia was significantly reduced in Group R, the prevalence of impaired glucose tolerance was similar at the follow-up as it was at the baseline. Finally, the differences of delta parameters were noted only in delta triglyceride and delta HDL cholesterol. In sum, the main clinical impact of dyslipidemia was noted in the obese Japanese men with at least 3 cm of waist circumference reduction. Tonstand et al. [12] also reported that a difference of 3.1 cm of waist circumference was noted between an intervention group with nurse-led lifestyle counseling and a control group. Although there was a difference in triglyceride between the two groups, the difference in blood pressure was not at a significant level. These results suggest that an improvement of metabolic risk factors may be different according to the level of waist circumference reduction.

There are several potential limits in this study. First, although we proved a link between a reduction in waist circumference and metabolic risk factors, and it seems that at least 3 cm of waist circumference reduction was beneficial for improving metabolic syndrome, we could not prove the precise threshold of waist circumference reduction as well as body weight reduction. Second, we could not directly measure visceral fat accumulation using computed tomography. Finally, the small number of subjects is a limitation of this study.

In conclusion, it may be beneficial for obese Japanese men to reduce their waist circumference by at least 3 cm for improving metabolic syndrome.

Conflict of interest statement

All co-authors have no conflict of interest.

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ORIGINAL ARTICLE

Resting energy expenditure can be assessed by dual-energy X-ray absorptiometry in women regardless of age and fitness

C Usui[1,2], E Takahashi[1], Y Gando[1], K Sanada[3], J Oka[4], M Miyachi[5], I Tabata[5] and M Higuchi[2,3]

[1]*Department of Sport Sciences, Graduate School of Human Sciences, Waseda University, Saitama, Japan;* [2]*Faculty of Sport Sciences, Waseda University, Saitama, Japan;* [3]*Consolidated Research Institute for Advanced Science and Medical Care, Waseda University, Tokyo, Japan;* [4]*Department of Home Economics, Tokyo Kasei University, Tokyo, Japan and* [5]*Health Promotion and Exercise Program, National Institute of Health and Nutrition, Tokyo, Japan*

Objective: To evaluate the possibility that measurement of the magnitude and distribution of fundamental somatic heat-producing units using dual-energy X-ray absorptiometry (DXA) can be used to estimate resting energy expenditure (REE) in both young and elderly women with different aerobic fitness levels.
Subjects and methods: Peak oxygen uptake (VO_2 peak) and REE_m were directly measured in 116 young (age: 22.3 ± 2.1 years) and 72 elderly (63.3 ± 6.4 years) women. The subjects were divided into four groups according to categories of age and VO_2 peak; young: high fitness (YH, $n=58$); low fitness (YL, $n=58$); elderly: high fitness (EH, $n=37$) and low fitness (EL, $n=35$). Using DXA, systemic and regional body compositions were measured, and REE_e was estimated from the sum of tissue organ weights multiplied by corresponding metabolic rate.
Results: Although there were remarkable differences in systemic and regional body compositions, no significant differences were observed between REE_m and REE_e in the four groups. REE_e significantly correlated with REE_m in elderly as well as young women; the slopes and intercepts of the two regression lines were statistically not different between the elderly and young groups (elderly: $y=0.60x+472$, $r=0.667$; young: $y=0.78x+250$, $r=0.798$; $P<0.001$, respectively). A Bland–Altman analysis did not indicate bias in calculation of REE for all the subjects.
Conclusion: These results suggest that REE can be estimated from tissue organ components in women regardless of age and aerobic fitness.
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Keywords: resting energy expenditure; age; aerobic fitness; body composition; female adults

Introduction

Resting energy expenditure (REE) accounts for 60–80% of total daily energy expenditure and is the basis for estimating the energy requirement. In the field of energy metabolism, early investigators showed intense interest in establishing the determinant factors of REE (Cunningham, 1980, 1991; Nelson *et al.*, 1992). To date, some earlier studies demonstrated that body mass, especially fat-free mass (FFM), has been a useful candidate in estimating REE (Ravussin and Bogardus, 1989; Fukagawa *et al.*, 1990; Tataranni and Ravussin, 1995).

