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## Changes in Metabolic Syndrome and Its Components with Lifestyle Modification in Japanese Men

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### Abstract

**Objective** Changes in metabolic syndrome and its components with lifestyle modification were evaluated in Japanese men.

**Methods** We used data for 160 Japanese men (45.6±8.8 years) with a 1-year follow up. Anthropometric, blood examination and blood pressure measurements were evaluated. Metabolic syndrome was defined by using a criterion in Japan. All subjects were given instructions by well-trained medical staff on how to change their lifestyle.

**Results** With a 1-year follow-up, anthropometric parameters, blood pressure (BP), triglyceride and HDL cholesterol were significantly improved and the prevalence of metabolic syndrome was significantly reduced. The number of subjects with abdominal obesity at baseline and at follow-up was higher (81 men) than that of subjects with other components at baseline and at follow-up. Parameters at baseline were significantly correlated with changes in parameters for one year. With lifestyle modification, the level of 163 mmHg in systolic BP (SBP), 115 mmHg in diastolic BP (DBP), 226 mg/dL in triglyceride and 33 mg/dL in HDL cholesterol at baseline was estimated to improve to the level without medications with a 1-year follow up.

**Conclusion** Lifestyle modification is useful for improving metabolic syndrome and its components. However, items of metabolic syndrome were improved, even when the abdominal circumference was greater than the normal value for Japanese men.

**Key words:** lifestyle modification, metabolic syndrome, blood pressure

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### Introduction

Metabolic syndrome, characterized by abdominal obesity, has become a public health challenge and common disorder in Japan (1). For example, we have previously described that 30.7% of men and 3.6% of women were diagnosed as having the metabolic syndrome (2). Metabolic syndrome is closely related to elevated hepatic enzymes (3), uric acid (4), reduced exercise capacity (5, 6) and cardiovascular disease (7). Therefore, proper management of metabolic syndrome is urgently required.

The recommendation for medication for hypertension is

based on the following from the Japanese Society of Hypertension (<http://www.jpnh.org/>, accessed on June 15, 2009.): blood pressure (BP)  $\geq 140/90$  mmHg, dyslipidemia is defined as triglyceride  $\geq 150$  mg/dL, LDL cholesterol  $\geq 140$  mg/dL, HDL cholesterol  $< 40$  mg/dL from the Japan Atherosclerosis Society (<http://jas.umin.ac.jp/>, accessed on July 15, 2009) and diabetes mellitus  $\geq 126$  mg/dL in fasting plasma glucose from the Japan Diabetes Society (<http://www.jds.or.jp/>, accessed on July 15, 2009). In addition, lifestyle modification has been considered as useful and an essential method for preventing and improving these disorders. However, whether a lifestyle modification is beneficial for improving metabolic syndrome and its components, and what

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**Table 1. Clinical Profiles and Changes in Parameters with Lifestyle Modification with a 1-year Follow Up in Japanese Men**

	Baseline	Follow up	p
Number of subjects	160		
Age	45.6 ± 8.8		
Height (cm)	168.7 ± 5.5		
Body weight (kg)	74.9 ± 11.1	73.5 ± 10.2	<0.0001
Body mass index (kg/m <sup>2</sup> )	26.3 ± 3.7	25.8 ± 3.3	<0.0001
Abdominal circumference (cm)	88.2 ± 9.9	86.5 ± 9.1	<0.0001
Hip circumference (cm)	96.7 ± 5.7	95.9 ± 5.2	<0.0001
SBP (mmHg)	130.8 ± 14.8	123.4 ± 12.4	<0.0001
DBP (mmHg)	82.5 ± 10.9	77.5 ± 9.3	<0.0001
Triglyceride (mg/dL)	145.2 ± 94.0	119.8 ± 76.5	0.0005
HDL cholesterol (mg/dL)	50.1 ± 14.4	56.1 ± 15.1	0.0109
Blood sugar (mg/dL)	102.0 ± 19.2	102.4 ± 25.6	0.7478
Mean ± SD			
SBP: Systolic blood pressure			
DBP: Diastolic blood pressure			

effects such a modification has on metabolic syndrome and its components remain to be investigated in a longitudinal analysis. In this study, we evaluated the effect of lifestyle modification on metabolic syndrome and its components in Japanese men with a 1-year follow up.

## Subjects and Methods

**Subjects.** We used data for 160 Japanese men, aged 45.6±8.8 years who met the following criteria: 1) received an annual health check-up every year with a follow up duration of 1-year, 2) received no medications for diabetes, hypertension, and/or dyslipidemia, and 3) provided written informed consent (Table 1).

In 2008, the Ministry of Health, Labor, and Welfare of Japan started to undertake a specific health check-up and special health guidance for preventing lifestyle-related diseases (<http://www.mhlw.go.jp/bunya/shakaihosho/iryouseido01/info02a.html>, accessed on Oct 11, 2009). At the first annual health check-up, all subjects were given instructions by well-trained medical staff on how to change their lifestyle as the special health guidance. Nutritional instruction was provided with a well-trained nutritionist, who planned the diet for each subject based on their data and provided simple instructions (i.e. not to eat too much and to consider balance when they eat). Exercise instruction was also provided by a well-trained physical therapist, who encouraged each subject to increase their daily amount of steps walked. At the second health check-up, medical staff subjectively evaluated changes in their lifestyle and the subjects with an evaluation of over the level of recommendation for medications were encouraged to receive medications.

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

**Anthropometric and body composition measurements.** Anthropometric and body compositions were evaluated based on the following parameters: height, body weight, abdominal circumference and hip circumference. Body mass index (BMI) was calculated by weight/[height]<sup>2</sup>(kg/m<sup>2</sup>). Abdominal circumference was measured at the umbilical level and hip circumference was measured at the widest circum-

ference over the trochanter in standing subjects after normal expiration (8).

**BP measurements at rest.** Resting systolic and diastolic BP (SBP and DBP) were measured indirectly using a mercury sphygmomanometer placed on the right arm of the seated participant after at least 15 minutes of rest.

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

**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 (1).

**Statistical analysis.** All data are expressed as mean ± standard deviation (SD) values. A statistical analysis was performed using a paired t test and  $\chi^2$  test: p<0.05 was considered to be statistically significant. Simple correlation analysis was used to test the significance of the linear relationship among continuous variables.

## Results

Clinical profiles and changes in parameters with lifestyle modification are summarized in Table 1. Body weight, BMI, abdominal circumference and hip circumference were significantly reduced after one year. SBP, DBP and triglyceride were also significantly reduced and HDL cholesterol was significantly increased with lifestyle modification. However, blood glucose at baseline was similar to that at follow up, and abdominal circumference was over the level of 85 cm at follow up.

We also evaluated the changes in prevalence of metabolic syndrome and its components (Table 2). Prevalence of metabolic syndrome and its components i.e. abdominal obesity, hypertension, dyslipidemia and impaired glucose tolerance was significantly reduced with a 1-year follow up. The number of subjects with abdominal obesity [81 men (50.6%)] at

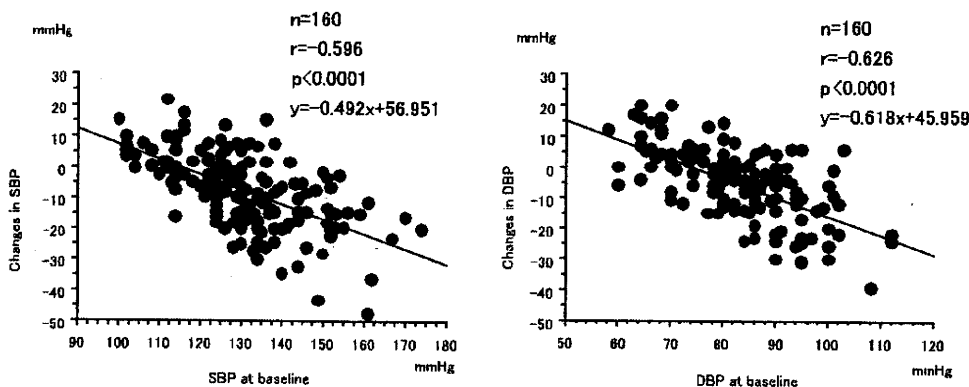
**Table 2. Changes in Metabolic Syndrome and Its Components with Lifestyle Modification after One Year**

