kenshin" in Japanese) aged 70 and older living in Itabashi-ku, Tokyo. "Otasha-kenshin," literally meaning "health examinations for successful aging," are comprehensive health examinations for community-dwelling older adults aimed at preventing geriatric syndromes including falls and fractures, incontinence, oral health and function, mild cognitive impairment, depression, and undernutrition. Details of the survey, such as the investigation methods and contents, have been described previously.[13,14]

The baseline survey for the present study was conducted in December 2002. Of 2,000 persons aged 70 to 84 randomly sampled from the resident registration records of Itabashi-ku in metropolitan Tokyo, 847 (456 men and 391 women) participated in the baseline survey. Of the 391 women, 205 (52.4%) also participated in the follow-up survey conducted in November 2004 and completed the interview, anthropometric measurements, blood analysis, and physical performance tests. Twenty-three people who participated in other intervention programs conducted at the Tokyo Metropolitan Institute of Gerontology for promoting independence were excluded. Thus the research subjects analyzed in this study consisted of 182 elderly women who participated in the baseline and follow-up surveys and had not participated in other intervention programs during the 2-year period. The ethics committee of the Tokyo Metropolitan Institute of Gerontology approved the study, and informed consent was obtained from all subjects.

Assessment of BMD

BMD was evaluated using dual-energy X-ray absorptiometry (DTX-200, Osteometer Medi-Tech, Hawthorne, CA) measured at the forearm. Specially trained personnel performed the measurements. The Osteometer DTX-200 can set region of interest automatically 24 mm proximal to the position where the radius and ulna are 8 mm apart. Baseline and follow-up examinations were conducted using densitometers of the same make and model. Annual percentage changes in BMD during the 2-year follow-up period were calculated using the following formula

$$100 \times (\text{BMD in 2004} - \text{BMD in 2002}) / (\text{BMD in 2002} \times \text{length of follow-up in years})$$

and summarized in quartiles of percentage change as follow: first (-12.57 to -4.18), second (-4.17 to -1.78), third (-1.77–0.72), and fourth (0.73–18.81).

Assessment of Physical Performance

Physical performance was assessed according to handgrip strength, functional reach, and walking speeds (usual and maximal). These assessments are routinely conducted as part of the Otasha-kenshin program, as described previously.[3,4]

Handgrip strength was measured using Smedley's Hand Dynamometer (Yagami, Tokyo, Japan). For functional reach, the subject stood sideways against a wall in a natural position and stretched both arms forward to the height of the shoulders. The positions of the fingertips were taken as the zero point. Then one arm was lowered. With the body tilted forward as far as possible, the subjects continued to stretch the arm parallel to the ground. The greatest distance of forward reach was measured. Three measurements were made, and the mean value was recorded.[15] To test walking speed, participants walked along a straight 11-m walkway on a flat floor. A stopwatch measured the time taken to walk 5 m, from the time when the foot touched the ground after the 3-m line to when the foot touched the ground after the 8-m mark. The participant first took the test by walking at usual speed and then by walking as fast as possible. Walking tests at usual and maximum speeds were repeated, and the faster speed was recorded in each walking test.

The change in physical performance was expressed as the change in value from 2002 to 2004 for each parameter. Annual percentage change in usual walking speed during the 2-year follow-up period was calculated by the formula

$$100 \times (\text{usual walking speed in 2004} - \text{usual walking speed in 2002}) / (\text{usual walking speed in 2002} \times \text{length of follow-up in years})$$

Assessment of Other Variables

An interview was conducted to assess the age, education level, subjective health status, regular exercise habits, chronic disease history, and higher-level functional capacity. Regular exercise per week was based on the following activities: walking outdoors, running, exercise, and sports. Chronic disease conditions were self-reported and included hypertension, stroke, heart attack, and diabetes mellitus. The higher-level functional capacity was measured using the Tokyo Metropolitan Institute of Gerontology Index of Competence.[16] This multidimensional 13-item index of competence comprises three subscales: instrumental activities of daily living, intellectual activity, and social roles. Blood samples were collected under a nonfasting state, in a sitting position. The analyses were performed centrally in one laboratory (Special Reference Laboratories, Inc., Tokyo, Japan). Serum albumin level was measured using a standard kit using the BCG method. Body mass index (BMI, kg/m^2) was calculated as weight (in kg) divided by the square of height (in m).

