cients of variation were 2±1%, 7±3%, and 5±2% for the carotid artery diameter, pulse pressure, and arterial compliance, respectively.

Measurements during Dynamic Resistance Exercise

Radial BP and ECG

To determine circulatory response, radial BP and ECG were recorded simultaneously in the sitting position at baseline, during exercise, and during the recovery period. ECG and radial BP waveforms were determined using arterial tonometry (JENTOW-7700; Colin Medical Technology) and standard lead electrocardiography (Life Scope 11; Nihon Kohden, Tokyo, Japan), respectively. Both ECG and arterial BP waveforms were sampled at 1,000 samples per second by connecting each device to a computer using an A/D converter (PowerLab; AD Instruments, Colorado Springs, USA). The principle of arterial tonometry is that BP at the radial artery can be obtained by measuring the reaction forces produced by flattening the radial artery. Recently, this method has become preferred over the conventional finger photoplethysmographic method (Finapres), and it has been confirmed that the accuracy and reliability of BP measured by tonometry are greater than those of BP measured by the intra-arterial method. A tonometric sensor was attached to the left wrist, and the wrist was placed on a padded platform at the level of the heart. The oscillometric calibrations were carried out for accurate tonometric measurement before, and sometimes during the main experiment (*29*).

Strength Testing

Maximal muscular strength was assessed with a leg press machine using air pressure (Keiser; Fitness Apollo Japan Co., Ltd. Tokyo, Japan). A one-repetition maximum (1RM) was determined by having the subjects perform single repetitions with progressively heavier weights, resting 2–3 min between attempts; the heaviest weight that subjects could lift once through a complete range of movement was considered their 1RM. The day-to-day coefficient of variation for 1RM strength in our laboratory is 4±2%.

Exercise Protocol I

Subjects rested under quiet conditions before beginning the leg press exercise. After a 60-s baseline period, all subjects randomly performed 10 repetitions of the leg press exercise for 40 s at each of 40%, 60%, and 80% 1RM, followed by an 80-s recovery period. One repetition was performed for 4 s (2 s for concentric and 2 s for eccentric contraction). To measure radial BP accurately, the subject's left arm was supported on an adjustable table during measurement. Subjects were stabilized in the apparatus during exercise using their right hand to hold the support handle on the seat. The left arm was allowed to rest freely by their side to avoid interference with the recording of radial BP from this arm. The subjects were encouraged to avoid deep inhalations while performing the Valsalva maneuver during the exercise. Exercise measurements were performed randomly in a day. The interval time between exercises was controlled at 10 min.

Table 1. Subject Characteristics

	Young	Middle-aged
N	12	9
Age, years	21.4±0.5	47.8±1.9
Height, cm	170.6±1.7	170.1±2.1
Body mass, kg	65.3±2.1	67.7±2.9
Resting heart rate, bpm	52.3±1.7	60.8±4.4
Brachial systolic BP, mmHg	118±3	123±4
Brachial diastolic BP, mmHg	67±2	80±3*
Brachial mean BP, mmHg	82±4	96±4*
Brachial PP, mmHg	55±4	43±2*
Carotid systolic BP, mmHg	109±2	119±6
Carotid diastolic BP, mmHg	67±2	80±3*
Carotid PP, mmHg	42±2	38±3
Carotid diastolic diameter, mm	5.9±0.1	6.7±0.3*
Carotid intima-media thickness, mm	0.48±0.02	0.63±0.02*
Carotid arterial compliance, $mm^2/mmHg$	0.17±0.01	0.11±0.01*
Carotid β-stiffness index, a.u.	3.95±0.28	7.30±0.76*
Brachial-ankle PWV, cm/s	1,092±38	1,291±46*
Augmentation index, %	−6.9±5.7	19.6±5.8*
Leg press maximum, kg	350±11	286±19*

Data are mean±SEM. BP, blood pressure; PP, pulse pressure; PWV, pulse wave velosity. Leg press maximum was evaluated by air pressure machine (Keiser; Fitness Apollo Japan Instruments). *Significant at $p<0.05$ *vs.* young.

Exercise Protocol II

Eleven young men and nine middle-aged men were studied using protocol II. All subjects performed 10 repetitions of the leg press exercise at individual absolute intensity (145 kgw) 10 min after the end of protocol I. Protocol II was performed using a procedure similar to that in protocol I.

Data Analysis

In the baseline period, during the leg press exercise and recovery periods, waveforms of ECG and radial BP were recorded continuously and simultaneously on a personal computer (iBook G3; Apple Computer, Cupertino, USA). Heart rate and systolic, diastolic, and mean BP were calculated using the Chart5 software package (AD Instruments). Baseline values of BP were taken as the average of the baseline period (1 min) before exercise. Average values every 4 s for one repetition and peak values of BP were obtained during the 40-s exercise period. Eight BP values in the recovery period were averaged at 0–4, 4–8, 16–20, 36–40, 56–60, 76–80, 96–

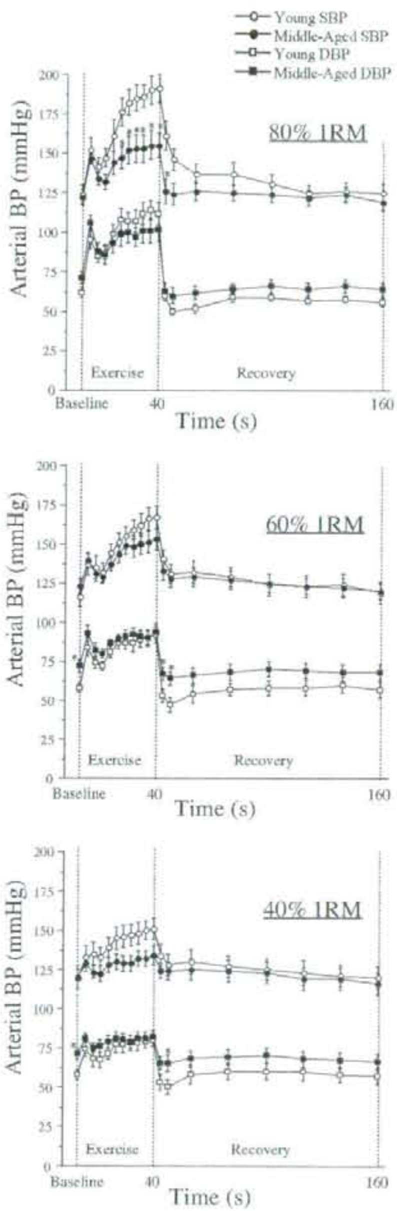

Fig. 1. *Systolic (circles) and diastolic (squares) blood pressure responses during resistance exercises and recovery periods at 40% (bottom), 60% (middle), and 80% (top) of 1RM in young (white) and middle-aged (black) men. Values are means±SEM.* **$p<0.05$ vs. young men.*