	Follow up		p
	Abdominal circumference (-)	Abdominal circumference (+)	
Abdominal circumference (-)	54	7	<0.0001
Abdominal circumference (+)	18	81	
	Hypertension (-)		<0.0001
Hypertension (-)	53	Hypertension (+)	
Hypertension (+)	48	11	
	Dyslipidemia (-)		<0.0001
Baseline Dyslipidemia (-)	88	Dyslipidemia (+)	
Dyslipidemia (+)	32	9	
	Impaired glucose tolerance (-)		<0.0001
Impaired glucose tolerance (-)	129	Impaired glucose tolerance (+)	
Impaired glucose tolerance (+)	8	3	
	Metabolic syndrome (-)		<0.0001
Metabolic syndrome (-)	110	Metabolic syndrome (+)	
Metabolic syndrome (+)	25	5	
		20	

**Table 3. Simple Correlation Analysis between Parameters at Baseline and Changes in Parameters with Lifestyle Modification with a 1-year Follow Up**

	r	p	Single regression line	Recommendation for medication	Baseline level without medications calculated by formula
SBP (mmHg)	-0.598	<0.0001	$y = -0.492x + 56.951$	$y + x = 140$	163
DBP (mmHg)	-0.626	<0.0001	$y = -0.618x + 45.959$	$y + x = 90$	115
Triglyceride (mg/dL)	-0.654	<0.0001	$y = -0.626x + 54.488$	$y + x = 150$	226
HDL cholesterol (mg/dL)	-0.270	0.0005	$y = -0.187x + 12.101$	$y + x = 39$	33
Blood sugar (mg/dL)	0.052	0.5118			

y: changes in parameters  
x: parameters at baseline



**Figure 1. Simple correlation analysis between BP at baseline and changes in BP with a 1-year follow-up in Japanese men.**

baseline and at follow up was higher than that of subjects with other components [hypertension: 48 men (30.0%), dyslipidemia: 31 men (19.4%), impaired glucose tolerance: 20 men (12.5%)] at baseline and at follow up. Therefore, abdominal obesity was persisted but metabolic parameters were improved.

We further investigated the link between parameters at baseline and changes in parameters (Table 3, Fig. 1). SBP, DBP, Triglyceride and HDL cholesterol at baseline were significantly correlated with changes in each parameter. The recommendation for medications was 140 mmHg in SBP, 90 mmHg in DBP, 150 mg/dL in triglyceride, 39 mg/dL in HDL cholesterol and 126 mg/dL in fasting plasma glucose. Therefore, the baseline level without medications was calculated by single regression line. The level of 163 mmHg in SBP, 115 mmHg in DBP, 226 mg/dL in triglyceride and 33

mg/dL in HDL cholesterol at baseline was estimated to improve to the level without medications with a 1-year follow up.

### Discussion

In this study, the prevalence of metabolic syndrome and its components was significantly reduced with lifestyle modification with a 1-year follow up. In addition, the metabolic parameters were improved without normalized abdominal circumference.

There are some reports that show the link between lifestyle modification and metabolic syndrome and its components in a longitudinal analysis. Katzmarzyk et al reported on the effects of 20 weeks supervised aerobic training program on the prevalence of metabolic syndrome in 621 men

and women who were enrolled in the HERITAGE Study. 30.5% of the participants with metabolic syndrome at baseline were classified as not having the syndrome after the intervention (9). Ekelund et al reported that the energy expenditure of physical activity predicts progression to metabolic syndrome independent of aerobic fitness, obesity, and other confounding factors followed by 5.6 years (10). The Kuopio Ischemic Heart Disease Risk Factor Study (11) followed several hundred men without the syndrome at baseline. After four years, subjects in the upper one-third of  $\dot{V}O_2\text{max}$  at baseline were 75% less likely than unfit men to develop metabolic syndrome. Muzio et al reported that metabolic syndrome was effectively treated by long-term diet (~500 calorie/day deficit) and lifestyle therapy alone in 37% of obese, nondiabetic patients (12). By using the criterion developed in Japan, Okura et al recently reported that 67 women with metabolic syndrome were treated with a 14-week weight loss program, which included a low-calorie diet and aerobic exercise. The adjusted odds ratios for metabolic syndrome improvement in the two interventions with diet alone and diet plus exercise were 1.0 and 3.68. In addition,  $\dot{V}O_2\text{max}$  in subjects on the low-calorie diet and aerobic exercise treatment was  $22.9 \pm 3.2$  mL/kg/min at baseline and  $27.0 \pm 3.8$  mL/kg/min after intervention ( $p < 0.001$ ) (13). In this study, although the difference of blood sugar between at baseline and at follow up was not noted, we found that the prevalence of metabolic syndrome and its components including impaired glucose tolerance was significantly reduced with lifestyle modification after one year. Abdominal obesity, which is one of the targets for management of metabolic syndrome, was not improved to the normal range. However, the metabolic parameters were improved without normalized abdominal circumference. The diagnosis of metabolic syndrome is a caution for the general people to be careful in the healthy life, and these are not criteria for diagnosis of a definite disease to be treated with drug administration or with specific medication (14, 15). Taken together, these changes in metabolic components with lifestyle modification would be expected to reduce the risk of cardiovascular diseases or glucose metabolism.

The Japan Society of Hypertension recommends that lifestyle modification is essential for improving hypertension and medications should be considered after one or three

months' lifestyle modification in subjects with low or moderate risk. Medications are immediately recommended in subjects with high risk (<http://www.jpns.org/>, accessed on June 15, 2009).

The Japan Atherosclerosis Society and the Japan Diabetes Society also recommended that lifestyle modification is essential in the first place. We explored that the clinical parameters i.e. BP, triglyceride and HDL cholesterol at baseline were closely correlated with changes in these parameters in subjects without medications with a 1-year follow up. In addition, by using single regression line and the recommendation for medications, the baseline level of parameters without medications was calculated. The level of 163 mmHg in SBP, 115 mmHg in DBP, 226 mg/dL in triglyceride and 33 mg/dL in HDL cholesterol at baseline was estimated to improve to the level without medications after one year. Through the concept of metabolic syndrome, the significance of encouraging a reduction of abdominal obesity by lifestyle modification as the first step for the management of individuals with abdominal obesity has become strengthened (14). Although these results may be affected by higher values and limited in the difference of parameters, the estimated level in this study may be one of reference data for improving metabolic syndrome with lifestyle modification in preference to medications in some Japanese men. Further intervention studies are necessary to test the effect of lifestyle modification on metabolic syndrome.

Potential limitations still remain in this study. First, the selected 160 subjects underwent an annual health check-up every year with a follow-up duration of 1-year and received no medication; they were, therefore, probably more health-conscious than most of the average person. Second, the small sample size makes it difficult to infer causality between lifestyle modification and metabolic syndrome. Third, blood sugar did not significantly reduce and blood sugar at baseline was not also associated with changes in blood sugar with a 1-year follow up. These results suggest that an improvement of metabolic risk factors may be different according to the level of lifestyle modification.

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## **Lack of carotid stiffening associated with MTHFR 677TT genotype in cardiorespiratory fit adults**

**Motoyuki Iemitsu, Haruka Murakami, Kiyoshi Sanada, Kenta Yamamoto, Hiroshi Kawano, Yuko Gando and Motohiko Miyachi**

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## Lack of carotid stiffening associated with MTHFR 677T genotype in cardiorespiratory fit adults

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<sup>1</sup>Health Promotion and Exercise Program, National Institute of Health and Nutrition, Tokyo; <sup>2</sup>Faculty of Sport and Health Science, Ritsumeikan University, Shiga; and <sup>3</sup>Faculty of Sport Sciences, Waseda University, Saitama, Japan

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**Iemitsu M, Murakami H, Sanada K, Yamamoto K, Kawano H, Gando Y, Miyachi M.** Lack of carotid stiffening associated with MTHFR 677T genotype in cardiorespiratory fit adults. *Physiol Genomics* 42: 259–265, 2010. First published April 20, 2010; doi:10.1152/physiolgenomics.00039.2010.—The TT genotype of C677T polymorphism in 5,10-methylenetetrahydrofolate reductase (MTHFR) induces elevation of homocysteine level and leads to atherosclerosis and arterial stiffening. Furthermore, cardiorespiratory fitness level is also associated with arterial stiffness. In the present study, a cross-sectional investigation of 763 Japanese men and women (18–70 yr old) was performed to clarify the effects of cardiorespiratory fitness on the relationship between arterial stiffness and MTHFR C677T gene polymorphism. Arterial stiffness was assessed by carotid  $\beta$ -stiffness with ultrasonography and tonometry. The study subjects were divided into high-cardiorespiratory fitness (High-Fit) and low-cardiorespiratory fitness (Low-Fit) groups based on the median value of peak oxygen uptake in each sex and decade. The plasma homocysteine level was higher in the TT genotype of MTHFR C677T polymorphism compared with CC and CT genotype individuals. MTHFR C677T polymorphism showed no effect on carotid  $\beta$ -stiffness, but there was a significant interaction effect between fitness and MTHFR C677T polymorphism on carotid  $\beta$ -stiffness ( $P = 0.0017$ ). In the Low-Fit subjects, carotid  $\beta$ -stiffness was significantly higher in individuals with the TT genotype than the CC and CT genotypes. However, there were no such differences in High-Fit subjects. In addition,  $\beta$ -stiffness and plasma homocysteine levels were positively correlated in Low-Fit subjects with the TT genotype ( $r = 0.71$ ,  $P < 0.0001$ ), but no such correlations were observed in High-Fit subjects. In CC and CT genotype individuals, there were also no such correlations in either fitness level. These results suggest that the higher cardiorespiratory fitness may attenuate central artery stiffening associated with MTHFR C677T polymorphism.