Statistical Analysis

All data were analyzed using SPSS software for Windows version 13.0 (SPSS Inc., Chicago, IL), and the level of significance was set at 5%. Population characteristics at baseline and at 2-year follow-up are expressed as frequency or mean ± standard deviation). Paired t tests were used to evaluate the changes in physical performance during the 2-year follow-up period. Simple correlation was used to test the association between changes in BMD and physical performance. Comparison of annual change in usual walking speed according to annual BMD change in quartile was conducted using analysis of covariance (ANCOVA). Trend analysis was conducted using linear regression and entering the quartiles of performance as ordinal variables.[9] The model was adjusted for age; subjective health status; regular exercise; BMI; serum albumin concentration; handgrip strength; functional reach; usual walking speed in 2002; and changes in BMI, serum albumin concentration, handgrip strength, and functional reach from 2002 to 2004.

Table 1. Characteristics of the Study Subjects (n = 182) in Baseline and Follow-Up Surveys

Characteristic	Value	*P*-value*
Age, mean ± SD	75.9 ± 3.6	
Education level ≥ high school, %	62.6	
Good subjective health status, %	80.2	
Regular exercise every day, %	42.3	
Chronic disease history, %		
Hypertension	50.5	
Stroke	5.5	
Heart attack	8.8	
Diabetes mellitus	4.9	
Higher-level functional capacity score, mean ± SD		
2002	12.2 ± 1.2	
2004	11.8 ± 1.4	<.001
Change 2004–2002	−0.48 ± 1.32	
Body mass index, kg/m^2, mean ± SD		
2002	22.8 ± 3.2	
2004	22.6 ± 3.2	.005
Change 2004–2002	−0.26 ± 1.23	
Bone mineral density, g/cm^2, mean ± SD		
2002	0.296 ± 0.068	
2004	0.286 ± 0.067	<.001
Change 2004–2002	−0.010 ± 0.023	
Serum albumin, g/dL, mean ± SD		
2002	4.25 ± 0.20	
2004	4.34 ± 0.20	<.001
Change 2004–2002	0.09 ± 0.16	
Handgrip strength, kg, mean ± SD		
2002	18.1 ± 4.4	
2004	17.4 ± 4.3	.001
Change 2004–2002	−0.74 ± 2.94	
Functional reach, cm, mean ± SD		
2002	32.0 ± 5.3	
2004	32.3 ± 5.3	.65
Change 2004–2002	0.16 ± 4.73	
Usual walking speed, m/sec, mean ± SD		
2002	1.15 ± 0.25	
2004	1.10 ± 0.26	.001
Change 2004–2002	−0.04 ± 0.18	
Maximal walking speed, m/sec, mean ± SD		
2002	1.61 ± 0.34	
2004	1.62 ± 0.39	.495
Change 2004–2002	0.01 ± 0.25	

* According to paired *t*-test.
SD = standard deviation.

RESULTS

Participants in the follow-up study were younger and had significantly better subjective health, higher scores in higher-level functional capacity, and higher scores in physical performance (functional reach, usual walking speed, and maximal walking speed) (data not shown) than nonparticipants.

Table 2. Correlations Between Changes in Bone Mineral Density (BMD) and Physical Performance During the 2-Year Follow-Up

Change in Physical Performance	Change in BMD (g/cm2) Correlation Coefficient	*P*-value*
Handgrip strength, kg	−0.036	.63
Functional reach, cm	0.062	.41
Usual walking speed, m/sec	0.212	.004
Maximal walking speed, m/sec	0.129	.08

* According to Pearson correlation analysis.