Changes in body weight (BW) including fat mass (FM) and FFM may be caused by various factors, such as biological aging, decreasing physical activity levels, nutritional status and health condition. Particularly in women, the menopause is also associated with increased body mass accompanied by elevated adiposity (Fukagawa *et al.*, 1990; Svendsen *et al.*, 1995; Guo *et al.*, 1999). Svendsen *et al.* (1995) have noted that postmenopausal women had significantly larger amounts of fat deposition, a higher abdominal fat distribution and lower lean tissue mass, including skeletal muscle, bone and intestinal organs than premenopausal women.

Correspondence: Dr M Higuchi, Faculty of Sport Sciences, Waseda University, 2-579-15 Mikajima, Tokorozawa, Saitama 359-1192, Japan.
E-mail: mhiguchi@waseda.jp
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Very little is known as to whether aerobically higher fitness individuals have higher metabolic rates in resting state. Ravussin and Bogardus (1989) reported that maximal O_2 uptake was not related to resting metabolic rate in non-diabetic, non-trained Pima Indians. However, they demonstrated that resting metabolic rate was significantly higher in well-trained men, when compared with sedentary men matched for BW, FFM and age (Ravussin and Bogardus, 1989). Thus, the question whether aerobic fitness level relates to REE remains unanswered.

Dual-energy X-ray absorptiometry (DXA) can easily and accurately assess the body composition, including bone mineral content (BMC), FM and FFM of the whole body and segments. Recently, Hayes *et al.* (2002) demonstrated that REE can be estimated from the summed heat productions from the weights of the brain, skeletal muscle mass (SM), adipose tissue (AT), bone and tissue organs by DXA. In view of the finding of Hayes *et al.* (2002), we decided to evaluate the possibility that measurement of the magnitude and distribution of fundamental somatic heat-producing units using DXA can be used to estimate REE in both young and elderly women with different aerobic fitness levels.

Materials and methods

Subjects

In total, 127 young women (age: 22.4 ± 2.2 years) and 83 elderly women (61.7 ± 8.1 years) were recruited for the study. Subjects who had too low and high body mass index (BMI <18.5 and BMI $>30\,\mathrm{kg\,m^{-2}}$) and had used medications that affect bone and estrogen replacement were eliminated from the analysis. Hence, 116 healthy young women (22.3 ± 2.1 years) and 72 healthy elderly women (63.3 ± 6.4 years) who had passed three years or more (13.5 ± 7.4 years) after menopause were selected for this study. The subjects were divided into four groups according to their aerobic fitness levels relative to BW (VO_2 peak: $\mathrm{ml\,kg^{-1}\,min^{-1}}$), and the median of VO_2 peak for each age, which were 36.4 (20–29 years), 27.1 (50–59 years), 25.8 (60–69 years) and 21.0 (70–79 years) $\mathrm{ml\,kg^{-1}\,min^{-1}}$ [young high fitness (YH): $n=58$; young low fitness (YL): $n=58$; elderly high fitness (EH): $n=37$ and elderly low fitness (EL): $n=35$]. All subjects were informed about the purpose and possible risks of the study and were then provided written informed consent, as approved by the Ethical Committee at the National Institute of Health and Nutrition in Japan.

Study protocol and direct measurement of REE

Participants came to the National Institute of Health and Nutrition in the morning. Subjects were asked to minimize any walking while en route from their home to the laboratory before REE determination. The subjects were restricted to perform any other exercises at least 24 h prior to the testing. The measured REEs (REE_m) was directly measured by open-circuit indirect calorimetry. Measurements were performed between 0700 and 0900 h after 10–12 h of fasting, except water, in a room at constant room temperature (23–25 °C). After entering the laboratory, subjects rested in the supine position for at least 30 min, and a Hans-Rudolph full face mask (Hans Rudolph Inc., Kansas City, MO, USA) was put on. Two samples of expired air were collected in Douglas bags for a duration of 10 min each, and the mean value was used for the analysis. For young subjects, all measurements were made during the follicular phase of the menstrual cycle.