peak oxygen uptake; arterial stiffness; homocysteine; 5,10-methylenetetrahydrofolate reductase

ELEVATED PLASMA HOMOCYSTEINE level is considered a risk factor for cardiovascular events and is associated with arterial stiffness and atherosclerosis in subjects with some cardiovascular risk factors (7, 15, 30, 36). High homocysteine levels may impair endothelial function, increase oxidative stress, and alter protein structure (5, 6, 37). Exposure of endothelial cells to elevated homocysteine levels results in decreased availability of nitric oxide (NO), which has vasodilatory and antiplatelet effects, and impaired vascular function, which are early events in atherogenesis (6, 29, 33, 35). Homocysteine metabolism represents an interesting model of gene-environment interaction (34, 38). Elevations in homocysteine may be caused by

genetic and environmental factors and by gene-gene and/or gene-environment interactions. The enzyme 5,10-methylenetetrahydrofolate reductase (MTHFR) catalyzes the irreversible conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate (4). A polymorphism of C677T (Ala $\rightarrow$ Val) in the gene encoding MTHFR is associated with decreased activity of the enzyme due to thermolability (1). In individuals homozygous for the T (Val) allele, a relative deficiency in the remethylation process of homocysteine into methionine leads to mild to moderate hyperhomocysteinemia, a condition recognized as an independent risk factor for arterial stiffness and atherosclerosis (1, 34). Thus the variation in MTHFR genetic sequence was shown to be associated with differences in the development of cardiovascular disease and related conditions, such as arterial stiffness and atherosclerosis.

Habitual exercise results in higher cardiorespiratory fitness and reduced risk of cardiovascular disease, such as arterial stiffness and atherosclerosis (8, 11, 12, 31). There have been several cross-sectional studies regarding the relationship between cardiorespiratory fitness and homocysteine status. These factors were reported to be independent regardless of sex (10) or to be negatively associated in women but not in men (19). Therefore, genetic variations in MTHFR, such as C677T polymorphism, may influence the effects of regular exercise and plasma homocysteine status on arterial stiffness. Recently, plasma homocysteine levels were shown not to be associated with cardiorespiratory fitness after controlling for potential confounders, including MTHFR C677T, in a cross-sectional study of Swedish children and adolescents (26). However, it remains unclear whether cardiorespiratory fitness level affects the relationship between arterial stiffness and genetic variations in MTHFR.

We hypothesized that single-nucleotide polymorphism (SNP) genotypes of C677T (Ala $\rightarrow$ Val) in exon 5 of MTHFR on chromosome 1 and cardiorespiratory fitness level may affect arterial stiffness in healthy Japanese subjects. The present study represents a cross-sectional investigation of 763 Japanese men and women (18–70 yr) to clarify the effects of cardiorespiratory fitness on the relationship between arterial stiffness and MTHFR C677T gene polymorphism.

### METHODS

**Subjects.** A total of 763 Japanese subjects (239 men and 524 women) between 18 and 70 yr of age participated in this cross-sectional study (mean:  $40 \pm 1$  yr). The study population consisted of sedentary or moderately active subjects who participated in swimming, stretching, and healthy gymnastics programs (at least 60 min/wk) and did not participate in any other vigorous sports activities. Subjects were divided into low-cardiorespiratory fitness (Low-Fit) and high-cardiorespiratory fitness (High-Fit) groups, with the dividing line set at the median value of peak oxygen uptake ( $\dot{V}O_{2\text{peak}}$ ), as an

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index of cardiorespiratory fitness, in each sex and decade [median value of  $\dot{V}O_{2peak}$  ( $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) for 18–30 yr old: men 47.1, women 36.7; 31–40 yr old: men 37.1, women 35.6; 41–50 yr old: men 34.7, women 31.9; 51–60 yr old: men 31.8, women 29.3; 61–70 yr old: men 31.0, women 27.2]. The median values of  $\dot{V}O_{2peak}$  in the present study were similar to the reference values included in the exercise guidelines established by the Ministry of Health, Labor, and Welfare of Japan for prevention of lifestyle-related diseases (<http://www.nih.go.jp/eiken/programs/pdf/epar2006.pdf>). Subjects were recruited for the present study by advertisement. All subjects were free of any overt signs or symptoms of chronic disease, and all were nonsmokers. Carotid  $\beta$ -stiffness ( $\beta$ -stiffness) and common carotid intima-media thickness (ccIMT) were determined as indexes of arterial stiffness in all subjects. Systolic blood pressure (SBP), diastolic blood pressure (DBP), percent body fat, and MTHFR gene C677T polymorphism were determined in all subjects. Body fat mass was determined for the whole body with dual-energy X-ray absorptiometry (DXA) (Hologic QDR-4500A scanner; Hologic, Waltham, MA). SBP and DBP were measured at rest with a vascular testing device (Colin Medical Technology, Tokyo, Japan). Serum cholesterol, triglyceride, and folic acid levels and plasma glucose and homocysteine levels were also measured.

The study was approved by the Ethical Review Board of the National Institute of Health and Nutrition. Written informed consent was obtained from all subjects before inclusion in the study.

**Measurement of  $\dot{V}O_{2peak}$ .**  $\dot{V}O_{2peak}$  was measured by an incremental cycle exercise test using a cycle ergometer (828E; Monark, Varberg, Sweden). The incremental cycle exercise began at a work rate of 90 W (60–120 W) in men and 60 W (30–90 W) in women, and power output was increased by 15 W/min until the subjects could not maintain a fixed pedaling frequency of 60 rpm. The subjects were encouraged during the ergometer test to exercise at the level of maximum intensity. Heart rate and rating of perceived exertion (RPE) were monitored minute by minute during exercise. RPE was obtained with the modified Borg scale (2).  $\dot{V}O_2$  was monitored during the last 30 s of each increase in work rate. Subjects breathed through a low-resistance two-way valve, and the expired air was collected in Douglas bags. Expired  $O_2$  and  $CO_2$  gas concentrations were measured by mass spectrometry (ARCO-1000A; Arco System, Chiba, Japan), and gas volume was determined with a dry gas meter (DC-5C; Shinagawa Seiki, Tokyo, Japan).  $\dot{V}O_{2peak}$  was assessed by the attainment of three of the following four criteria: 1) a plateau in  $\dot{V}O_2$  with increases in external work, 2) maximal respiratory exchange ratio  $\geq 1.1$ , 3) maximal heart rate of the age-predicted maximum [ $208 - 0.7 \times \text{age (yr)}$ ]  $\geq 90\%$  (32), and 4) RPE  $\geq 18$ ; the highest value of  $\dot{V}O_2$  during the exercise test was then designated as  $\dot{V}O_{2peak}$ .

**Measurement of ccIMT.** Carotid artery IMT was measured from the images obtained with a Vivid i ultrasound system (GE Medical Systems, Milwaukee, WI) equipped with a high-resolution linear array broadband transducer as described previously (12, 18, 24). Ultrasound images were analyzed with image analysis software (Image J; National Institutes of Health, Bethesda, MD). At least 10 IMT measurements were taken at each segment, and the mean values were used for analysis. This technique has excellent day-to-day reproducibility (coefficient of variation  $3 \pm 1\%$ ) for ccIMT.

**Measurement of  $\beta$ -stiffness.** 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 noninvasive determination of arterial compliance (31). The carotid artery diameter was measured from images obtained with an ultrasound system 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.

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) (31). Because baseline levels of blood pressure are subject to hold-down force, the pressure signal obtained by tonometry was calibrated by equating the carotid mean arterial and diastolic blood pressures to the brachial artery value (12, 18, 24, 31). The  $\beta$ -stiffness indexes were calculated with the equation  $[\ln(P1/P0)]/(D1 - D0)/D0$ , where D1 and D0 are the maximal (systolic) and minimal (diastolic) diameters and P1 and P0 are the highest (systolic) and lowest (diastolic) blood pressures, respectively. The day-to-day coefficients of variation for carotid artery diameter, pulse pressure, and  $\beta$ -stiffness were  $2 \pm 1\%$ ,  $7 \pm 3\%$ , and  $5 \pm 2\%$ , respectively.