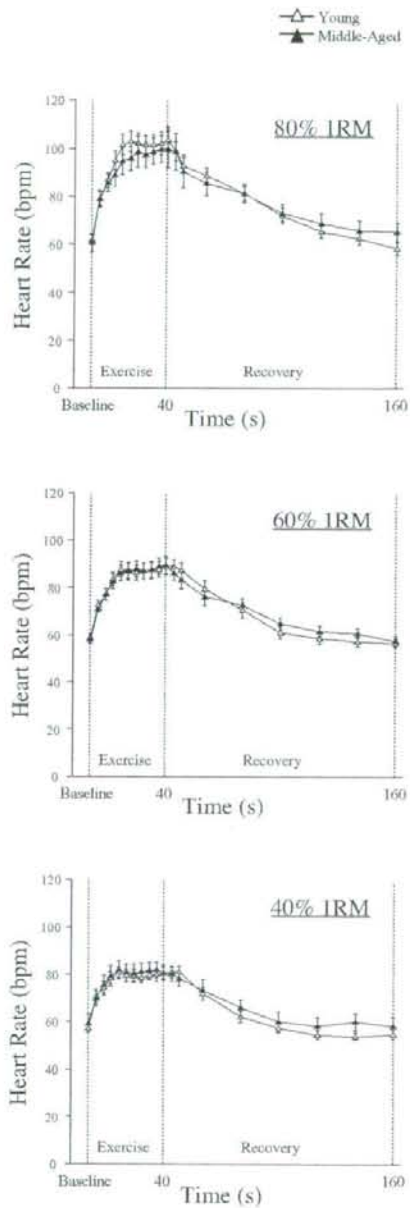

Fig. 2. *Heart rate responses during resistance exercises and recovery periods at 40% (bottom), 60% (middle), and 80% (top) of 1RM in young (white) and middle-aged (black) men. Values are means±SEM.*

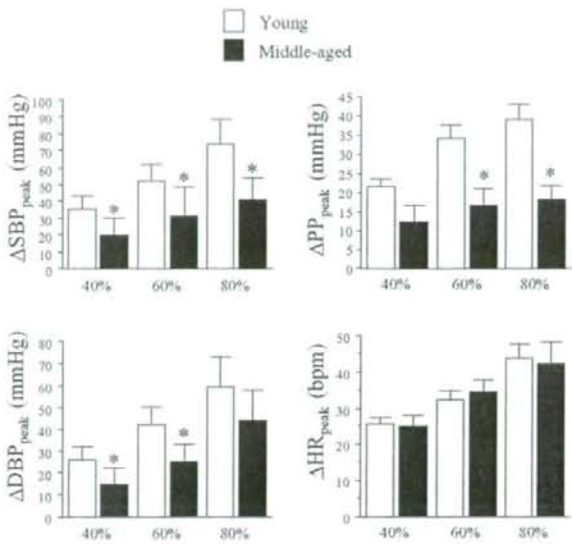

Fig. 3. *The amounts of change in systolic (SBP; top left) and diastolic (DBP; bottom left) blood pressure, pulse pressure (PP; top right) and heart rate (HR; bottom right) responses to resistance exercises at 40%, 60%, and 80% of 1RM in middle-aged (black bar) and young (white bar) men. Values are means±SEM. *$p<0.05$ vs. young men at the same intensity.*

100, and 116–120 s. Heart rate was calculated as the peak value during exercise.

Statistical Analysis

Changes during the leg press exercise were assessed by two-way analysis of variance (group × time) with repeated measures. In the case of significant F-values, a post hoc test (Newman-Keuls method) was used to identify significant differences among mean values. Peak values were analyzed using the t-test. All data are presented as the means±SEM. Statistical significance was set at $p<0.05$ for all comparisons.

Results

Subject Characteristics

Subjects' characteristics at rest are shown in Table 1. There were no significant differences in height, weight, heart rate, or carotid BP between young and middle-aged men in the present study. Brachial diastolic and mean BP and carotid diastolic diameter were higher in the middle-aged men than in the young group ($p<0.05$). Brachial systolic BP and carotid pulse pressure were not significantly different between the two groups. β-Stiffness, augmentation index, and baPWV in the middle-aged men were significantly higher than those in the young group ($p<0.05$). The carotid arterial compliance and leg press maximum of the middle-aged men were significantly lower than those of the young men ($p<0.05$).

Exercise Protocol I

Radial systolic and diastolic BP responses during the exercise and recovery periods are shown in Fig. 1. Baseline values of radial diastolic BP under the 40% and 60% 1RM conditions were higher in middle-aged than in young men, and there were no significant differences between groups in other baseline BP values. Systolic BP for 20–40 s during exercise in the middle-aged men at only 80% 1RM was significantly lower than that in the young group ($p<0.05$). There were no significant differences in heart rate response to resistance exercise between middle-aged and young men at any intensity examined (Fig. 2). Systolic and diastolic BP returned to the baseline values within 60 s during the recovery period. The amounts of change in systolic and diastolic BP and pulse pressure from baseline to the peak response during resistance exercise were significantly lower in the middle-aged men than in the young group at all exercise intensities examined, but there was no significant difference in Δ heart rate (Fig. 3).

Exercise Protocol II

The amounts of change in systolic and diastolic BP and pulse pressure from baseline to the peak response during resistance

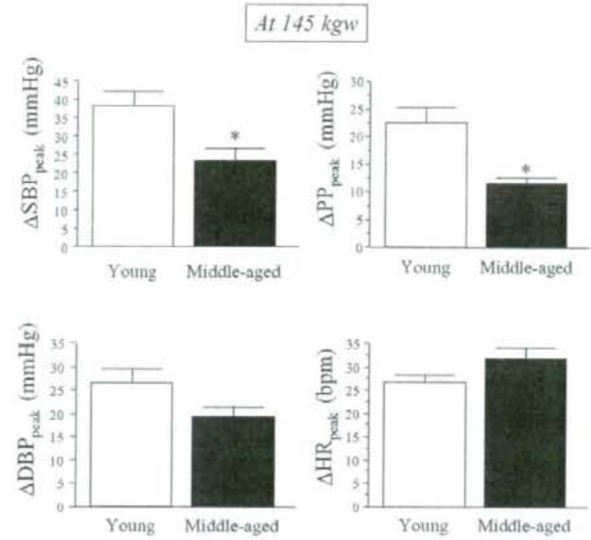

Fig. 4. *The amounts of change in systolic (SBP; top left) and diastolic (DBP; bottom left) blood pressure, pulse pressure (PP; top right) and heart rate (HR; bottom right) responses to resistance exercise at 145 kgw in middle-aged (black bar) and young (white bar) men. Values are means±SEM. *$p<0.05$ vs. young men.*

exercise were lower in the middle-aged men than in the young men at individual absolute intensity, but there was no significant difference in Δheart rate (systole, $p=0.019$; diastole, $p=0.091$; pulse pressure, $p=0.003$; Fig. 4).

Discussion

The major findings of the present study were as follows. 1) The absolute value of BP response to dynamic resistance exercise at 80% 1RM was lower in middle-aged men with stiffening arteries than in young men with compliant arteries. 2) At all relative intensities, the amounts of change in peak BP response to resistance exercise were lower in middle-aged than in young men. 3) At individual absolute intensity, the amounts of change in peak systolic BP response to resistance exercise were lower in middle-aged than in young men. In contrast to our hypothesis, these results suggest that BP responses during dynamic resistance exercise may be attenuated with advancing age at either individual relative or absolute intensity, despite age-related stiffening of the arteries.