An oxygen and carbon dioxide analyzer (Arco-1000A; Arco system, Japan) was used to analyze the rate of oxygen consumption and carbon dioxide production. The volume of expired air was determined using a dry gas volume meter (DC-5; Shinagawa, Japan) and converted to standard temperature, standard pressure and dry gas. Gas exchange results were converted to REE ($\mathrm{kcal\,day^{-1}}$) using Weir's equation (Weir, 1949).

Body composition analysis

Anthropometric measurements. BW was measured to the nearest 0.1 kg by using an electronic scale (Inner Scan BC-600; Tanita Co., Japan), and height was measured to the nearest 0.1 cm by using a stadiometer (YL-65; Yagami Inc., Japan). BW and height were measured with subjects wearing light clothing and no shoes. BMI was calculated by dividing BW in kilograms by the square of height in meters ($\mathrm{kg\,m^{-2}}$).

DXA. The percentage of fat (% body fat) and BMC of the whole body and appendicular lean soft tissue (LST) were measured by DXA (Hologic QDR-4500 DXA Scanner; Hologic Inc., Whaltham, MA, USA). Manufacturer's software version 11.2 for Windows was used to analyze the % body fat, BMC and LST. FFM and FM were calculated by BW and % body fat.

Test of aerobic capacity (VO_2 peak)

Young subjects were habituated to pedaling a dynamically calibrated Monark Model 828E cycle ergometer (Monark Exercise AB, Varberg, Sweden). On the other hand, aerobic capacity in elderly subjects was assessed by a progressive continuous test to exhaustion on a motor-driven treadmill with walking and running. All subjects wore a Hans-Rudolph full face mask. Oxygen consumption and carbon dioxide production of all subjects were measured during the last 30 s of each stage and analyzed using an oxygen and carbon dioxide analyzer. Heart rate was monitored electrocardiographically during the last 15 s of each minute, and a 'steady state' was regarded to have occurred if consecutive readings differed by <3 $\mathrm{beats\,min^{-1}}$. Four criteria were used to determine a successful maximal test: (1) a leveling or plateauing of VO_2 (defined as an increase in oxygen uptake $<2\,\mathrm{ml\,kg^{-1}\,min^{-1}}$); (2) maximal heart rate >195 or (220–age); (3) respiratory exchange ratio $\geqslant 1.0$ and (4) rating of perceived exertion $\geqslant 18$ (Johnson *et al*., 2000; Santa-Clara *et al*., 2006). VO_2 peak was defined by the attainment of at least two of the four criteria.

Calculation of tissue organ mass and estimation of REE

Tissue organ mass was calculated using the previously reported prediction model as follows.

Bone mass (BM) was calculated by multiplying BMC times 1.85 (Snyder *et al*., 1975; Heymsfield *et al*., 1990). AT was assumed to be 85% fat (Heymsfield *et al*., 2002), leading to the model based on FM. Thus, AT was calculated by multiplying FM times 1.18. SM was calculated using the prediction model of Kim *et al*. (2002) ($R^2 = 0.96$; $\text{SEE} = 1.58\,\text{kg}$; $P < 0.001$). Finally, residual mass (RM) was calculated as the difference between BW and the sum of the calculated BM, AT and SM.

$\mathbf{BM\ (kg) = BMC\ (g) \times 1.85/1000}$

$\mathbf{AT\ (kg) = FM\ (kg) \times 1.18}$

$\mathbf{SM\ (kg) = 1.13 \times LST\ (kg) - 0.02 \times age\ (years) + 0.97}$

$\mathbf{RM\ (kg) = BW - (BM + AT + SM)}$

Estimation of REE (REE_e) was based on the sum of four body compartments (BM, AT, SM and RM) times the corresponding tissue respiration rate as follows. The specific resting metabolic rate of the four compartments was assumed from previously reported data, bone ($2.3\,\text{kcal}\,\text{kg}^{-1}$), AT ($4.5\,\text{kcal}\,\text{kg}^{-1}$), skeletal muscle ($13\,\text{kcal}\,\text{kg}^{-1}$) and residual ($53\,\text{kcal}\,\text{kg}^{-1}$) (Holliday *et al*., 1967; Grande, 1989; Elia, 1992; Hayes *et al*., 2002; Heymsfield *et al*., 2002).