**SNP genotyping.** Genomic DNA was extracted from plasma buffy coats and buccal cells with a QIAamp DNA Blood Maxi Kit (Qiagen, Tokyo, Japan). MTHFR SNP genotypes were determined by real-time PCR with TaqMan probes and an ABI Prism 7700 Sequence Detector (Perkin-Elmer Applied Biosystems, Foster City, CA) as described previously with minor modifications (16, 23). The gene-specific primers and TaqMan probes for each SNP were synthesized with Primer Express v.1.5 software (Perkin-Elmer Applied Biosystems) according to the published DNA sequences for each SNP as follows: C677T (Ala→Val) in exon 5 of MTHFR (NCBI accession no. rs1801133). The sequences of the oligonucleotides used were as follows: MTHFR forward: 5'-GCACCTGAAGGAGAAGGTGTCT-3', MTHFR reverse: 5'-CCTCAAAGAAAAGCTGCCGTGATG-3', MTHFR/G probe: 5'-ATGAAATCGCTCCCGC-3', MTHFR/A probe: 5'-ATGAAATCGACTCCCGC-3'.

PCR 96-well plates were read on an ABI-7700 with the end-point analysis mode of the SDS v.1.7a software package (Perkin-Elmer Applied Biosystems). Genotypes were determined automatically by the signal processing algorithms in the software.

**Measurements of serum cholesterol, triglyceride, and folic acid levels and plasma glucose and homocysteine levels.** Fasting serum concentrations of cholesterol and triglycerides and plasma concentrations of glucose were determined by standard enzymatic techniques. Plasma homocysteine level was analyzed by gas chromatography-mass spectrometry. Serum folic acid level was determined by micro-biological methods.

**Statistical analysis.** The MTHFR allelic frequencies were calculated with a gene-counting method, and Hardy-Weinberg equilibrium was confirmed with the  $\chi^2$ -test. Student's *t*-test for unpaired values was used to evaluate differences between High-Fit and Low-Fit groups, and ANOVA was used to evaluate differences among genotype groups and differences among each genotype and fitness group. Furthermore, the  $\beta$ -stiffness, ccIMT, and plasma homocysteine level comparisons between the genotype groups in each High-Fit and Low-Fit group were assessed by an analysis of covariance (ANCOVA) model that included age as covariates. Values are expressed as means  $\pm$  SE, and  $P < 0.05$  was taken to indicate significance.

## RESULTS

**Comparison of characteristics in low- and high-cardiorespiratory fitness groups.** In the High-Fit group, body weight, %fat, and triglyceride levels were significantly lower than those in the Low-Fit group. High-density lipoprotein (HDL) level was significantly higher in the High-Fit group than in the Low-Fit group (Table 1). There were no significant differences in age, height, SBP, DBP,  $\beta$ -stiffness, ccIMT, total cholesterol, glucose, homocysteine, or folic acid levels between the High-Fit and Low-Fit groups (Table 1).

**Comparison of characteristics between genotypes.** We analyzed the MTHFR genotypes of the study subjects (Table 2), and no significant differences were found in the frequency of these polymorphisms between sexes. In addition, the allele frequencies did not deviate from the expected Hardy-Weinberg equilibrium.

Table 1. Characteristics of subjects in high-cardiorespiratory fitness and low-cardiorespiratory fitness groups

	High-Fit	Low-Fit
Age, yr	39 ± 1	38 ± 1
Body weight, g	58 ± 1*	60 ± 1
Height, cm	163 ± 1	163 ± 1
%Fat	21.2 ± 0.3*	26.4 ± 0.4
SBP, mmHg	112 ± 1	112 ± 1
DBP, mmHg	65 ± 1	66 ± 1
β-Stiffness, AU	8.4 ± 0.2	8.8 ± 0.3
ccIMT, mm	0.59 ± 0.01	0.59 ± 0.01
Total cholesterol, mg/dl	191 ± 2	190 ± 2
HDL cholesterol, mg/dl	69 ± 1*	63 ± 1
Triglycerides, mg/dl	67 ± 1*	72 ± 2
Glucose, mg/dl	89 ± 1	90 ± 1
Homocysteine, mmol/l	7.7 ± 0.2	7.6 ± 0.2
Folic acid, ng/ml	9.8 ± 0.3	9.3 ± 0.2
VO <sub>2peak</sub> , ml·kg <sup>-1</sup> ·min <sup>-1</sup>	40.9 ± 0.5*	31.1 ± 0.4

Values are means ± SE. High-Fit, high cardiorespiratory fitness; Low-Fit, low cardiorespiratory fitness; SBP, systolic blood pressure; DBP, diastolic blood pressure; β-stiffness, carotid β-stiffness; AU, arbitrary units; ccIMT, common carotid intima-media thickness; HDL, high-density lipoprotein; VO<sub>2peak</sub>, peak oxygen uptake. \**P* < 0.05 vs. Low-Fit.

We next compared the characteristics of subjects with different gene polymorphisms (Table 3). In the MTHFR C677T genotypes, plasma homocysteine level was significantly higher in the TT genotype than in the CC and CT genotypes. There were no significant differences in age, body weight, height, %fat, SBP, DBP, β-stiffness, ccIMT, total cholesterol, HDL cholesterol, triglycerides, glucose, homocysteine, folic acid, or VO<sub>2peak</sub> between these groups.

**Comparison of characteristics between genotypes and cardiorespiratory fitness groups.** We compared the characteristics of subjects with different genotypes and fitness levels (Table 4). In the MTHFR C677T genotypes in the High-Fit group, body weight (vs. CT and TT genotypes), %fat (vs. all genotypes), and triglycerides (vs. TT genotypes) were significantly lower than those in the Low-Fit group, and HDL cholesterol level (vs. CT and TT genotypes) and VO<sub>2peak</sub> (vs. all genotypes) were significantly higher than those in the Low-Fit group. VO<sub>2peak</sub> in the High-Fit group with TT genotype was lower than those in the CC and CT genotypes. There were no significant differences in age, height, SBP, DBP, ccIMT, total cholesterol, HDL cholesterol, glucose, or folic acid between genotypes or cardiorespiratory fitness groups.

**Comparison of arterial stiffness and plasma homocysteine levels between genotypes and cardiorespiratory fitness groups.** There was a significant interaction effect of fitness and

Table 2. Distribution of gene polymorphisms of MTHFR (C677T) and allele frequency in study subjects

	Total	Male	Female
Genotypes, %			
CC	35 (268)	41 (97)	33 (171)
CT	50 (384)	44 (106)	53 (278)
TT	15 (111)	15 (36)	14 (75)
Allele frequency			
MTHFR (C allele)	0.65	0.59	0.67

Numbers of subjects are indicated in parentheses. Genotype frequencies did not deviate from Hardy-Weinberg equilibrium. No difference was found between sexes. MTHFR, 5,10-methylenetetrahydrofolate reductase.

Table 3. Genotypes of MTHFR C677T and subject characteristics

	MTHFR C677T		
	CC	CT	TT
Age, yr	40 ± 1	39 ± 1	41 ± 2
Body weight, g	59 ± 1	58 ± 1	59 ± 1
Height, cm	164 ± 1	162 ± 1	162 ± 1
%Fat	23.3 ± 0.5	24.1 ± 0.4	24.3 ± 0.7
SBP, mmHg	113 ± 1	112 ± 1	114 ± 1
DBP, mmHg	66 ± 1	66 ± 1	67 ± 1
β-Stiffness, AU	8.5 ± 0.3	8.2 ± 0.2	9.2 ± 0.6
ccIMT, mm	0.59 ± 0.01	0.59 ± 0.01	0.60 ± 0.01
Total cholesterol, mg/dl	191 ± 2	191 ± 2	196 ± 4
HDL cholesterol, mg/dl	66 ± 1	66 ± 1	65 ± 1
Triglycerides, mg/dl	71 ± 2	69 ± 1	70 ± 2
Glucose, mg/dl	90 ± 1	89 ± 1	90 ± 1
Homocysteine, mmol/l	7.4 ± 0.1	7.4 ± 0.1	9.7 ± 0.5*†
Folic acid, ng/ml	9.8 ± 0.2	9.5 ± 0.3	8.7 ± 0.4
VO <sub>2peak</sub> , ml·kg <sup>-1</sup> ·min <sup>-1</sup>	36.4 ± 0.7	35.9 ± 0.6	35.7 ± 0.9

Values are means ± SE. \**P* < 0.05 vs. CC; †*P* < 0.05 vs. CT.