The baseline characteristics and changes in BMD and physical performance during the 2-year follow-up period of the 182 study participants are shown in Table 1. The mean age in 2002 was 75.9 ± 3.6 (range 70–84). The frequency of good self-rated health was 80.2%, and the mean higher-level functional capacity score was 12.2 ± 1.2 out of a full score of 13. During the follow-up period, higher-level functional capacity ($P < .001$), BMI ($P = .005$), BMD ($P < .001$), handgrip strength ($P = .001$), and usual walking speed ($P = .001$) decreased significantly. Alternatively, serum albumin concentration increased significantly ($P < .001$). There were no significant changes in functional reach and maximal walking speed during the 2-year follow-up period.

Table 2 shows the correlation between the change in BMD and change in physical performance during the 2-year follow-up period. Change in BMD was significantly related only to change in usual walking speed (correlation coefficient = 0.212, $P = .004$). There was no significant relationship between changes in BMD, handgrip strength, functional reach, and maximal walking speed.

Figure 1 compares the change in usual walking speed according to the change in BMD presented in quartiles. Mean annual BMD change rate was −1.57 ± 4.12% (range −12.57–18.81), and mean annual usual walking speed change rate was −1.54 ± 8.58% (range −23.84–47.78). A significant association was observed between mean annual change in usual walking speed and annual BMD change presented in quartiles ($P = .03$, according to ANCOVA). Elderly women whose BMD decreased (−3.5% in the first quartile and −3.1% in the second quartile) over the 2-year follow-up showed significantly ($P = .01$) greater decline in usual walking speed than women whose BMD increased (1.5% in the fourth quartile). More-rapid annual bone loss was associated with greater decline in usual walking speed ($P = .005$, according to trend test). This result was adjusted for age; subjective health status; regular exercise; BMI; serum albumin concentration; handgrip strength; functional reach; usual walking speed in 2002; and changes in BMI, serum albumin concentration, handgrip strength, and functional reach from 2002 to 2004.

DISCUSSION

The present 2-year longitudinal follow-up study evaluated the association between changes in BMD and physical per-

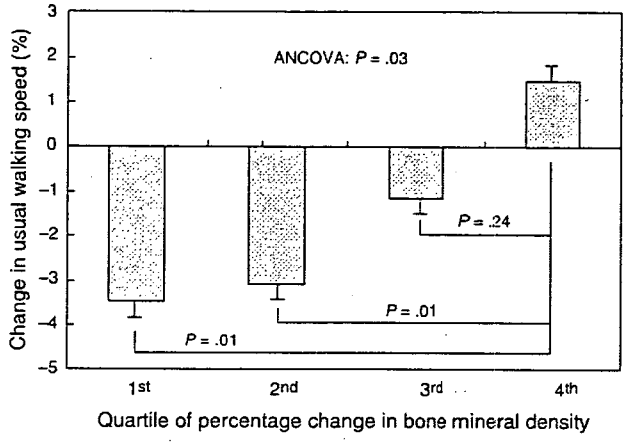

Figure 1. Associations between change in bone mineral density (expressed in quartiles) and change in usual walking speed during the 2-year follow-up. First quartile: −12.57 to −4.18; second quartile: −4.17 to −1.78; third quartile: −1.77–0.72; fourth quartile: 0.73–18.81. Annual percentage change = 100 × (data from 2004–data from 2002)/(data of 2002 × 2 (length of follow-up in years)). ANCOVA = analysis of covariance.

formance in a population-based random sample of 182 Japanese women aged 70 and older. It found that elderly women with more-rapid bone loss had a greater decline in usual walking speed.

To promote independence and to maintain quality of life in older people, the maintenance of physical performance, including muscle strength, balance capacity, and walking speed, is important.[1–4] Of these measures of physical performance, walking speed, especially usual walking speed, is the most sensitive predictor of functional dependence in older people.[3] Walking speed decreases with aging, is influenced by multiple factors, and should be modified through a lifestyle that strengthens muscles of the lower extremities.[4,17,18] For example, exercise and nutritional interventional interventions in relatively healthy community-dwelling elderly people have been shown to improve walking speed.[17,18]

BMD decreases with age, decreasing 1% per year after menopause in women,[19] although adequate dietary protein,[20] calcium and dairy,[21,22] and vitamin C intake;[23] weight maintenance;[21,23] higher BMI;[21] maintenance of daily physical activity;[21,22] supplementation;[24] and hormone replacement therapy[25] may contribute to healthy bones and prevent decline in bone mass.