$\mathbf{REE_e = 2.3BM + 4.5AT + 13SM + 53RM}$

Statistical analysis

The data were presented as mean ± s.d. Statistical analyses were carried out with the Sigma Stat 2.03 (Systat Software Inc., CA, USA). A two-way analysis of variance was used to test for interaction effects between the age and aerobic fitness levels among the mean values for the four groups. Where appropriate, the *Tukey* test was employed to locate the source of the significant differences. To determine the associations between measured and estimated REE, Bland–Altman plots were used (Bland and Altman, 1986). For all the statistical analyses, the level of significance was defined as less than 0.05.

Results

Table 1 presents the comparisons of characteristics, composition of whole body and aerobic fitness levels. BW and FFM were significantly higher in the YH group than in the YL group and EH group. The % body fat tended to be higher in the EL group compared with the other groups, but this interaction between age and aerobic fitness level was just short of statistical significance (age: $P < 0.001$; aerobic fitness level: $P < 0.001$; interaction: $P = 0.056$). However, no significant interaction in BMI and FM was noted in the four groups.

REE_m in the YH group was ~15% higher than in the other three groups (Table 2).

Table 2 Measured and estimated resting energy expenditure

	Young		*Elderly*	
	YH (n = *58)*	*YL* (n = *58)*	*EH* (n = *37)*	*EL* (n = *35)*
REE_m	1265 ± 155	1118 ± 114^a	1080 ± 125^b	1093 ± 92
REE_e	1246 ± 161	1108 ± 101^a	1128 ± 108^a	1128 ± 89
$\text{REE}_m - \text{REE}_e$	19 ± 105	9 ± 89	−48 ± 92	−35 ± 79

Abbreviations: REE_m, measured by expiratory gas exchange; REE_e, estimated by four tissue organs.
Values are means ± s.d., kcal day^{-1}.
$\text{REE}_e = 13\text{SM} + 2.3\text{BM} + 4.5\text{AT} + 54\text{RM}$, significance was determined by two-way analysis of variance (ANOVA).
$^a P < 0.05$ vs high-fitness group (same age group).
$^b P < 0.05$ vs young group (same fitness category).

Table 1 Subject characteristics for the healthy female adults

	Young		*Elderly*	
	YH (n = 58)	*YL* (n = *58)*	*EH* (n = *37)*	*EL* (n = *35)*
Age (years)	21.8 ± 1.9	22.8 ± 2.2	62.4 ± 6.7	64.3 ± 6.1
Ht (cm)	163.2 ± 6.6	159.5 ± 6.3^a	153.1 ± 5.4^b	154.7 ± 5.0^b
BW (kg)	57.1 ± 6.8	53.9 ± 5.9^a	53.2 ± 6.0^b	55.5 ± 5.9
BMI ($\text{kg}\,\text{m}^{-2}$)	21.4 ± 1.9	21.2 ± 1.9	22.7 ± 2.1	23.2 ± 2.5
FFM (kg)	44.7 ± 5.6	39.5 ± 4.0^a	37.6 ± 3.7^b	37.9 ± 3.3
FM (kg)	12.3 ± 2.6	14.3 ± 3.0	15.5 ± 3.6	17.7 ± 4.1
% body fat	21.6 ± 3.6	26.5 ± 3.6	29.0 ± 4.5	31.5 ± 4.8
VO_2 peak ($\text{ml}\,\text{kg}^{-1}\,\text{min}^{-1}$)	42.3 ± 4.8	32.1 ± 2.9^a	29.8 ± 4.2^b	22.2 ± 2.8^{a,b}

Abbreviations: BMI, body mass index; BW, body weight; FFM, fat-free mass; FM, fat mass; Ht, height.
Values are means ± s.d.
Significance was determined by two-way analysis of variance (ANOVA).
$^a P < 0.05$ vs high-fitness group (same age group).
$^b P < 0.05$ vs young group (same fitness category).