MTHFR C677T polymorphism on β-stiffness (*P* = 0.0017) but not on ccIMT (*P* = 0.6020). The β-stiffness of subjects with the TT genotype of MTHFR C677T in the Low-Fit group was significantly higher than that of individuals with the CC and CT genotypes, but there were no significant differences in β-stiffness of subjects with CC, CT, and TT genotypes in the High-Fit group (Fig. 1). However, there were no significant differences in ccIMT between MTHFR genotypes in the Low-Fit and High-Fit groups (Table 4). In addition, there was a significant association between plasma homocysteine level and MTHFR C677T polymorphism (*P* < 0.0001). The plasma homocysteine concentrations in subjects with the TT genotype of MTHFR in both Low-Fit and High-Fit groups were significantly higher than those of individuals with the CC and CT genotypes in each fitness group (Fig. 2).

To further explore the possible relationship between arterial stiffness (β-stiffness) and plasma homocysteine levels, we performed regression analyses between β-stiffness and plasma homocysteine level (Fig. 3). In the Low-Fit group, there were positive and significant correlations between β-stiffness and plasma homocysteine level in the individuals with the TT genotype of MTHFR ( $y = 0.78x + 2.80$ ,  $r = 0.71$ ,  $P < 0.0001$ ). There were no significant correlations for the CC and CT genotypes. In the High-Fit group, there were no significant correlations for any of the MTHFR genotypes (Fig. 3). The slopes of the regression lines were significantly different between High-Fit and Low-Fit groups in TT genotype of MTHFR (*P* < 0.05). There was a slight significant correlation between plasma homocysteine and VO<sub>2peak</sub> ( $y = 0.04x + 6.06$ ,  $r = 0.16$ ,  $P < 0.05$ ).

## DISCUSSION

The present cross-sectional study demonstrated the associations among arterial stiffness, cardiorespiratory fitness, and polymorphisms in the MTHFR gene in Japanese subjects. Plasma homocysteine concentrations were significantly higher in individuals with the TT genotype of MTHFR than in those with the CC and CT genotypes in each fitness group. Interestingly, in the Low-Fit subjects carotid β-stiffness was higher in the TT genotype individuals than in those with the CC and CT

Table 4. Characteristics of subjects in each cardiorespiratory fitness and genotype of MTHFR C677T group

	Low-Fit			High-Fit		
	CC	CT	TT	CC	CT	TT
Age, yr	39 ± 1	38 ± 1	37 ± 2	38 ± 1	38 ± 1	41 ± 2
Body weight, g	60 ± 1	60 ± 1	61 ± 2	59 ± 1	58 ± 1*	57 ± 1*
Height, cm	164 ± 1	162 ± 1	164 ± 1	164 ± 1	163 ± 1	162 ± 1
%Fat	25.3 ± 0.7	26.9 ± 0.5	27.1 ± 1.1	20.7 ± 0.6*	21.0 ± 0.5*	22.7 ± 0.8*
SBP, mmHg	111 ± 1	112 ± 1	115 ± 3	113 ± 1	112 ± 1	111 ± 2
DBP, mmHg	66 ± 1	66 ± 1	69 ± 1	66 ± 1	65 ± 1	66 ± 1
ccIMT, mm	0.60 ± 0.01	0.59 ± 0.01	0.58 ± 0.01	0.58 ± 0.01	0.58 ± 0.01	0.60 ± 0.02
Total cholesterol, mg/dl	190 ± 3	189 ± 3	193 ± 6	189 ± 3	191 ± 3	195 ± 5
HDL cholesterol, mg/dl	65 ± 1	63 ± 1	65 ± 1	67 ± 1	70 ± 1*	70 ± 2*
Triglycerides, mg/dl	75 ± 3	70 ± 2	75 ± 4	68 ± 3	67 ± 2	64 ± 4*
Glucose, mg/dl	89 ± 1	90 ± 1	90 ± 1	90 ± 1	89 ± 1	89 ± 1
Folic acid, ng/ml	9.8 ± 0.4	9.2 ± 0.3	8.4 ± 0.8	9.9 ± 0.4	9.9 ± 0.4	9.0 ± 0.6
VO <sub>2peak</sub> , ml·kg <sup>-1</sup> ·min <sup>-1</sup>	31.1 ± 0.8	30.6 ± 0.5	32.9 ± 1.4	41.4 ± 0.9*	41.2 ± 0.8*	38.1 ± 1.1*†

Values are means ± SE. \**P* < 0.05 vs. each genotype in Low-Fit; †*P* < 0.05 vs. CC and CT in High-Fit.

genotypes of MTHFR C677T. However, there were no such differences in High-Fit subjects. In addition,  $\beta$ -stiffness and plasma homocysteine levels were positively correlated in the Low-Fit subjects with the TT genotype ( $r = 0.71$ ,  $P < 0.0001$ ) but were not correlated in the other groups.

The TT genotype at C677T of the MTHFR gene was associated with elevated plasma homocysteine level but showed no effect on carotid arterial stiffness in the present study. Elevated plasma homocysteine level is associated with vascular function and increased risk of arterial stiffness (7, 15, 30, 36), because exposure of endothelial cells to elevated homocysteine levels leads to decreased availability of NO and results in impairment of endothelium-dependent vasodilation in humans (6, 29, 33, 35). In subjects with lower fitness, the TT genotype at C677T of the MTHFR gene increased arterial stiffness, but this was not seen in higher-fitness subjects. Moreover, homocysteine level was positively associated with

arterial stiffness only in lower-fitness subjects with the TT genotype. Regular exercise improves endothelial function through increased NO production and decreased endothelin-1 concentration (22). Hayward et al. (14) reported that exercise training improved endothelium-dependent vasodilation under conditions of homocysteine exposure, and this may contribute to the increased endothelial nitric oxide synthase (eNOS) protein levels and eNOS activity in the aorta of rats. Exercise training induced changes in expression levels of vasodilation-related molecules, including eNOS, in the aorta of rats with improvement of arterial stiffness (21). Therefore, regardless of elevated homocysteine level induced by the T allele of the MTHFR C677T polymorphism, regular exercise is considered to decrease stiffening in the central artery via improvement of endothelial function. Thus regular exercise, which can maintain and obtain sufficient cardiorespiratory fitness, may be needed to cancel the genetic negative effects of MTHFR polymorphism in subjects with the TT genotype at C677T of the MTHFR gene.

In the present study, higher cardiorespiratory fitness did not seem to be associated with elevated plasma homocysteine

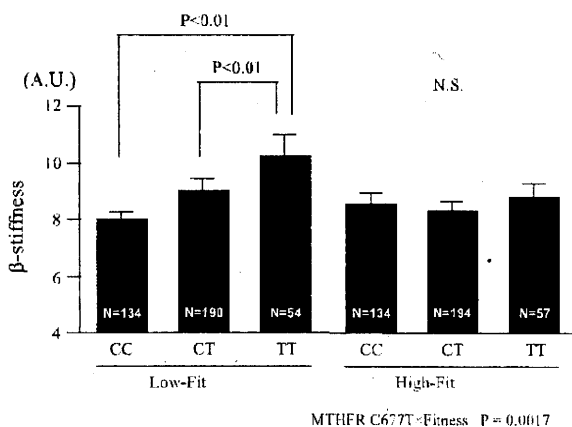


Fig. 1. Carotid  $\beta$ -stiffness ( $\beta$ -stiffness) of each fitness group and genotype of 5,10-methylenetetrahydrofolate reductase (MTHFR) gene polymorphism (C677T; CC, CT, TT genotypes) of subjects in a cross-sectional study. Subjects were divided into low-cardiorespiratory fitness (Low-Fit) and high-cardiorespiratory fitness (High-Fit) groups, with the dividing line set at the median value of peak oxygen uptake (VO<sub>2peak</sub>), as an index of cardiorespiratory fitness, in each sex and decade as a cutoff. Differences in  $\beta$ -stiffness between each fitness group and genotype were assessed by an analysis of covariance (ANCOVA) model that included age as a covariate. Data are expressed as means ± SE for numbers of subjects indicated. AU, arbitrary units; NS, not significant.