Cross-sectional studies have reported that BMD in elderly people is significantly associated with physical performance.[9,10,12] Elderly women with lower BMD had significantly lower grip strength and knee extension power and poorer balance. These results suggest a strong role of maintaining muscular strength in the prevention of bone loss in healthy and functionally independent women. In the absence of neurological and degenerative disorders, poor physical performance in elderly people is likely to result from reduced physical activity, and a consequence of the reduced mechanical loading would be reduced bone mass and density.[9]

In the present study, elderly women with more-rapid bone loss during 2 years of follow-up had a greater risk of decline in usual walking speed than those with greater BMD. Because the directionality of the association between the change in mineral density and usual walking speed cannot be ascertained from this study design, the result does not imply that modification or improvement of BMD would have any effect upon walking speed. Intervention trials are needed to assess the effect of treatment of osteoporosis on walking speed and the effect of interventions targeting gait speed on bone density.

This study has some limitations. First, the characteristics of the subjects must be considered. Although the subjects analyzed were selected randomly from the population of an urban district, they were relatively healthy elderly persons who were able to travel from their homes to the health examination center at baseline and 2 years later. As a result, the present results may not be applicable to frail older people or those with multiple comorbidities who have low physical functional capacity. Second, BMD has been measured at virtually all available measurement sites (spine, proximal femur, forearm, whole body, calcaneus, and tibia) in other reports.[26] In the present study, only forearm BMD was used as indicator of bone loss. Therefore, the findings may not be directly comparable with those in other groups. To generalize this result, a more-comprehensive approach, including measuring bone mass at various sites in a large sample of elderly people and evaluating the associations between bone loss at different sites and changes in physical performance, is necessary. Forearm BMD measurement was chosen, because it is a quick, easy, and accurate method to evaluate the bone health of older people.[27] In addition, forearm BMD may be useful to assess osteoporosis in postmenopausal women because forearm BMD is significantly associated with BMD of the lumbar spine and hip.[28] Third, this study did not control for the type and dose of drugs that affect bone turnover, such as calcium, estrogens, vitamin D, and calcitonin, all of which may affect BMD. Finally, this study focused on the association between change in BMD and change in walking speed during the 2-year follow-up period and did not provide information on the cause-and-effect relationship. However, the relationship between the two parameters that were used in this study is expected to form a basis for further study. The number of elderly people with low bone mass and walking ability is going to increase in the future. Therefore, there will be an increasing need for strategies to strengthen these two parameters.

In conclusion, elderly women with more-rapid bone loss had greater decline in usual walking speed, even after multivariate adjustment including changes in muscle strength, balance capability, and other potential confounders. Further studies are needed to investigate the cause-and-effect relationship between BMD and walking speed.

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Age-specific change of prevalence of metabolic syndrome: Longitudinal observation of large Japanese cohort

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Abstract

To examine real age-related changes in the prevalence of metabolic syndrome, we studied longitudinal changes in the prevalence of metabolic syndrome in a single cohort of individuals. The participants included 112,960 Japanese (70,996 men, 14–94 years and 41,946 women, 17–85 years), who had received annual examinations between 1989 and 2004. Metabolic syndrome was defined according to the Japan Metabolic Syndrome Criteria Study Group and the US National Cholesterol Education Program (NCEP) guidelines. Overweight was defined as BMI $\geqq 25\,kg/m^2$. Longitudinal changes indicated a birth cohort effect in the prevalence rate of metabolic syndrome with a lower or higher prevalence in the younger birth cohort than in the older for females or males, respectively. The estimation of the age-specific prevalence of metabolic syndrome demonstrated that in males, the prevalence of metabolic syndrome increased up to 50 decades of life for the Japanese and 60 decades of life for the NCEP criteria. In females, the prevalence increased with age up to 80 years old for both criteria. The estimated secular trends suggested that the prevalence rate of metabolic syndrome decreased in females and increased in males during study periods.