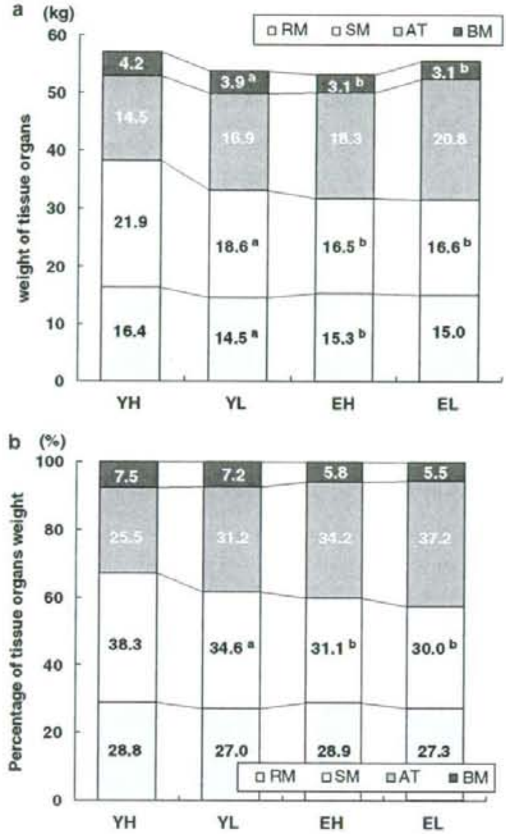

Figure 1 Four tissue organ components in women expressed as a weight (**a**) and as their respective fractional contributions to body weight (**b**). RM, residual mass; SM, skeletal muscle; AT, adipose tissue; BM, bone mass. Significance was determined by two-way analysis of variance (ANOVA). $^{a}P<0.05$ vs high-fitness group (same age group) and $^{b}P<0.05$ vs young group (same fitness category).

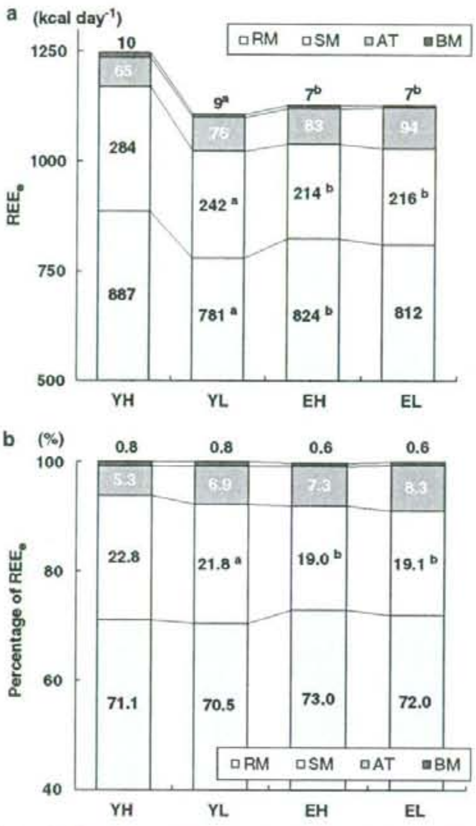

Figure 2 Four tissue organ components in women expressed as a specific energy expenditure (**a**) and as their respective fractional contributions to REE_e (**b**). RM, residual mass; SM, skeletal muscle; AT, adipose tissue; BM, bone mass; REE_e, resting energy expenditure estimated by four tissue organs. $REE_e = 13SM + 2.3BM + 4.5AT + 54RM$. Significance was determined by two-way analysis of variance (ANOVA). $^{a}P<0.05$ vs high-fitness group (same age group) and $^{b}P<0.05$ vs young group (same fitness category).

The absolute and relative values of the weight of the four tissue organs are presented in Figures 1a and b, respectively. SM and BM in YH were significantly higher than in YL, and were also significantly higher in young women than in elderly women of the same fitness category. The absolute value of RM was also significantly higher in YH than in YL and EH. However, no significant interaction in AT was noted among the four groups. When these four tissue masses were expressed as a percentage of BW, SM in YH was significantly higher than in YL, and was also significantly higher in young women than in elderly women of the same fitness category. This result was similar to that for SM mass. The relative mass of AT in EL tended to be higher than in the respective group, whereas no statistical significance in this interaction between age and aerobic fitness levels was observed.