Previous studies have suggested that the arteries of middle-aged men appear to be stiffer than those of young men based on measurements of carotid arterial compliance, β-stiffness, augmentation index, and baPWV (*5, 6, 22, 23, 30*). Our results also showed that arterial stiffening develops at a greater rate in middle-aged men than in young men. However, remarkable hypertrophy (>1.1 mm) of IMT, which is a characteristic of atherosclerosis, was not observed in any of the subjects in the present study. The maximal muscle strength estimated by the leg press exercise was lower in middle-aged men than in young men. These results indicate that the middle-aged men in the present study had developed arteriosclerosis without atherosclerosis and had lower maximal muscle strength than the young men. Although all BP values at rest in middle-aged men were higher than those in young men, all subjects were normotensive (<140/90 mmHg). Carotid diastolic diameter in middle-aged men was higher than that in young men. This result was consistent with the results of a previous epidemiological study (*31*). This alteration may be a physiological adaptation to suppress marked reductions in arterial compliance and vessel diameter induced by hypertrophied IMT with advancing age.

Dynamic resistance exercise is mainly used for health promotion and strength conditioning as it has greater effects on strength and volume of skeletal muscle in comparison with static (isometric) exercise (*32*). Understanding the pressor response during dynamic resistance exercise using large muscle groups is essential for exercise prescription. However, most previous studies have focused on static resistance exercise (*11, 12, 16, 33*), and have provided little information regarding the cardiovascular response during dynamic resistance exercise (*10*), or the interaction between age and BP response to dynamic resistance exercise using large muscle groups. We found that pressor responses during dynamic resistance exercise at relative intensities were lower in middle-aged than in young men, suggesting that the BP response to dynamic resistance exercise may be attenuated with advancing age despite age-associated arterial stiffening.

From the relative intensities, it is reasonable to hypothesize that the attenuated BP response to resistance exercise in middle-aged men may be induced by the age-related reduction in maximal muscular strength, because of the exercise intensity-associated increase in BP response to resistance exercise in both groups. In the present study, the 1RM estimated by the leg press exercise was lower in middle-aged than in young men, suggesting that the absolute intensities during exercise at individual relative intensities were lower in the former than in the latter. Accordingly, we determined BP response during the dynamic leg press exercise at individual absolute intensity (145 kgw) in the middle-aged and young men. The results indicated that the amount of change in BP response to resistance exercise was lower in middle-aged than in young men. These results suggest that age-associated reduction in muscle strength did not contribute to the attenuated pressor response to dynamic resistance exercise in middle-aged as compared with young men.

It is unclear what physiological mechanisms explain the attenuated BP responses during dynamic resistance exercise using large muscle groups in middle-aged as compared with young men. However, we speculate that the mechanism may be as follows. In middle-aged men, the muscle sympathetic nerve activity is higher at rest than in young men (*16*), whereas during exercise it is lower in the former than the latter (*16*). This results in attenuation of the increases in cardiac output and peripheral vasoconstriction induced by sympathoexcitation during exercise with advancing age (*34–36*). The ratio of high-glycolytic muscle fiber type II in skeletal muscle falls from 59% to 48% between the third and sixth decades of life (*37*), and the transformation to oxidative skeletal muscle fibers results in a lower pressor response evoked by static contraction as compared with glycolytic fibers (*38*). Therefore, alterations in sympathetic nerve activity and/or skeletal muscle fiber type with advancing age may contribute to the attenuated BP response to resistance exercise in middle-aged as compared with young men.

Sarcopenia and osteoporosis with advancing age are social problems in developed countries with aging populations. The leg press exercise used in this study, as a form of dynamic resistance exercise using predominantly the lower body, is widely accepted in exercise prescription for the prevention and rehabilitation of sarcopenia and osteoporosis, which can lead to falls and femur bone fracture, and may even result in patients becoming bedridden. However, BP rises rapidly and remarkably during high-intensity leg press exercise (*10*). Indeed, it has been reported the accidents, such as artery dissociation and subarachnoid hemorrhage, occur during resistance exercise (*39–42*). Therefore, care should be taken regarding the rapid and marked increases in BP response to resistance exercise, particularly in middle-aged and older men. In contrast to our expectations, the results of the present study indicated that pressor responses during dynamic resistance exercise at individual relative and absolute intensities were not higher in middle-aged men with stiffening arteries than in young men with compliant arteries. These results may contribute to our understanding of the cardiovascular responses to resistance exercise at appropriate intensities recommended by the major health organizations in middle-aged men who have developed arterial stiffening.

As it is the simplest parameter of arterial buffering function, pulse pressure was evaluated along with systolic and diastolic BP responses to resistance exercise in the present study. The results indicated that the amounts of change in pulse pressure response to resistance exercise at either relative or absolute intensities were lower in middle-aged men than in young men despite age-related increases in arterial stiffness. The attenuation of pulse pressure response to resistance exercise with advancing age may be affected by systolic function in the left ventricle. Of course, this function is greater in young than in middle-aged men during exercise as well as at rest. Thus, lower pulse pressure response to resistance exercise in middle-aged men may be appropriate. Pulse pressure at rest was also lower in middle-aged than in young men. As pulse pressure at rest increases progressively in normotensive subjects from the fifth decade (*43*), further studies are needed to determine BP response to resistance exercise in older men with augmented pulse pressure.

The present study had several limitations. Although there have been several reports on BP responses to isometric or aerobic exercise, we did not attempt to compare the BP responses to isometric resistance or aerobic exercise with those to dynamic resistance exercise. Compared to isometric or aerobic exercise, dynamic resistance exercise is more often used for health promotion, strength conditioning and prevention of sarcopenia or osteoporosis in middle-aged and older individuals. Therefore, as a primary approach, it was necessary to clarify the differences in BP response to dynamic resistance training using large muscle groups between young and middle-aged men. Although increases in central arterial BP during exercise may be more important than those in peripheral arterial BP from the standpoint of cardioprotection, we performed noninvasive assessment of only the radial arterial BP response to resistance exercise. Therefore, the results of the present study must be confirmed in future prospective studies focusing on central arterial BP responses to resistance exercise. Finally, the muscular strength maximum was evaluated with a leg press machine using air pressure. The value of muscular strength assessed by this machine may be different from that of muscular strength evaluated using real weights. Although the muscular strength maximum of subjects in the present study was relatively high, our results may not have been affected by this difference.

In conclusion, this study demonstrated that, at either individual relative or absolute intensity, the BP response during dynamic resistance exercise using large muscle groups was attenuated in middle-aged men as compared with young men despite age-related stiffening of the arteries. These findings may contribute to our understanding of the BP response during dynamic resistance exercise and aid in the safe performance of exercise prescription for prevention and rehabilitation of sarcopenia and osteoporosis in middle-aged and older men.

Acknowledgements

We thank Dr. Kenta Yamamoto and Dr. Izumi Tabata for their advice.

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Required muscle mass for preventing lifestyle-related diseases in Japanese women

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Published: 18 August 2008

BMC Public Health 2008, 8:291 doi:10.1186/1471-2458-8-291

Received: 14 January 2008
Accepted: 18 August 2008

This article is available from: http://www.biomedcentral.com/1471-2458/8/291

Abstract

Background: Since it is essential to maintain a high level of cardiorespiratory fitness to prevent life-style related disease, the Ministry of Health, Labour and Welfare of Japan in 2006 proposed to determine the maximal oxygen uptake (Vo_2max: mL·kg^{-1}·min^{-1}) reference values to prevent life-style related diseases (LSRD). Since muscle mass is one of the determinant factors of Vo_2max, it could be used as the reference parameter for preventing LSRD. The aim of this study was to determine and quantify the muscle mass required to maintain the Vo_2max reference values in Japanese women.