Keywords: Metabolic syndrome; Aging; Secular trends; Longitudinal study

Metabolic syndrome has become one of the major public-health challenges worldwide [1,2]. The most important dimension of metabolic syndrome is its association with the risk of developing type 2 diabetes mellitus and atherosclerotic cardiovascular disease [3–9]. A number of metabolic syndrome definitions have been proposed, including the World Health Organization (WHO) Consultation for diabetes and its complications [10], the European Group for the Study of Insulin Resistance [11], the National Cholesterol Education Program (NCEP) Expert Panel [12], and, more recently, the International Diabetes Federation (IDF) [13] have formulated definitions for metabolic syndrome. In addition, the American Heart Association in conjunction with the National Heart, Lung, and Blood Institute have proposed a revised version of the NCEP-ATPIII definition [14]. In Japan, the National Metabolic Syndrome Criteria Study Group has proposed new criteria for metabolic syndrome in the Japanese [15].

Since several definitions of the syndrome are in use, it is difficult to compare the prevalence and impact between countries. However, a very consistent finding is that the prevalence of metabolic syndrome is highly age-dependent [16–18]. These previous findings were based on the cross-sectional observations, which may represent cohort, period, and/or survivorship effects rather than a true aging effect. Although longitudinal studies are required to examine real age-related changes in the prevalence of metabolic syndrome, to our knowledge, no studies have examined the longitudinal changes in the prevalence of metabolic syndrome in individuals over time.

We therefore studied longitudinal changes in the prevalence of metabolic syndrome in a single cohort of individuals to observe the effect of the natural aging process on the prevalence of metabolic syndrome as well as on obesity,

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hypertension, impaired glucose tolerance, and dyslipidemia as components of metabolic syndrome.

1. Methods

1.1. Study population

The study population consisted of office workers and their families residing in Aichi Prefecture in central Japan. The subjects included 112,960 Japanese (70,996 men and 41,946 women) with an average age of 44.6 years in men and 43.4 years in women, who had received annual examinations at a health examination center in Japan between 1989 and 2004 (Table 1). About 57% of the cohort (41,709 men and 23,001 women) had attended at least one follow-up examination. The average visits for the follow-up examinations were 3.4 times for men and 3.0 times for women.

1.2. Procedures and laboratory methods

The examinations included a questionnaire, physical examination, blood pressure measurement, an anthropometric measurement, and laboratory analysis of blood samples, all taken on the same day as described previously [19–21]. The anthropometric measurements included height and body weight. The body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Blood pressure was measured after the participants had been comfortably seated for at least 5 min.

All serum samples were obtained following a 12–14 h fast. The serum was separated promptly, and all lipid analyses were conducted at the clinical laboratory in the health examination center. Serum glucose and triglycerides were measured using enzymatic methods. HDL-cholesterol was measured after dextran sulfate-magnesium precipitation. No differences were seen in the sample collection, laboratory apparatus, or techniques used between 1989 and 2004.

1.3. Definition of metabolic syndrome

We applied both the Japanese criteria of metabolic syndrome [15] and the NCEP Expert Panel on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III; ATPIII) criteria [12]. According to the Japanese definition, someone has metabolic