Figures 2a and b present the absolute and relative values of the energy expenditure of the four different tissue organs. Our data noted significant differences in only SM as a percentage of the energy expenditure in the four groups. Specifically, the energy expenditure of SM as a percentage of the whole body in elderly women was lower than in the same fitness category (percentage energy expenditure of RM, AT and BM did not differ among the groups).

Tissue organ-derived REE_e was significantly higher in the YH than in the YL and EH groups (Table 2). There was also no

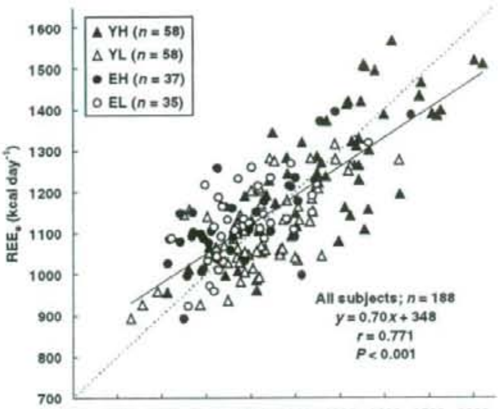

Figure 3 Relationship between the measured and estimated resting energy expenditure. REE_m, measured by expiratory gas exchange; REE_e, estimated by four tissue organs. $REE_e = 13SM + 2.3BM + 4.5AT + 54RM$.

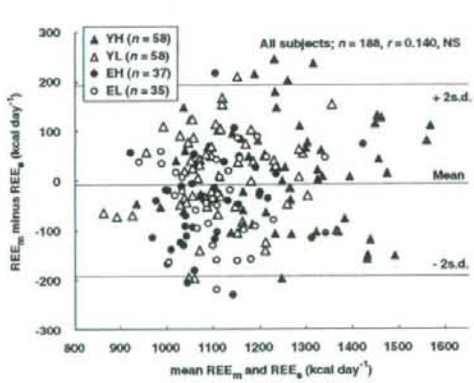

Figure 4 Bland–Altman analysis. Plots of the differences between REE_m and REE_e. REE_m, measured by expiratory gas exchange; REE_e, estimated by four tissue organs. $REE_e = 13SM + 2.3BM + 4.5AT + 54RM$.

significant difference between REE_m and REE_e in the four groups. In addition, a significant relationship between REE_m and REE_e was observed in all subjects (Figure 3). A Bland–Altman analysis did not indicate any bias in the calculation of REE for all subjects (Figure 4).

Discussion

The major finding from the present study is that REE in adult women can be accurately estimated from tissue organ components by using DXA regardless of age and aerobic fitness levels.

Measured and estimated REEs

A strongly significant relationship between REE_m and REE_e was observed in all subjects ($r = 0.771$, $P < 0.001$; Figure 3) and a Bland–Altman analysis did not indicate bias in the estimation of REE (all subjects: $r = 0.140$; young: $r = 0.041$; elderly: $r = 0.133$, NS, respectively; Figure 4). Furthermore, our study indicated that REE_e was related significantly to REE_m in both young and elderly women (elderly: $y = 0.60x + 472$, $r = 0.667$; young: $y = 0.78x + 250$, $r = 0.798$; $P < 0.001$ for both), and the slopes and intercepts of the two regression lines were statistically not different between the young and elderly groups (slopes: $t = 1.652$; intercept: $t = 1.881$; NS for both). This suggests the possibility that the difference in the ratio of SM and RM to FFM is important rather than the decline in the specific metabolic rate with advancing age.

It is well known that REE decreases after menopause in women, potentially contributing to changes in body composition (Vaughan *et al*., 1991; Hunter *et al*., 2001). It is unclear, however, whether the decrease in REE is a consequence of an age-dependent decrease in FFM, which includes skeletal muscle, bone and tissue organs. In the present study, the absolute REE_ms (kcal day^{-1}) are ~15% lower in the YL, EH and EL groups compared with the YH group (Table 2). When REE_m is expressed in terms of FFM, however, no significant differences in absolute REE_m were obtained among the groups (YH vs YL vs EH vs EL: 28.4 ± 2.3 vs 28.4 ± 2.3 vs 28.8 ± 2.7 vs 29.0 ± 2.1 kcal kg^{-1} day^{-1}). This result did not correspond to previous reports on sedentary adult women and men (Van Pelt *et al*., 1997, 2001; Piers *et al*., 1998). Van Pelt *et al*. (1997, 2001) and Piers *et al*. (1998) reported that the effect of age on REE was significantly negative in healthy sedentary adults, even after adjusting for age-related differences in body composition.