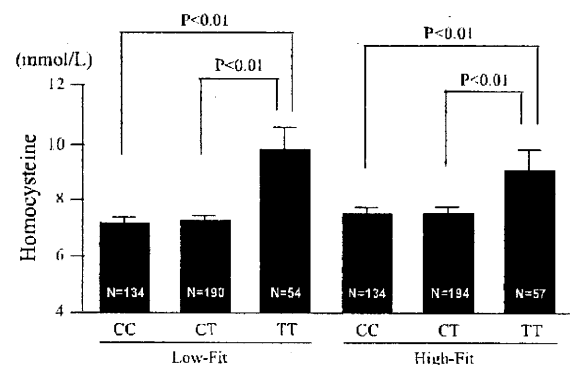


Fig. 2. Plasma homocysteine levels of each fitness group and genotype of MTHFR gene polymorphism (C677T; CC, CT, TT genotypes) of subjects in a cross-sectional study. Subjects were divided into Low-Fit and High-Fit groups, with the dividing line set at the median value of VO<sub>2peak</sub>, as an index of cardiorespiratory fitness, in each sex and decade as a cutoff. Differences in plasma homocysteine levels between each fitness group and genotype were assessed by an ANCOVA model that included age as a covariate. Data are expressed as means ± SE for numbers of subjects indicated.

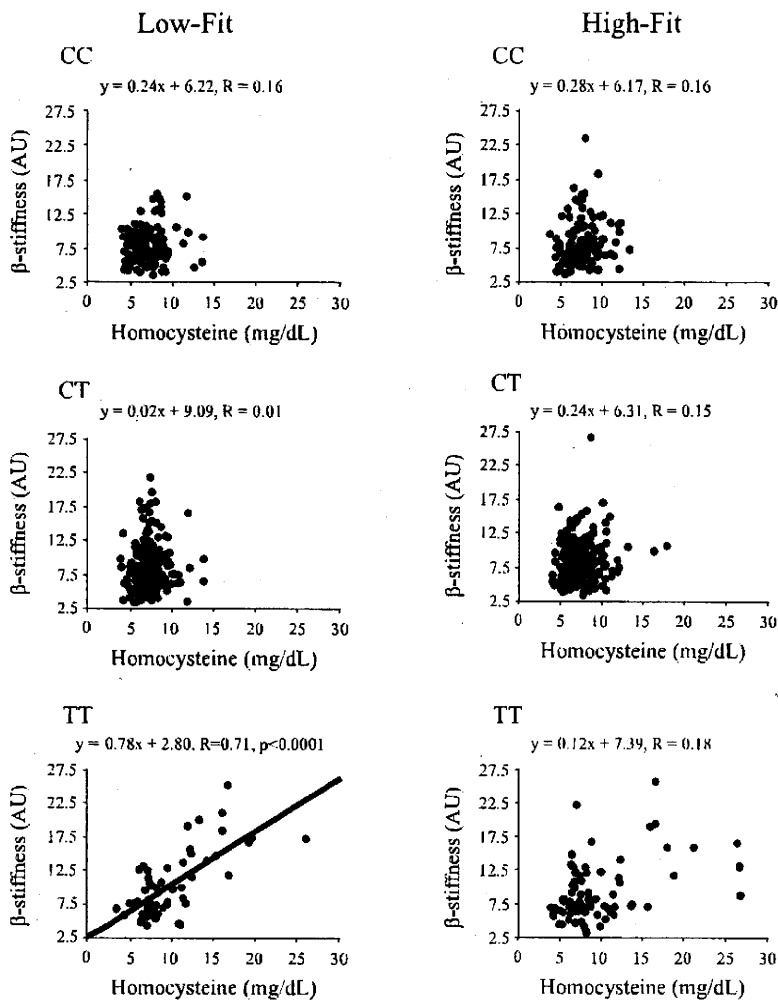


Fig. 3. Correlations between  $\beta$ -stiffness and plasma homocysteine levels of each genotype of MTHFR gene polymorphism [C677T; CC (top), CT (middle), TT (bottom) genotypes]. Subjects were divided into Low-Fit (left) and High-Fit (right) groups, with the dividing line set at the median value of  $\dot{V}O_{2peak}$ , as an index of cardiorespiratory fitness, in each sex and decade as a cutoff.

levels in individuals with the TT genotype at C677T of the MTHFR gene. There have been several studies regarding the association with homocysteine status according to varied cardiorespiratory fitness levels and age. The relationship between  $\dot{V}O_{2peak}$  and plasma homocysteine is unaffected in men or women aged 30–59 yr (10) and inversely associated in women (mean age 33.5 yr) but not in men (mean age 33.1 yr) (19). Moreover, the relationship was unaffected in children and adolescents (26), and a negative association was observed in women but not in men (27). Inconsistent results were also reported in athletes, in whom plasma homocysteine levels were elevated (25) or decreased compared with untrained control subjects (13). Thus the relationship between cardiorespiratory fitness and homocysteine status was not consistent. This discrepancy may be influenced by differences in physical fitness level, age, and genetic effects, such as MTHFR C677T, in each study. Although we extended our research effort to the association with MTHFR genotype, the present results could not account for the discrepancy. Therefore, further studies are required to examine differences in the relationship between different physical fitness levels and plasma homocysteine levels in various age groups.

In the present study, subjects were divided into Low-Fit and High-Fit groups, with the dividing line set at the median value of  $\dot{V}O_{2peak}$  in each sex and decade, which were similar to the respective mean values for the Japanese population. It is considered that a higher level of exercise than the mean value for the Japanese population may be required to attenuate arterial stiffening in the TT genotype. However, further studies are necessary to determine the required amount of exercise.

Carotid  $\beta$ -stiffness was higher in the TT genotype at C677T of the MTHFR gene in subjects with lower cardiorespiratory fitness but was not altered in those with CC and CT genotypes. However, there were no effects of SNP on arterial stiffness in individuals with higher cardiorespiratory fitness. In contrast, ccIMT, evaluated as the thickness of the carotid arterial wall, was unaffected by the relationship between MTHFR C677T genotype and fitness level. Previous studies demonstrated the relationship between ccIMT and homocysteine levels in female smokers (17), whereas no relationship was observed in patients with atherosclerotic disease (28). de Bree et al. (10) reported no effect of ccIMT or pulse wave velocity on increases in plasma homocysteine levels in healthy middle-aged French subjects. Thus measurements using carotid  $\beta$ -stiffness may be a sensi-

tive means of detecting the effect of cardiorespiratory fitness on stiffening in the central artery induced by MTHFR C677T polymorphism in healthy subjects.

A previous study indicated the effects of plasma homocysteine level on the association between C677T and A1298C or G1793A (3). Further studies are required to determine the effects of fitness on the association between arterial stiffness and MTHFR haplotype. In addition, Labayen et al. (20) recently reported the effects of polymorphisms in the UCP3 gene on plasma homocysteine levels during youth. Plasma homocysteine level was higher in the TT and CT genotypes of the rs1800849 polymorphism in the UCP3 gene compared with individuals with the CC genotype after adjustment for sex, age, pubertal status, folate and vitamin B<sub>12</sub> intake, and MTHFR C677T polymorphism. Moreover, the T allele of the rs1800849 polymorphism was associated with elevated homocysteine levels in young subjects with low fitness, but not with moderate or high cardiorespiratory fitness, indicating that cardiorespiratory fitness modifies the association between the rs1800849 polymorphism and homocysteine. The UCP3 gene polymorphism-induced increase in plasma homocysteine level in subjects with low fitness may affect arterial stiffness. Therefore, further studies are required to examine the effects of UCP3 gene polymorphism on the relationships among homocysteine, fitness, and arterial stiffness. Furthermore, although homocysteine is affected by endothelial function, we did not measure endothelial function, such as flow-mediated diameter, plasma NO, plasma endothelin-1, etc., in the present study. Therefore, further studies are required to determine the endothelial function parameters and the effects of gene polymorphism and fitness on homocysteine and endothelial function. Although it is well known that dietary folate intake is a major determinant of plasma homocysteine level, it could not be assessed in all subjects in the present study. Further studies are required to determine the effects of folate intake. Finally, the present study population included only Asian (Japanese) subjects; therefore, our data may not be applicable to other populations because genotypic distribution appears to show ethnic differences.

We investigated the associations among cardiorespiratory fitness, arterial stiffness, and C677T polymorphism of the MTHFR gene in healthy Japanese subjects. The results of this study indicated a lack of arterial stiffening associated with the TT genotype at C677T of the MTHFR gene in cardiorespiratory fit subjects. Thus habitual exercise-induced cardiovascular fitness may affect cardiovascular adaptations to molecular variation in the MTHFR gene in Japanese subjects. However, further studies are required to clarify the effects of fitness or physical activity on the risk of cardiovascular disease associated with genetic factors.