Methods: A total of 403 Japanese women aged 20–69 years were randomly allocated to either a validation or a cross-validation group. In the validation group, a multiple regression equation, which used a set of age and the percentage of muscle mass (%MM, percentage of appendicular lean soft tissue mass to body weight), as independent variables, was derived to estimate the Vo_2max. After the equation was cross-validated, data from the two groups were pooled together to establish the final equation. The required %MM for each subject was recalculated by substituting the Vo_2max reference values and her age in the final equation.

Results: The mean value of required %MM was identified as (28.5 ± 0.35%). Thus, the present study proposed the required muscle mass (28.5% per body weight) in Japanese women to maintain the Vo_2max reference values determined by the Japanese Ministry of Health Labour and Welfare.

Conclusion: The estimated required %MM (28.5% per body weight) can be used as one of the reference parameters of fitness level in Japanese women.

Background

Previous epidemiologic and clinical evidence indicate that a poor cardiorespiratory fitness is a major risk factor for life-style related diseases (LSRD) such as obesity, hypertension, hypercholesterolaemia, arteriosclerosis and diabetes [1-4]. Moreover, low cardiorespiratory fitness has been found to be a predictor of cardiovascular disease (CVD) mortality, and all-cause mortality [5-8]. Thus, it is essential to maintain a high level of cardiorespiratory fitness to prevent LSRD.

Cardiovascular fitness is usually evaluated as the maximal oxygen uptake per body mass (Vo_2max, $mL \cdot kg^{-1} \cdot min^{-1}$). The Japanese Ministry of Health Labour and Welfare in 2006 proposed Vo_2max reference values for each age group to prevent LSRD [9]. These Vo_2max reference values were determined by the "Committee for the Determination of the Recommended Exercise Allowance and Exercise Guide" established in August 2005, and were referenced in the "Exercise and Physical Activity Reference Quantity for Health Promotion 2006 (EPAR2006)". Originally, the "Recommended Quantity of Exercise for Health Promotion (1989)" had been formulated to mainly target the prevention of coronary artery disease. With the passage of more than 15 years following the establishment of this standard, the morbidity pattern of people has worsened and LSRD have increased in prevalence. In order to face this situation, the EPAR2006 was made based on the latest scientific evidence, and was designed to maintain and promote the health of people and prevent LSRD by improving their capacity for physical activity and exercise. These Vo_2max reference values proposed in the EPAR2006 were determined by experts through the systematic review of literature regarding the relationship between Vo_2max and LSRD such as obesity, hypertension, hypercholesterolemia, diabetes, cerebrovascular disease, CVD mortality and all-cause mortality.

It is well known that Vo_2max decreases with age [10-20]. It has been suggested that the age-related decline in Vo_2max is a consequence of attenuation of central and peripheral functions such as stroke volume, heart rate max (HR_{max}), peripheral O_2 extraction, and lean body mass (LBM) or muscle mass [19,21-25]. Among these determinants, reductions in HR_{max} and LBM or muscle mass have been suggested to be primary factors [26,27]. While many studies on cardiovascular fitness have focused on cardiac measurements, it should be emphasized that muscle mass is one of the critical determinants of Vo_2max [13,14,19,24,26,28-30] since the amount of tissue available to extract oxygen during maximal exercise, i.e., muscle, can directly contribute to the value of Vo_2max. For example, Sanada et al. reported the MRI-measured lower body skeletal muscle mass was closely associated to the absolute Vo_2max during running [28,30]. Additionally, the age-related decrement in Vo_2max can be related to the age-associated muscle loss [24,19]. Further, it is important to notice that LBM or muscle mass can be maintained to some degree by exercise training, while such training cannot prevent age-related declines in HR_{max}, [26,27].

Therefore, we hypothesized that a certain level of muscle mass required to maintain sufficient cardiovascular fitness is present and that it could be a limiting factor of age-related Vo_2max attenuation. Based on this hypothesis, it is advantageous to Japanese women's health to propose such muscle mass required to maintain sufficient Vo_2max. Thus, the purpose of this study was to determine a required value of muscle mass to maintain the Vo_2max reference value determined by the Japanese Ministry of Health Labour and Welfare in 2006 (Ministry of Health, Labour and Welfare of Japan 2006).

Methods

Subjects

A group of 403 Japanese women aged 20 to 69 years were randomly allocated to either a validation group (V-group, n = 201) or a cross-validation group (CV-group, n = 202). The subjects were recruited from the community around the National Institute of Health and Nutrition. All subjects were active and free of overt CVD assessed using a medical history questionnaire. All assessments were conducted at the National Institute of Health and Nutrition between February 2004 and October 2006. The study was approved by the Ethics Committee of the National Institute of Health and Nutrition, and written consent was obtained from all participants.

Percentage of muscle mass

The lean soft tissue mass of legs and arms were measured with a whole-body Dual Energy X-ray Absorptiometry (DXA) scanner (Hologic QDR-4500, Hologic INC., Waltham, MA, USA). The body regions were delineated according to specific anatomical landmarks using manual DXA analysis software (version11.2.3). The appendicular lean soft tissue mass was calculated as a sum of the lean soft tissue mass of the legs and the arms. The lean soft tissue mass of extremities assessed using DXA was assumed to represent appendicular skeletal muscle mass along with a small and relatively constant amount of skin and underlying connective tissues. The percentage of muscle mass (%MM) was calculated as follows;

%MM (%) = (Appendicular lean soft tissue mass)/Body weight × 100.

Vo_{2max}

We assessed peak oxygen uptake (Vo_{2peak}: $mL \cdot kg^{-1} \cdot min^{-1}$) instead of Vo_{2max} as an index of cardiorespiratory fitness, which is defined as the highest level of oxygen uptake that is determined by the protocol of a graded exercise load. The Vo_{2peak} was measured using the incremental cycle exercise. An initial work intensity of 30 W or 60 W was selected for each patient based on the patient's fitness level. The work intensity was increased thereafter by a step of 15 W/min, until the subject was not able to maintain the required pedaling frequency of 60 rpm. The heart rate and rating of perceived exertion (RPE) were monitored throughout the exercise. The O_2 consumption and the minute ventilation were monitored during each 1-min exercise stage (two 30 sec samplings for each stage), after RPE reached 18. The expired air was collected using Douglas bags. Expired O_2 and CO_2 gas concentrations were measured using a mass spectrometer (ARCO-1000A, ARCO SYSTEM, Chiba, Japan), and gas volume was measured using a dry gas meter (DC-5C Shinagawa Seiki, Tokyo, Japan). If the subject became exhausted and was not able to keep the pedaling frequency at 60 rpm, it was decided that the maximum effort had been achieved and the test was terminated. The highest value of Vo_2 during the exercise test was designated as Vo_{2peak}. Note that the oxygen uptake obtained in this procedure is referred to as Vo_{2peak}, to discriminate this from Vo_{2max} in the strict definition. However, we equate the obtained Vo_{2peak} to Vo_{2max} in the present study since the Vo_{2max} reference value was determined using both Vo_{2max} and Vo_{2peak} as mentioned in the next section.

Vo_{2maxk} reference values

The Japanese Ministry of Health Labour and Welfare proposed Vo_2max reference values to prevent life-style related illness for women [9]. The Vo_{2max} reference values are provided for each age group. The procedure to determine Vo_{2max} reference values was described in the EPARQ2006 [9]. In brief, these Vo_{2max} reference values were determined by experts through a systematic review of literature. The target age was 6 years and older. The target LSRD were obesity, hypertension, hyperlipemia, diabetes mellitus, cerebrovascular disorders, death due to circulatory diseases, osteoporosis, ADL and total mortality. By means of this systematic review, the threshold values of the Vo_{2max} or Vo_{2peak} at which the morbidity of LSRD statistically increases in each age group were collected from the literature. The average values of these threshold values for each age group were then calculated and designated as the Vo_{2max} reference values for preventing LSRD. The identified Vo_{2max} reference values ($mL \cdot kg^{-1} \cdot min^{-1}$) were 33 (20–29 yr), 32 (30–39 yr), 31 (40–49 yr), 29 (50–59 yr), and 28 (60–69 yr).