On the basis of the different tissue masses and their specific metabolic rates (Elia, 1992), Gallagher *et al*. (1998, 2000) examined the relationship between REE and body composition divided into numerous tissues and organs. In addition, Hayes *et al*. (2002) investigated whether the REE can be calculated from the summed heat productions from the weight of tissue organs estimated by DXA. Their study showed that no bias was detected between measured and predicted REEs (Hayes *et al*., 2002).

Aerobic fitness level and body composition

Our present data showed that the aerobic fitness level in the elderly was ~30% lower than in young adults in both high- and low-fitness level groups. The reduction rate of VO_2 peak/BW was ~7.5% per decade of age. Earlier study showed a 7.5% reduction per decade in VO_2 max for 20–75 years of age (Pollock *et al*., 1987).

In the present study, the % body fat in high fitness or young group was lower than in low fitness or elderly group of the same category, but this interaction between age and aerobic fitness level was just short of statistical significance ($P = 0.056$). On the other hand, FFM was significantly higher in YH than in the other three groups, and no significant differences in FFM were noted among the YL, EH and EL groups (Table 1). These findings are in accordance with earlier studies (Van Pelt *et al.*, 1997, 2001), suggesting that keeping aerobically fit can prevent an increase in % body fat with aging.

Our present study also focused on the weight or energy expenditure of DXA-estimated tissue organs, as a component of the whole body, to assess the relationship between FFM and REE_m. The percentage of AT mass suggested that keeping a high aerobic fitness level may suppress the age-related increase in total body fat. In contrast, SM decreases in elderly women regardless of their aerobic fitness levels (Figures 1a and b). These results suggested that, in elderly women, it could be difficult to prevent a decrease in the volume of skeletal muscle, by performing aerobic exercise, such as swimming, walking or jogging. Resistance exercise should be combined with aerobic exercise for elderly women.

Limitations

Our investigation has a few limitations. First, the weight of tissue organs could not be directly measured by using apparatus, such as a magnetic resonance imaging. Second, we did not observe directly the magnitude of the summed heat produced by the tissue organs. Third, we did not test middle-aged (30–49 years) adults. Future studies should widen the characteristics of the subjects to include lean and obese adults or middle-aged adults. Future studies are needed to extend these observations and to analyze gender-related, hormonal, ethnic and other determinant factors of REE.

In conclusion, the present investigation demonstrated that estimation of the four tissue organs by using DXA allows successful calculation of REE in female adults regardless of age and aerobic fitness levels. The findings suggest the possibility that REE is regulated mainly by the mass of the tissue organs with lower and higher metabolic rates, including skeletal muscle and intestinal organs, rather than a decline in the specific metabolic rate of different tissue organs associated with advancing age and decreasing aerobic fitness levels in young and elderly women.

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Experimental **Physiology**

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 Kawano, Michiya Tanimoto, Kenta Yamamoto, Kiyoshi Sanada, Yuko Gando, Izumi Tabata, Mitsuru Higuchi and Motohiko Miyachi

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Experimental Physiology

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 Kawano[1,2], Michiya Tanimoto[1], Kenta Yamamoto[2], Kiyoshi Sanada[2], Yuko Gando[1,2],
Izumi Tabata[1], Mitsuru Higuchi[2] and Motohiko Miyachi[1]

[1]*National Institute of Health and Nutrition Program for Health Promotion, 1-23-1 Toyama, Shinjuku 162-8636, Japan*
[2]*Wasada 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 β-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.