Table 1
Characteristics of participants

	Males	Females
Number of subjects	70996	41946
Total number of measurements for 16 years	239879	122624
Number of subjects for whom measurements were taken at least twice	41709	23001
Number of measurements per subject for 16 years, mean (S.D.)	3.4 (3.4)	3.0 (2.9)
Average follow-up periods (years), mean (S.D.)	3.4 (4.3)	3.1 (4.1)
Initial measurements		
Age (years), mean (S.D.), age range (years)	44.6 (9.3), 14–94	43.4 (9.5), 17–85
Number of subjects in each age group, *n* (%)		
10–29 years	1914 (2.7)	2183 (5.2)
30–39 years	21173 (29.8)	1398 (31.5)
40–49 years	26583 (37.4)	15287 (36.4)
50–59 years	16783 (23.6)	9199 (21.9)
60–69 years	4152 (5.8)	1830 (4.4)
70–79 years	361 (0.5)	230 (0.6)
≥80 years	30 (0.04)	19 (0.05)
Hight (cm), mean (S.D.)	168.6 (6.0)	156.0 (5.5)
Body weight (kg), mean (S.D.)	65.7 (9.4)	52.4 (7.4)
BMI (kg/m^2), mean (S.D.)	23.1 (2.9)	21.6 (2.9)
Total cholesterol (mg/dl), mean (S.D.)	199.4 (35.0)	199.0 (36.5)
Triglyceride (mg/dl), mean (S.D.)	142.0 (103.5)	87.0 (49.7)
HDL-cholesterol (mg/dl), mean (S.D.)	55.2 (13.3)	67.8 (14.6)
Fasting plasma glucose levels (mg/dl), mean (S.D.)	98.5 (18.6)	91.4 (11.1)
Systolic blood pressure (mmHg), mean (S.D.)	121.2 (16.2)	113.7 (7.4)
Dyastolic blood pressure (mmHg), mean (S.D.)	73.0 (11.7)	66.5 (5.5)
Prevalence of obesity (%, BMI ≧ 25 kg/m^2)	24.1	11.5
Prevalence of hypertension (%, BP ≧ 130/85 mmHg or treated)	30.6	17.0
Prevalence of glucose intolerance (%, FSG ≧ 110 mg/dl or treated)	11.4	4.0
Prevalence of high triglyceride (%, ≧150 mg/dl)	32.2	8.0
Prevalence of low HDL (%, HDL male < 40, female < 50 mg/dl)	9.1	9.1
Prevalence of dyslipidaemia (%, TG ≧ 150 or HDL < 40 mg/dl)	35.1	8.5
Prevalence of metabolic syndrome		
Modified Japanese criteria, % (95% CI)	7.8 (7.6–8.0)	2.2 (2.0–2.3)
ATPIII-BMI25, % (95% CI)	11.6 (11.4–11.9)	4.0 (3.8–4.1)

BMI: body mass index, BP: blood pressure, FSG: fasting serum glucose, TG: triglyceride.

syndrome if he or she has central adiposity plus two or more of the following three factors [15]: (1) raised concentration of triglycerides, ≥150 mg/dl or reduced concentration of HDL-cholesterol, <40 mg/dl; (2) raised blood pressure: systolic blood pressure, ≥130 mmHg or diastolic blood pressure, ≥85 mmHg or treatment of previously diagnosed hypertension; and (3) raised fasting plasma glucose concentration, ≥110 mg/dl. The thresholds for waist circumference to define central adiposity: ≥85 cm for men and ≥90 cm for women. The ATPIII proposed the following five abnormalities to define metabolic syndrome [12]: (1) abdominal obesity (abdominal circumference >102 cm for men and >88 cm for women); (2) elevated serum triglyceride level (≥150 mg/dl); (3) decreased HDL-cholesterol level (<40 mg/dl for men and <50 mg/dl for women); (4) elevated blood pressure (systolic and diastolic blood pressure 130/85 mmHg); and (5) an elevated fasting glucose level (≥110 mg/dl). Individuals with three or more of the five abnormalities were considered to have metabolic syndrome. Because waist measurements were not available for the entire study sample, we substituted a BMI of 25 kg/m^2 or greater for all participants as an index of obesity for both criteria (the modified Japanese criteria and ATPIII-BMI25). A BMI of 25 kg/m^2 or greater has been proposed as a cutoff for the diagnosis of obesity in Asian people [22]. Individuals who were using antihypertensive or antidiabetic medications met the criteria for high blood pressure or high fasting glucose.

1.4. Data analysis

The data were analyzed with the Statistical Analysis System (SAS), release 8.2. We demonstrated that there is a birth cohort effect on the prevalence rate of metabolic syndrome based on a 16-year longitudinal analysis of the same cohort. Therefore, the pooled cross-sectional data at the initial examination of each subject from 1989 through 2004 were adjusted for the year of the examination using the logistic regression model, and estimated for the examination in 1997. The prevalence rate of metabolic syndrome for the modified Japanese and ATPIII-BMI25 definitions was estimated from an age younger than 40 years through age 70 years and older at 10-year intervals, and compared between these two definitions in each age group by paired *t*-test.