Analyses

First, a single regression analysis was used to test the correlation between age and Vo_2max, and between %MM and Vo_2max in V-group. Then, a multiple regression analysis was performed using Vo_2max as a dependent variable, and age and %MM as the independent variables. This analysis was based on the hypothesis that Vo_2max can be accounted for by age and %MM. In this hypothesis, we assumed that the age factor included Vo_2max determinant factors related to aging except for muscle mass, such as HR_{max}, maximal stroke volume, and peripheral O_2 extraction [21-23,25,27]. The validity of the prediction by the obtained regression equation was tested by applying the obtained regression equation to the CV-group. After the equation was cross-validated, the data from the two groups were pooled together to obtain the final prediction equation and in the subsequent analysis.

The purpose of the final prediction equation was to obtain the required %MM to maintain the reference Vo_2max value in each age group. Thus, the required %MM for each subject was recalculated by assigning the Vo_2max reference values and age in the final prediction equation. If the difference of the required %MM among the age groups was very small, the mean value of the required %MM was calculated to be used in the following analysis. To test the validity of the required %MM, the correlation between the sufficiency of Vo_2max, i.e., individual's Vo_2max as the percentage of the Vo_2max reference values (% Vo_2max reference values), and the sufficiency of the required %MM, i.e., individual's %MM as the percentage of the required %MM (%required-%MM), were tested.

All data are reported as means ± standard deviations (SD). $P < 0.05$ was used as a level of significance for all comparisons.

Results

Physiological characteristics

The physiological characteristics for each group are shown in Table 1. There were no significant physiological differences between V-group and CV-group.

Relationship between age and Vo_2max in V-group

Vo_2max in V-group was from 16.4 to 56.9 $ml.kg^{-1}min^{-1}$ (mean 33.5 ± 7.9) (Table 1). As expected, a strong nega-

Table 1: Characteristics of validation and cross-validation group

	V-group	CV-group
n	202	201
Age (yr)	41.4 ± 16.7	41.6 ± 16.9
Height (cm)	158.5 ± 6.4	157.9 ± 6.1
Body weight (kg)	54.4 ± 7.4	53.9 ± 7.3
Body mass index (kg/m^2)	21.6 ± 2.7	21.7 ± 2.9
Appendicular muscle mass (kg)	16.4 ± 2.4	16.1 ± 2.3
% MMI (%)	30.3 ± 3.2	30.0 ± 3.4
Vo_2max ($ml \cdot kg^{-1} \cdot min^{-1}$)	33.5 ± 7.9	32.7 ± 7.7

mean ± SD, V-group, Validation group; CV-group, Cross-validation group; %MM, percentage of muscle mass tive linear correlation was found between Vo_2max and age (Figure 1). The decrement was 2.58 ml.kg^{-1}min^{-1} per decade. The Vo_2max reference values for each age group in the EPAR2006 were superimposed in Figure 1. With increasing age, the proportion of subjects with Vo_2max values below the reference Vo_2max values increased.

Relationship between Vo_2max and %MM in V-group

%MM in V-group was from 18.7 to 37.3% (mean 30.3 ± 3.2%) (Table 1). There was also a strong correlation between Vo_2max and %MM, while the correlation was positive (Figure 2).

Multiple-regression analysis in V-group

Multiple regression analysis in V-group revealed that age ($R^2 = 0.286$) and %MM ($R^2 = 0.540$) were significant ($p < 0.0001$) contributors to the prediction of the measured Vo_2max. The multiple regression equation obtained in the V-group was the following: $Vo_2max = -0.135 \times Age + 1.315 \times \%MM - 0.799$. In this equation, R^2 and SEE were 0.522 and 5.4 mL·kg^{-1}·min^{-1}, respectively.

Cross-validation of the multiple regression equation

The multiple regression equation derived from the V-group was used to predict Vo_2max in the CV-group. Figure 3 shows the residual plot. There was not statistically significant correlation between the predicted Vo_2max and residual error ($p > 0.05$). Thus, the residual plot indicates that there was no bias in the prediction of Vo_2max of the CV-group using the multiple regression obtained in the V-group.

Final prediction equation

Data from the two groups were pooled to generate the final equations:

$$Vo_2max = -0.131 \times Age + 1.344 \times \%MM - 2.035. \quad (1)$$

In the final equation, analysis revealed that age ($R^2 = 0.282$) and %MM ($R^2 = 0.570$) were significant ($p < 0.0001$) independent contributors to the prediction of the measured Vo_2max. Figure 4 shows the residual plot of the multiple-regression. There was no statistically significant correlation between the predicted Vo_2max and residual error ($p > 0.05$). Thus, the residual plot indicates that there was no bias in the prediction of Vo_2max.

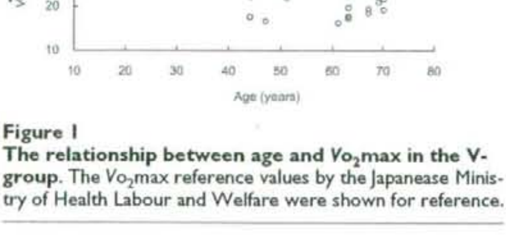

Figure 1
The relationship between age and Vo_2max in the V-group. The Vo_2max reference values by the Japanese Ministry of Health Labour and Welfare were shown for reference.

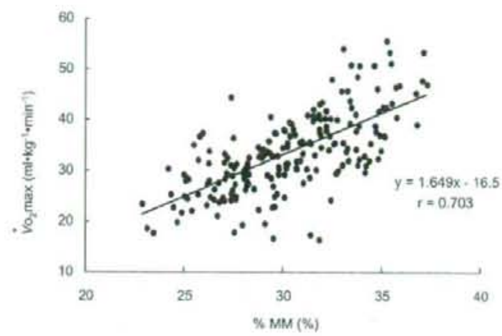

Figure 2
Relationship between percentage of muscle mass (%MM) and Vo_2max in the V-group.

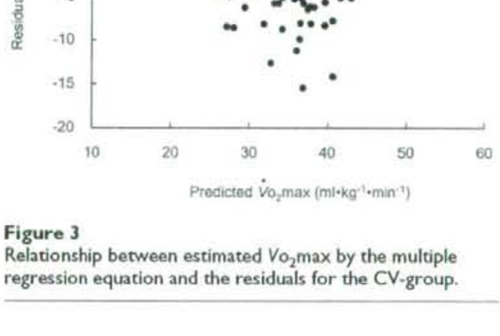

Figure 3
Relationship between estimated Vo_2max by the multiple regression equation and the residuals for the CV-group.