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#### DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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# METs in Adults While Playing Active Video Games: A Metabolic Chamber Study

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## ABSTRACT

MIYACHI, M., K. YAMAMOTO, K. OHKAWARA, and S. TANAKA. METs in Adults While Playing Active Video Games: A Metabolic Chamber Study. *Med. Sci. Sports Exerc.*, Vol. 42, No. 6, pp. 1149–1153, 2010. **Purpose:** Active video game systems controlled through arm gestures and motions (Nintendo Wii Sports) and video games controlled through force plate (Wii Fit Plus) are becoming increasingly popular. This study was performed to determine the energy expenditure (EE) during Wii Fit Plus and Wii Sports game activities. **Methods:** Twelve adult men and women performed all the activities of Wii Sports (five activities: golf, bowling, tennis, baseball, and boxing) and Wii Fit Plus (63 activities classified as yoga, resistance, balance, and aerobic exercises). Each activity was continued for at least 8 min to obtain a steady-state EE. Because EE was assessed in an open-circuit indirect metabolic chamber consisting of an airtight room (20,000 or 15,000 L), subjects were freed of apparatus to collect expired gas while playing the games. MET value was calculated from resting EE and steady-state EE during activity. **Results:** The mean MET values of all 68 activities were distributed over a wide range from 1.3 METs (Lotus Focus) to 5.6 METs (single-arm stand). The mean MET values in yoga, balance, resistance, and aerobic exercise of Wii Fit Plus and Wii Sports were 2.1, 2.0, 3.2, 3.4, and 3.0 METs, respectively. Forty-six activities (67%) were classified as light intensity (<3 METs), and 22 activities (33%) were classified as moderate intensity (3.0–6.0 METs). There were no vigorous-intensity activities (>6.0 METs). **Conclusions:** Time spent playing one-third of the activities supplied by motion- and gesture-controlled video games can count toward the daily amount of exercise required according to the guidelines provided by the American College of Sports Medicine and the American Heart Association, which focus on 30 min of moderate-intensity daily physical activity  $5 \text{ d} \cdot \text{wk}^{-1}$ . **Key Words:** ENERGY EXPENDITURE, HUMAN CALORIMETER, METABOLIC EQUIVALENTS, Wii

Adults in developed countries are currently recommended to take more than a half hour of moderate to vigorous physical activity each day (6). However, many individuals spend many hours sitting in front of their TV playing video games. More than half of American adults (53%) play video games, and about one in five adults (21%) play every day or almost every day (9). This type of sedentary behavior is causally linked to chronic diseases and obesity (5,13).

The active video game systems controlled through arm gestures and motions (Wii Sports; Nintendo Inc., Kyoto, Japan) as well as the video games controlled through force plate (Wii Fit Plus; Nintendo Inc.) are becoming increasingly popular. These systems may attenuate a sedentary lifestyle and permit video game enthusiasts to increase their

energy expenditure (EE), which is associated with prevention of obesity and lifestyle-related diseases (7,10). Several studies indicated that playing new-generation active computer games involves significantly greater EE than playing sedentary computer games but does not use as much energy as playing sport itself (3,4,8). The energy spent while playing active Wii Sports games was not of sufficiently high intensity to contribute toward the recommended daily amount of exercise (3,4,8). However, EE for these activities may have been underestimated because measurements were obtained using the Intelligent Device for Energy Expenditure and Activity (IDEEA) system (3) or indirect calorimeter with a facemask connected directly to an analyzer (4,8). The IDEEA does not detect arm or trunk movements well, considering the principle for physical activity evaluation (4,15), and therefore may underestimate EE. During measurement of EE with a facemask, the subjects' movements were tightly restricted (4,8). This may result in misleading conclusions regarding whether sufficient EE can be obtained while playing any mode of Wii Sports or Wii Fit Plus. Therefore, further research is needed to understand the energy load of the new modes of computer interaction and game play.

The present study was performed to determine EE and MET during various modes of activity in Wii Sports and Wii Fit Plus software using an open-circuit indirect metabolic chamber. The metabolic chamber can correctly

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measure whole-body EE and MET intensities while subjects are freely playing the game.

## METHODS

**Subjects.** Twelve Japanese men ( $n = 7$ ) and women ( $n = 5$ ) participated in this study. All subjects were adults (25–44 yr) and were free of chronic diseases that could affect metabolism or daily physical activity. They had not engaged in regular intensive sports or physical activity for the past year. Informed consent was obtained from all subjects. The study protocol was approved by the ethical committee of the National Institute of Health and Nutrition.

**Experimental design.** Each subject completed metabolic chamber measurement under three different protocols on three different days: sitting rest, Wii Fit Plus balance and resistance exercises, Wii Fit Plus yoga and aerobic exercises, and Wii Sports. The order of these protocols was randomly assigned for each subject. Resting metabolic rate was evaluated immediately before performing activities of Wii Fit Plus balance and resistance exercises in the morning. Subjects abstained from meals and drink, except water, for at least 5 h before entering the metabolic chamber. Weight, height, and body composition analyzed by bioelectrical impedance were measured immediately before each session.

Wii Fit Plus software contains various activities consisting of 18 modes of yoga, 15 modes of resistance exercise, 16 modes of balance exercise, and 14 modes of aerobic exercise. Wii Sports software includes five activities: golf, bowling, tennis, baseball, and boxing. Each activity was continued for at least 8 min to obtain the steady-state EE separated by appropriate rest periods. Although game lengths of each activity were initially from 1 to 4 min, personal skills, fitness, and type of game resulted in fluctuations in the game lengths. The games in all activities were restarted immediately over and over again for 8 min. All subjects began each activity at the beginner level, and they performed these in an active fashion.

**Metabolic chamber.** The open-circuit indirect metabolic chamber used consisted of an airtight room (20,000 or 15,000 L) equipped with a bed, a desk, a chair, a TV with a video game player, a telephone, and a toilet. Thus, subjects were freed of apparatus to collect expired gas while playing the games. The temperature and the relative humidity in the room were controlled at 25°C and 55%, respectively. The oxygen ( $O_2$ ) and carbon dioxide ( $CO_2$ ) concentrations of the air supply and exhaust were measured by mass spectrometry. For each experiment, the gas analyzer (ARCO-1000A-CH; Arco System, Kashiwa, Japan) was initially calibrated using a certified gas mixture and atmospheric air. The flow rate exhausted from the chamber was measured by pneumotachography (FLB1; Arco System). The flowmeter was calibrated before each measurement, and the flow rate was maintained at 60 L·min<sup>-1</sup> ambient temperature pressure (ATP).  $O_2$  consumption and  $CO_2$

production ( $\dot{V}O_2$  and  $\dot{V}CO_2$ , respectively) were determined from the flow rate of exhaust from the chamber and the concentrations of the inlet and outlet air of the chamber, respectively (12). EE was estimated from  $\dot{V}O_2$  and  $\dot{V}CO_2$  using Weir's (14) equation. The accuracy and the precision of our metabolic chamber for measuring EE as determined by the alcohol combustion test were 99.2% ± 0.7% (mean ± SD) over 6 h and 99.2% ± 3.0% over 30 min (2).

Each activity was continued for at least 8 min. The metabolic chamber continuously analyzed  $O_2$  and  $CO_2$  concentrations for each gas and flow rate five times per minute and calculated EE for each minute. The EE increased progressively in the first 2–3 min of each activity, and then steady-state EE was obtained from 3 to 8 min. Therefore, we defined the mean value of EE for the last 5 min as steady-state EE of each activity. This increase in EE within a few minutes and the subsequent steady-state EE indicated that our metabolic chamber method has sufficient sensitivity. MET value was calculated from resting and steady-state EE during the activity.

**Data calculation and analysis.** All data are expressed as the means ± SD. Data were analyzed using one-way repeated-measures ANOVA with corrected *post hoc* paired *t*-test. We used the Statistical Package for the Social Sciences for Windows (SPSS Inc., Chicago, IL) for statistical analyses, and  $P < 0.05$  was taken to indicate statistical significance.

## RESULTS

The characteristics of the study subjects were as follows: age = 34 ± 6 yr, height = 167.4 ± 7.6 cm, body weight = 64.3 ± 15.0 kg, and percent fat = 22.3% ± 3.9%. Figure 1 shows the MET intensities during gaming. There were no significant differences in MET values between men and women. Therefore, mean MET values of each activity were calculated from the data of both sexes combined. The mean MET values of all 68 activities were distributed over a wide range from 1.3 METs (Lotus Focus: balance exercise) to 5.6 METs (single-arm stand: resistance exercise). The mean MET values in yoga, balance, resistance, and aerobic exercise of Wii Fit Plus and Wii Sports were 2.1 ± 0.6, 2.0 ± 0.6, 3.2 ± 1.2, 3.4 ± 0.9, and 3.0 ± 0.9 METs, respectively. The MET values of yoga and balance exercise were significantly lower than those of resistance and aerobic exercise of Wii Fit Plus or Wii Sports. Forty-six activities (67%) were classified as light intensity (<3 METs), and 22 activities (33%) were classified as moderate intensity (3.0–6.0 METs). There was no activity with intensity >6.0 METs.