Longitudinal changes in the prevalence of metabolic syndrome were analyzed by a generalized-estimating-equation (GEE), which adjusts for repeated measurements in the same persons. For the longitudinal analyses, the subjects who did not receive follow-up examination were excluded. Age-related changes in the prevalence rate of metabolic syndrome, obesity, hypertension, impaired glucose tolerance and dyslipidemia were estimated by quadratic curve of age controlling for the observation year during which the subjects attended at least one follow-up examination. The GEE was also used to test for trends in the prevalence of metabolic syndrome during 1989–2004. The year of examination was used to test for temporal trends in prevalence. Age adjustment was performed by a least-squares regression approach. The model included age, square of age and year of examination as independent variables. A result was considered statistically significant if the P value was less than 0.05.

2. Results

Based on the pooled cross-sectional data of each subject at initial examination from 1989 through 2004, the mean prevalence rate of metabolic syndrome defined by the modified Japanese or ATPIII-BMI25 criteria was 7.8% in males and 2.2% in females, or 11.6% in males and 4.0% in females, respectively (Table 1). The prevalence of metabolic syndrome defined by two criteria was shown by age group and gender after adjusting for the examination year (Table 2). The prevalence rate of metabolic syndrome increased with age, with the highest rate in the 60–69 years group followed by a decline in the 70 years and older group in females with both criteria. In males, the highest prevalence rate was observed in the 50–59 years group or the 60–69 years group in the modified Japanese or ATPIII-BMI25 criteria, respectively. There was a significant difference between the two definitions in both genders and any age group with a higher prevalence rate in the ATPIII-BMI25 definition.

Longitudinal changes for 16 years in the prevalence rate of metabolic syndrome by birth cohort using the both criteria indicate the birth cohort effect in the prevalence rate of metabolic syndrome for females from the fifth decade of life, since at those ages, the prevalence rate of the younger

Table 2
The cross-sectional data of prevalence of metabolic syndrome at initial examination of each subject from 1989 through 2004

Age (years)	Females					Males				
	N	Modified Japanese		ATPIII-BMI25		*N*	Modified Japanese		ATPIII-BMI25	
		Mean (%)	95% CI	Mean (%)	95% CI		Mean (%)	95% CI	Mean (%)	95% CI
≤39	15381	0.5	(0.4, 0.6%)	1.1	(0.9, 1.3%)	23087	5.7	(5.4, 6.0%)	8.3	(7.9, 8.6%)
40–49	15287	1.9	(1.7, 2.1%)	3.5	(3.2, 3.7%)	26583	8.1	(7.7, 8.4%)	11.9	(11.5, 12.3%)
50–59	9199	4.0	(3.6, 4.5%)	7.4	(6.9, 8.0%)	16783	9.9	(9.4, ,10.3%)	15.0	(14.4, 15.5%)
60–69	1830	7.8	(6.6, 9.1%)	13.7	(12.1, 15.2%)	4152	9.6	(8.7, 10.5%)	15.2	(14.1, 16.3%)
≥70	249	7.2	(4.0, 10.5%)	12.1	(8.0, 16.1%)	391	7.4	(4.8, 10.0%)	13.6	(10.2, 17.0%)

Data were adjusted for year of initial examination, and estimated for the examination in 1997. Significant difference between two definitions in both genders and any age group with higher prevalence rate in ATPIII-BMI25 definition $P < 0.0001$.