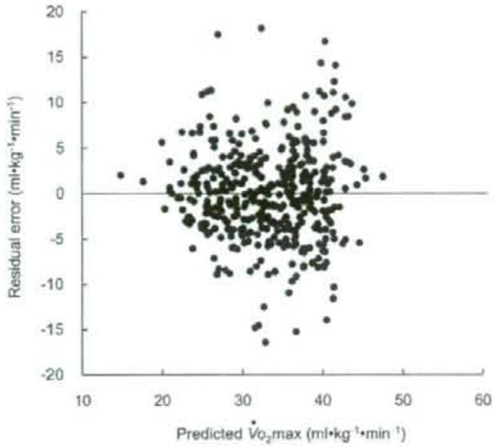

Figure 4
Relationship between estimated Vo_2max by the multiple regression equation and the residuals for both the V-group and the CV-group.

Estimation of the required %MM

The equation (1) was rearranged to predict required %MM as follow;

$$\%MM = (0.131 \times Age + 2.035 + Vo_2max)/1.344. \quad (2)$$

The required %MM was calculated by assigning the Vo_2max reference values, and age in the equation (2). The calculated required %MM was shown in Table 2. The mean value and standard deviation of required %MM was 28.5 ± 0.35%. Figure 5 shows the relationship between the measured %MM and age with the required %MM superimposed on the plot. The older people tended to have a %MM lower than the required. With increasing age, the proportion of subjects with %MM below the required %MM increased.

The validity of the required %MM

Figure 6 shows the relationship between %Vo_2max reference values and %required-%MM. The %Vo_2max reference values positively correlated with %required-%MM ($r = 0.651$, $p < 0.05$).

Discussion

The primary finding of the present study is that appendicular muscle mass of 28.5% of body weight is needed to maintain the Vo_2max reference values determined by the Japanese Ministry of Health Labour and Welfare in Japanese women. By use of the multiple-regression analysis, the regression equation of Vo_2max from age and %MM was obtained in the V-group at first. Then the validity of the regression equation was confirmed in the CV-group (Figure 3). The required %MM to maintain the Vo_2max reference values was obtained using the final regression equation using the data of V- and CV-groups (equation (2)) and the Vo_2max reference values for each age group (Table 2). There was strong correlation between percentages of the required %MM and Vo_2max reference values (Figure 6).

Required muscle mass

We propose the required %MM in Japanese women as a reference value of muscle mass for the usage of maintaining the reference value of Vo_2max proposed by the Ministry of Health Labour and Welfare of Japan. Interestingly, the calculated required %MM was not different among age groups (Table 2). Thus, we proposed the averaged required muscle mass (28.5%) as the general value for all age groups. A large portion of the subjects (68%) satisfied the required muscle mass, while with increasing age, the proportion of subjects with %MM below the required %MM increased (Figure 5). This tendency was similar to Vo_2max, i.e., with increasing age, the proportion of subjects with Vo_2max values below the reference Vo_2max values increased (Figure 1). Additionally, there was strong positive relation between percentages of Vo_2max reference values and required %MM (Figure 6). The results indicate that subjects with total muscle mass lower than 100% of the required %MM also tended to have lower Vo_2max when compared to levels of Vo_2max reference values. Thus, our result suggests that one of the reasons for insufficient Vo_2max may be insufficient %MM. Women who have %MM less than the required %MM are encouraged to increase their %MM above the required %MM to achieve the Vo_2max reference values. The required %MM can be used as an additional parameter for preventing LSRD together with the Vo_2max reference values. The

Table 2: Required %MM for Vo_2max reference values of each age group

Age roup Y	20 3 Y	0 4 Y	0 5 Y	0 6 Y	0	Total
n	143	48	55	73	84	403
Required MMI (%)	28.3 ± 0.26	28.6 ± 0.29	28.9 ± 0.27	28.4 ± 0.25	28.6 ± 0.30	28.5 ± 0.35

Mean ± SD; %MMI, percentage of muscle mass

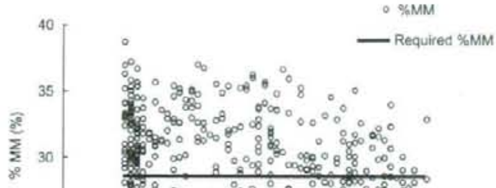

Figure 5
The relationship between age and the percentage of muscle mass (%MM) in the V-group and the CV-group. Required %MM is shown for reference.

required %MM obtained in this study is practical and appropriate for most Japanese women, because it is slightly less than the average %MM of the total number of subjects. Thus, the value is an achievable goal for most of Japanese women. Although strength training is not typically included in exercise programs targeting prevention

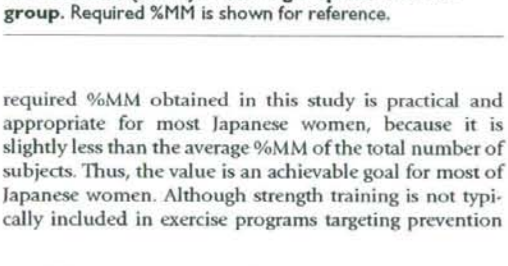

Figure 6
The relationship between the sufficiency of Vo_2max (%Vo_2max reference values) and the sufficiency of the required %MM (% required %MM) in both the V-group and the CV-group. Solid line: regression line, dashed line: lines of 100% of Required %MM and 100% of Vo_2max reference values.

of the age-related decline in Vo_2max or to increase Vo_2max, it would be advisable to recommend some form of strength training as well as aerobic training especially for individuals who do not achieve the required %MM.

Several prior studies demonstrated the significance of fat free mass, muscle mass, and/or muscle function to morbidity and mortality, although there are few researches targeting women [31-33]. The Japanese Ministry of Health Labour and Welfare also has admitted the importance of muscle mass and muscle function to prevent LSRD and/or mortality in EPAR2006. However practical target values have not been offered in the statement due to the lack of evidences compared to Vo_2max. In this present study we determined the target value of muscle mass through the Vo_2max reference values, which already has strong evidences. Although we have not confirmed the direct relation between muscle mass and LSRD morbidity and/or mortality, we believe Japanese women could aim to achieve the required %MM as one of targets for their health. Whether an increase of skeletal muscle mass would result in an improvement of exercise capacity and or reduce morbidity and mortality needs to be confirmed by future studies.

It should note that some individuals may have a large muscle mass, yet be at a high mortality risk. For example, it is well known that central obesity is one of risk factor of LSRD morbidity. Thus, it is important to remember that muscle mass is not the only important parameter but also, other risk factor should be monitored and considered together.

Prediction of Vo2max from age and muscle mass

The residuals of the multiple regression might be due to the approximation that all age-related determinant factors were included in age in the multiple regression. In the present model, we hypothesized that determinants such as HR_{max}, maximal stroke volume, and peripheral O_2 extraction were age-related, and therefore their effects were included in the factor of age. It was suggested that HR_{max} [14,22,26,29,34-39] and peripheral O_2 extraction [21,34] do decline with age, and are not influenced by exercise training. However, although maximum stroke volume was also suggested to decline with age in sedentary individuals [23], it was suggested that age-related decline of maximum stroke volume was prevented by exercise [21,34]. Thus, the simplification must be the error factor, and it is likely in future to improve the multiple regression equations using these age-related Vo_2max determinants, and to improve the estimation of the required MMI.

We studied only a statistical relationship between Vo_2max and muscle mass. Therefore, the results do not necessarily suggest a cause-effect relationship. It is possible that muscle mass and Vo_2max are physiologically unrelated but indirectly correlated, i.e., people with a high Vo_2max may be more physically active and perform activities that increase muscle mass. However, muscle mass is highly likely physiologically important determinant of Vo_2max because the amount of tissue available to extract oxygen during maximal exercise directly contribute to the value of Vo_2max.