The MET values of playing Wii Sports versions of activities were markedly lower than those of actual sports activities reported previously as follows (1): golf = 3.0–4.5 METs, bowling = 3.0, tennis = 5.0–7.0 METs, baseball = 5.0 METs, and boxing = 6.0–12.0 METs. However, the MET values of the Wii Fit Plus versions of yoga and



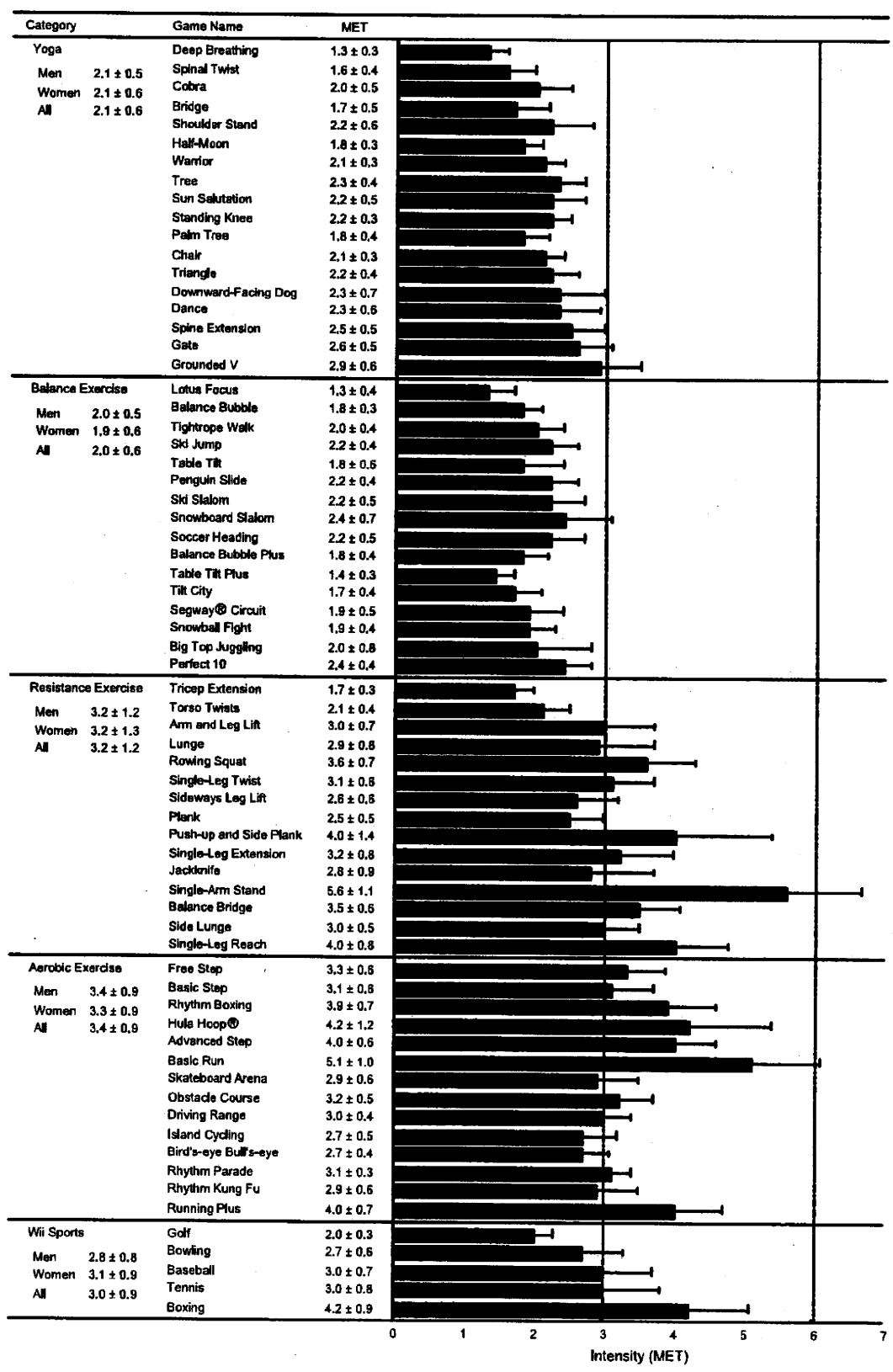


FIGURE 1—Mean values ± SD of METs while playing Wii Fit Plus and Wii Sports.

resistance exercise were similar to actual yoga (2.5 METs) and resistance exercise (3.0 METs) (1).

## DISCUSSION

We determined EE and MET values during Wii Sports and Wii Fit Plus game activities using an open-circuit indirect metabolic chamber. The main findings of the present study were as follows. First, the mean MET values in yoga, balance, resistance, and aerobic exercise of Wii Fit Plus and Wii Sports were 2.1, 2.0, 3.2, 3.4, and 3.0 METs, respectively. Second, 46 activities (67%) were classified as light intensity (<3 METs), and 22 activities (33%) were classified as moderate intensity (3.0–6.0 METs). There were no vigorous-intensity activities (>6.0 METs). These findings suggest that time spent playing one-third of the activities supplied by motion- and gesture-controlled video games can partially count toward the daily amount of exercise required according to the guidelines provided by the American College of Sports Medicine (ACSM) and the American Heart Association (AHA) (6).

The ACSM or AHA physical activity guidelines (6) focus on 30 min of moderate-intensity daily physical activity 5 d·wk<sup>-1</sup> or vigorous-intensity aerobic activity for a minimum of 20 min for 3 d·wk<sup>-1</sup>. Moderate and vigorous physical activities were generally defined as intensities of 3.0–6.0 and >6.0 METs, respectively (6). Twenty-two (33%) of the 68 activities in Wii Fit Plus and Wii Sports were classified as moderate-intensity activities on the basis of MET intensity. Taken together, the observations of the present study suggest that the time spent playing Wii Fit Plus or Wii Sports can partially count toward the daily amount of exercise required according to the guidelines provided by the ACSM and the AHA (6). On the other hand, Graves et al. (3) concluded that Wii Sports games were not sufficiently vigorous to meet the guidelines for daily physical activity in children. We speculate that this discrepancy may be associated with differences in age of subjects and of measurement methods in EE and MET values (15).

Wii Sports gaming or Wii Fit Plus aerobic exercise involved less EE than authentic sports or exercises (1) because playing these active video games involved little horizontal locomotion. However, these light to moderate activities may

contribute to increased EE, and even the small energy gap induced by the increased EE may be effective for prevention of weight gain (7). Furthermore, there were no moderate- or vigorous-intensity activities in Wii Fit Plus yoga and balance exercise. However, we should emphasize that yoga and balance exercise are effective in improving flexibility and in fall prevention, respectively (11). In addition, active computer games stimulated positive activity behaviors: the players were on their feet, and they moved in all directions while performing basic motor control and fundamental movement skills that were not evident during seated gaming. Given the current prevalence of overweight and obesity, such positive behaviors should be encouraged.

The strength of the present study is that the metabolic chamber method could replicate the conditions under which the subjects play the games in their home because subjects were free from apparatus used to measure EE when playing the game. In fact, the MET values of Wii Sports activities in our study were slightly higher than those in previous reports using the IDEEA system (3) or indirect calorimeter (4,8). On the other hand, the limitations of this study were that the sample size was small and the results were applicable only to healthy adults and to the Wii Fit Plus and Wii Sports computer games, which are more active than other Wii games.

## CONCLUSIONS

We determined the MET values of Wii Sports and Wii Fit Plus game activities under free-living conditions using an open-circuit indirect metabolic chamber in healthy adults. Time spent playing one-third of the activities supplied by Wii Sports and Wii Fit Plus can count toward the daily amount of exercise required according to the guidelines provided by the ACSM and the AHA, which focus on 30 min of moderate-intensity daily physical activity 5 d·wk<sup>-1</sup>. Further research is needed to investigate the efficacy of the games on health promotion.

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The results of the present study do not constitute endorsement by the authors and the American College of Sports Medicine.

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## **Longer Time Spent in Light Physical Activity Is Associated With Reduced Arterial Stiffness in Older Adults**

Yuko Gando, Kenta Yamamoto, Haruka Murakami, Yumi Ohmori, Ryoko Kawakami, Kiyoshi Sanada, Mitsuru Higuchi, Izumi Tabata and Motohiko Miyachi

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