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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 (Zeiher *et al.* 1989; O'Rourke, 1990; Taddei *et al.* 1995; Tanaka *et al.* 2000; Najjar *et al.* 2005). Therefore,

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Table 1. Subject characteristics

	Control	Resistance trained
Number of subjects	17	12
Age (years)	36.8 ± 1.2	38.7 ± 1.7
Height (cm)	171.0 ± 1.2	171.0 ± 1.8
Body weight (kg)	71.9 ± 1.9	74.9 ± 2.1
Percentage body fat (%)	19.4 ± 1.2	12.3 ± 0.9*
Total cholesterol (mmol l^{-1})	5.0 ± 0.2	4.7 ± 0.2
HDL cholesterol (mmol l^{-1})	1.3 ± 0.1	1.6 ± 0.1*
Plasma glucose (mmol l^{-1})	5.0 ± 0.1	5.1 ± 0.1
Triglycerides (mmol l^{-1})	1.5 ± 0.3	0.9 ± 0.1
Resting heart rate (beats min^{-1})	58 ± 2	56 ± 2
Maximal heart rate (beats min^{-1})	186 ± 3	183 ± 4
$\dot{V}_{O_2max}$ (l min^{-1})	2.7 ± 0.1	2.8 ± 0.1
$\dot{V}_{O_2max}$/body weight (ml kg^{-1} min^{-1})	37.7 ± 1.4	36.9 ± 1.3
Leg extension power (W)	1719 ± 91	2293 ± 155*
Handgrip (kg)	45.6 ± 1.6	51.0 ± 2.0*

Data are means ± S.E.M.; $\dot{V}_{O_2max}$, maximal oxygen consumption. *$P < 0.05$ *versus* control subjects.

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

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.* 1995*b*; 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 ($\dot{V}_{O_2max}$) 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

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

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.

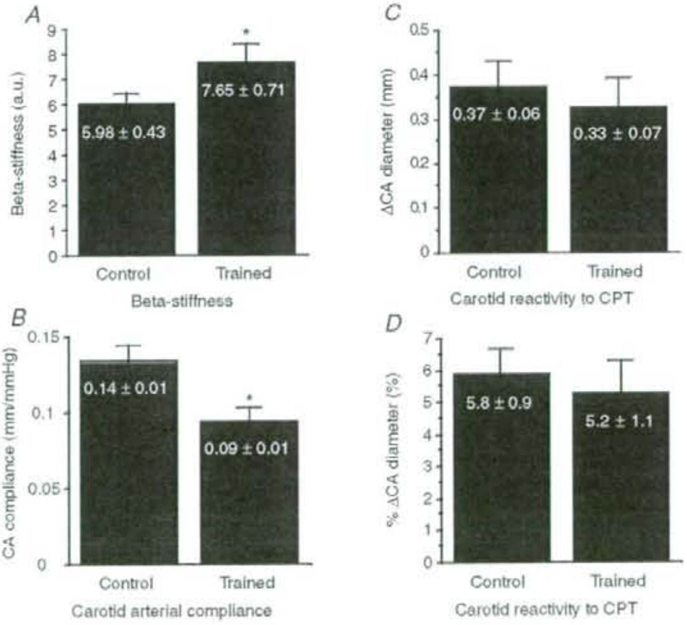

Figure 1. Carotid arterial β-stiffness index (*A*), carotid arterial (CA) compliance (*B*), and amount (*C*) and percentage change (*D*) in carotid artery diameter in response to CPT in resistance-trained men and control subjects

Values are means ± S.E.M. *$P < 0.05$ *versus* control subjects.

Carotid arterial β-stiffness (Fig. 1*A*) was higher and compliance (Fig. 1*B*) was lower in resistance-trained men compared with control subjects. There were no significant differences in the amount (Fig. 1*C*) or percentage change (Fig. 1*D*) of carotid artery diameter in response to CPT between resistance-trained men and control subjects. The differences in carotid arterial compliance and β-stiffness index between resistance-trained men and control subjects disappeared after normalizing carotid arterial compliance and β-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 β-stiffness index between resistance-trained men and control subjects were affected after normalizing carotid arterial compliance and β-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.* 1995*a*). 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 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; Rakobowchuk *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 vasoreactivity 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.

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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 Kawano, Michiya Tanimoto, Kenta Yamamoto, Kiyoshi Sanada, Yuko Gando, Izumi Tabata, Mitsuru Higuchi and Motohiko Miyachi

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