Study limitations

The current study has limitations that require caution when interpreting and generalizing the findings reported herein. This study included only the cross-sectional design, and it did not investigate the relationship between the required %MM and the morbidity of LSRD or mortality by using a prospective design. Thus, it has not been clarified how the required %MM reflects these risks in this present study. Further investigation is required to validate the required %MM through a prospective study with the morbidity and/or mortality as an endpoint. Additionally, the potential difference between methods using %MM or absolute muscle mass (kg) as the indicator of health should be also investigated. Another limitation of this study is the results of this study are applicable to only Japanese women. The decided %MM in this study may not be able be applicable to men and/or other racial group since they may have different characteristics of the relationship between muscle mass and Vo_2max.

Conclusion

In conclusion, the present study proposed the required muscle mass (28.5% per body weight) in Japanese women to maintain the Vo_2max reference values determined by the Japanese Ministry of Health Labour and Welfare. This required muscle mass can be used as one of the reference parameters of fitness level in Japanese women.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MM performed analysis and data interpretation as well as drafted and revised the manuscript. KM participated in the conception of this study, interpretation of the analysis and critically reviewed this manuscript, and provided comment as Statistical expertise. HK, YG, KY, MT, TO, CU and SK performed data analysis and interpretation, and provided comment and review of the manuscript. MH and IT designed the project, assisted with data interpretation and provided comment and revisions for the manuscript. MM designed the project, participated in the conception of this study, interpretation of the analysis and critically reviewed this manuscript. All authors read and give final approval of the final manuscript for publication.

Acknowledgements

We thank Ms. Andrea Brown for her assistance with the manuscript preparation. This study was supported by the Health and Labour Sciences Research Grants of I. Tabata for the research on exercise and physical activity guidelines, awarded from the Ministry of Health, Labour and Welfare, Japan, the Health and Labour Sciences Research Grants of M. Miyachi, awarded from the Ministry of Health, Labour and Welfare, Japan, and Japan and Research Resident Fellowship of M. Miyatani awarded from Japan Foundation for Aging and Health.

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Pre-publication history

The pre-publication history for this paper can be accessed here:

http://www.biomedcentral.com/1471-2458/8/291/prepub

5ヵ月間の生活習慣改善教室参加者女性における体重変化量と腹囲変化量との関連

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日本予防医学会雑誌
Journal of Preventive Medicine
VOL.3 NO.2, pp. 13～16, 2008

原　著

5ヵ月間の生活習慣改善教室参加者女性における体重変化量と腹囲変化量との関連

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(平成20年2月23日受理)

(目的) 日本肥満学会ではメタボリックシンドロームの予防、改善のため、まず3 kg の減量と3 cm の腹囲の減少を提唱しているが、その関連ついては明らかでない。今回、5ヵ月間の生活習慣改善における体重変化量とウエスト変化量との関連を検討した。

(対象と方法) 対象は、岡山県南部健康づくりセンターにおいて、5ヵ月間の生活習慣改善教室に参加し、薬物治療を受けていない女性95名 (47.5±9.6歳) であった。測定項目は、体重、腹囲、血圧、中性脂肪、HDL コレステロール、空腹時血糖であった。ウエスト囲は臍部、立位呼気時で計測した。

(結果) 教室前では、体重と腹囲との間には有意な相関を認めた。78名が教室に継続して参加し、教室後には教室前に比較して体重、腹囲、中性脂肪が有意に減少した。体重の変化量と腹囲の変化量との間には、有意な関連が認められた【(腹囲変化量) =1.052× (体重変化量) -0.326】。

(結論) 5ヵ月間の生活習慣改善教室参加者女性では、体重1 kg の変化は、ウエスト囲1 cm の変化にほぼ相当した。

(日本予防医学会雑誌 2008, 3: 13−16)

—キーワード—

体重、腹囲、生活習慣改善、メタボリックシンドローム

Introduction

Metabolic syndrome, characterized by abdominal obesity, has become public health challenge in Japan [1]. We preciously reported that 30.7 % of men and 3.6 % of women were diagnosed as having the metabolic syndrome [2] and reducing abdominal circumference is considered to be critical therapeutic approach [1].

In 2006, reducing -3kg of body weight and -3 cm of abdominal circumference is recommended for preventing and improving the metabolic syndrome by Japan society for the study of obesity (JASSO) (http://wwwsoc.nii.ac.jp/jasso/, accessed on Jan 25, 2007). In addition, we also explored that -3 kg of delta (delta represents positive changes in parameters) body weight was almost corresponded to -3 cm of delta abdominal circumference with 1-year follow up by using a large sample of Japanese who received an annual health check up [3]. However, further investigation should be recommended on the association between delta body weight and delta abdominal circumference by using other population and intervention. Therefore, we evaluated how delta body weight is linked to delta abdominal circumference with 5-months follow up by life style modification at Okayama Southern Institute of Health in Okayama prefecture, Japan.

Subjects and Methods

Subjects

Japanese women (n=95), aged 23-67 years (47.5±9.6) were enrolled into this study with written informed consent (Table 1). The average BMI (body mass index) of subjects was 25.9±3.6 kg/m^2. Subjects did not receive any medications for diabetes, hypertension, and/or dyslipidemia throughout the observation period. In a cross-sectional analysis, we used baseline data for 95 subjects (Table 1) and investigated the relationship between body weight and abdominal circumference. In a longitudinal analysis, we used follow up data for 78 subjects (47.3 ± 10.2 years) who met the following criteria: 【1】 no electrocardiogram changes in response to exercise, 【2】 a repeat blood examination and blood pressure measurements at follow up, 【3】 a follow up duration of 5-months, 【4】 joining the education program regularly at Okayama Southern Institute of Health.

The participants visited Okayama Southern Institute of Health weekly and were monitored for 5-months. All of the subjects were instructed to change their eating habits by trained nutritionists *i.e.* not to eat too much and consider balance when they eat. The subjects were also registered in an exercise program at Okayama Southern Institute of Health every week. Aerobic exercise *i.e.* walking, aerobic dance, swimming and resistance training *i.e.* leg extension, leg flexion, sit-ups were lasted for 90 minutes and were supervised by a physical educator to ensure compliance to the prescribed program [4].

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

Table 1 Clinical profiles of enrolled subjects at baseline

Number of subjects	95
Age	47.5 ± 9.6
Height (cm)	155.7 ± 5.7
Body weight (kg)	62.7 ± 9.5
Body mass index (kg/m^2)	25.9 ± 3.6
Abdominal circumference (cm)	79.1 ± 8.6
Systolic blood pressure (mmHg)	121.9 ± 14.4
Diastolic blood pressure (mmHg)	75.4 ± 9.6
Triglyceride (mg/dl)	101.5 ± 73.7
HDL cholesterol (mg/dl)	68.1 ± 19.5
Blood glucose (mg/dl)	95.1 ± 9.6
	Mean ± SD

Anthropometric and body composition measurements

Their anthropometric and body composition were evaluated by using the following respective parameters such as height, body weight, body mass index (BMI), abdominal circumference. BMI was calculated by weight / [height] ^{2} (kg/m^2). The abdominal circumference was measured at the umbilical level in standing subjects after normal expiration [5].

Blood sampling and assays

After subjects fasted overnight for 10 to 12 hours, we collected blood samples in order to determine serum levels of glucose, triglyceride and HDL cholesterol.

Blood pressure (BP) measurements at rest

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

Definition of metabolic syndrome

Women with a abdominal circumference in excess of 90 cm [6] were defined as having metabolic syndrome if they also had 2 or more of the following components: 1) Dyslipidemia: triglycerides≧150 mg/dl and/or HDL cholesterol＜40 mg/dl, 2) High BP: BP≧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. Statistical analysis was performed by paired t test: p<0.05 was considered to be statistically significant. Relations of interested parameters were identified by univariate regression analysis. The Pearson's correlation coefficients were calculated as well as tested for the significance of the linear relationship among continuous variables.

Results

In a cross-sectional analysis at baseline, body weight was significantly correlated with abdominal circumference (r=0.831, p<0.0001) in 95 women (Fig. 1).

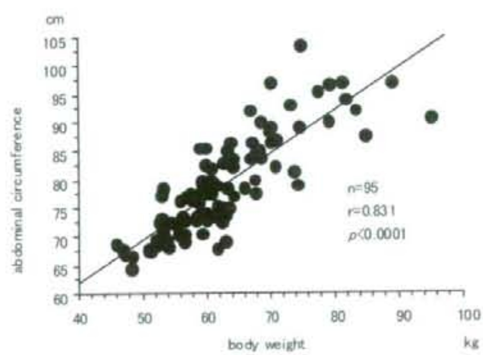

Fig. 1: Simple correlation analysis between body weight and abdominal circumference at baseline.

In a longitudinal analysis with 5-months education, body weight, BMI, abdominal circumference and triglyceride were significantly reduced in 78 women. However, BP, HDL cholesterol and blood glucose were similar to baseline (Table 2). In 78 women, 59 women decreased their body weight (Group I) and 19 women increased their body weight (Group D) at the time of 5-months follow up. There were no significant differences between two groups in clinical parameters at baseline *i.e.* age, body weight, BMI, abdominal circumference, blood pressure, triglyceride, HDL cholesterol and blood sugar. Although three subjects were diagnosed as having the metabolic syndrome at baseline, no subjects were diagnosed as having the metabolic syndrome at follow up.

Table 2 Clinical profiles and changes in parameters in 78 students

	Baseline	Follow up	p
Number of subjects	78		
Age	47.3 ± 10.2		
Height (cm)	155.6 ± 5.8		
Body weight (kg)	62.5 ± 9.2	60.9 ± 9.0	<0.0001
Body mass index (kg/m^2)	25.8 ± 3.4	25.1 ± 3.3	<0.0001
Abdominal circumference (cm)	78.8 ± 8.1	76.8 ± 8.3	<0.0001
Systolic blood pressure (mmHg)	121.7 ± 14.7	120.8 ± 14.1	0.4618
Diastolic blood pressure (mmHg)	75.4 ± 9.8	75.1 ± 8.6	0.7304
Triglyceride (mg/dl)	105.3 ± 78.5	93.5 ± 58.7	0.0314
HDL cholesterol (mg/dl)	66.5 ± 16.2	67.2 ± 16.9	0.4910
Blood glucose (mg/dl)	95.0 ± 9.0	94.1 ± 8.0	0.2701

Mean ± SD

We evaluated the relationship between delta body weight and delta abdominal circumference. Delta body weight was significantly correlated with delta abdominal circumference (Fig. 2). Furthermore, the slope of regression line (delta abdominal circumference vs delta body weight) was 1.052, respectively. Accordingly, we found that the reduction of 1 kg of body weight corresponded to -1.052 cm of abdominal circumference in women with 5-months' lifestyle modification (Fig. 2).

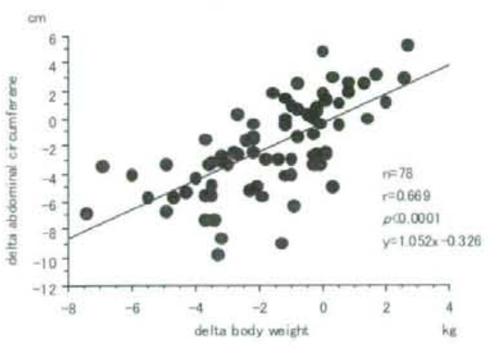

Fig. 2: Univariate regression and correlation analysis between changes in (delta) body weight and changes in (delta) abdominal circumference.

In addition, we found that the reduction of 1kg of body weight corresponded to -1.136cm (Group I) and -0.790 cm (Group D) of abdominal circumference.

Discussion

The main finding of this study was to explore that -1 kg of delta body weight corresponded to -1 cm of delta abdominal circumference at the umbilical level in Japanese women with 5-months' life style modification.

There are few studies to investigate the association between delta body weight and delta abdominal circumference in a large sample of the Japanese population. In Exercise Guideline 2006 edited by ministry of health, labor and welfare of Japan (http://www.mhlw.go.jp/shingi/2006/07/dl/s0719-3b.pdf. accessed on July 1, 2007), delta 1kg of body weight was corresponded to delta 1 cm of abdominal circumference. We also previously reported that, with 1-year follow up, -3 kg of delta body weight was almost corresponded to -3 cm of delta abdominal circumference at the umbilical level by using 2635 Japanese men and women who received an annual health check up at Okayama Southern Institute of Health in Okayama prefecture, Japan [3], which agreed with the recommendation of JASSO and Exercise Guideline 2006. In this study, with 5-months' lifestyle modification, -1 kg of delta body weight was also corresponded to -1 cm of delta abdominal circumference at the umbilical level in Japanese women. In addition, no subjects were diagnosed as having the metabolic syndrome at follow up.

Potential limitations still remain in this study. First, although we proved the link between delta body weight and delta abdominal circumference, we could not prove the threshold of body weight and abdominal circumference reduction for preventing and improving metabolic syndrome. Second, we neither directly measured the visceral fat accumulation by using computed tomography nor investigated the correlation between visceral fat accumulation and body composition parameters. The third, 95 women in our study enrolled in the program of lifestyle modification at Okayama Southern Institute of Health: they were therefore more health-conscious than the average. 78 women joined in the program every week with a follow up duration of 5-months and received no medications; they were therefore more health-conscious than subjects at baseline. They were also instructed to change their lifestyle by well-trained medical staff and anthropometric body composition parameters and triglyceride were significantly reduced. Finally, the small sample size in our study makes it difficult to infer causality between delta body weight and delta abdominal circumference in Group I and Group D.

Further intervention studies by using other population are necessary to explore the link between delta body weight and delta abdominal circumference in Japanese.

Acknowledgement

This research was supported in part by Research Grants from the Ministry of Health, Labor, and Welfare, Japan.

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Relationship between Changes in Abdominal Circumference and Body Weight in Japanese Women with 5-months' Lifestyle Modification

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We investigated the link between delta (delta represents positive changes in parameters) body weight and delta abdominal circumference in Japanese women. We used data for 95 Japanese women (47.5±9.6 years) at baseline and followed for 5-months with lifestyle modification. Body weight, abdominal circumference at the umbilical level, blood pressure, triglyceride, HDL cholesterol and fasting blood sugar were measured. Significant relationship between body weight and abdominal circumference was noted at baseline. After 5-months follow up (n=78), body weight, abdominal circumference and triglyceride were significantly reduced. Delta abdominal circumference was significantly correlated with delta body weight [(delta abdominal circumference) = 1.052 (delta body weight) - 0.326]. In conclusion, -1 kg of delta body weight is almost corresponded to -1 cm of delta abdominal circumference at the umbilical level in Japanese women with 5-months' education.

Key words: body weight, abdominal circumference, lifestyle modification, metabolic syndrome