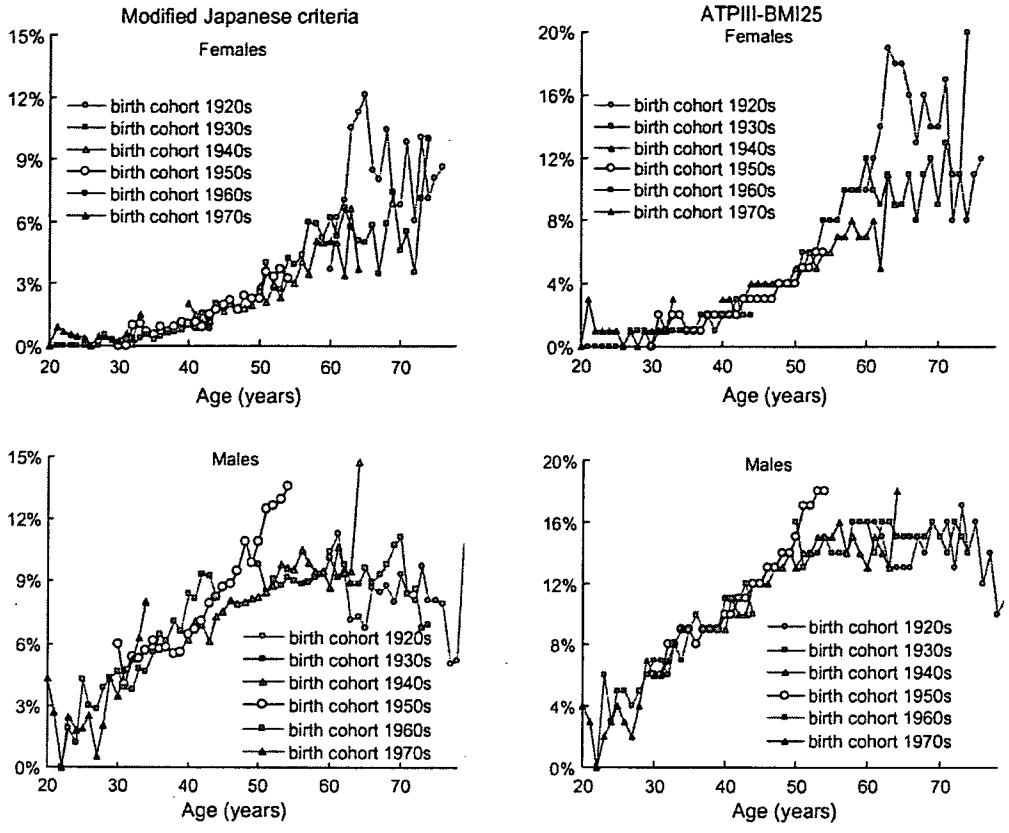

Fig. 1. Longitudinal changes for 16 years in the prevalence rate of metabolic syndrome by birth cohort in females and males using the modified Japanese and ATPIII-BMI25 criteria.

birth cohorts were lower than those of the older birth cohorts in both definitions (Fig. 1). There was a birth cohort effect in males at least between 40 and 55 years, indicating that the younger birth cohorts scored higher than the older birth cohorts in both criteria (Fig. 1).

Fig. 2 shows the prevalence rates of the individual components of metabolic syndrome in the modified Japanese criteria. There was no birth cohort effect on the prevalence rate of obesity in females, except for the cohort of the 1930s, which demonstrated a higher prevalence rate than that of the 1940s between age 50 and 64 years. However, the apparent birth cohort effect on the prevalence rate of obesity was detected in males with a higher prevalence in the younger cohort than the older one. Regarding the prevalence rate of hypertension, no apparent birth cohort effect was detected in either gender. There was no apparent birth cohort effect of the prevalence rate of impaired glucose tolerance in females, but there was an apparent effect in males with a higher prevalence rate in the younger cohort than that the older one. There seemed to be a birth cohort effect of the prevalence rate of dyslipidemia in both genders, with a lower prevalence rate in the younger cohort than the older one, at least for the birth cohort of the 1950s and older cohorts.

Fig. 3A shows the estimated prevalence rate of metabolic syndrome at individual ages according to the two different criteria after adjusting for the examination year (estimation at 1997). In male, the highest prevalence rate of metabolic syndrome was observed around 60 years for the ATPIII-BMI25 criteria and around 55 years for the modified Japanese criteria. In females, the highest rate was detected at the 70 years and older age group for both criteria.

Fig. 3B showed the estimated prevalence rate of each component of metabolic syndrome defined in the modified Japanese criteria at individual ages after adjusting for the examination year (estimation at 1997). The prevalence rates of obesity and dyslipidemia increased between 20 and 50 years, or 70 years in males, or females, respectively. The prevalence rate of hypertension increased in both genders from 20 years through the 80 years. Regarding impaired glucose tolerance, the prevalence rate increased up to the 60th or 70th decade and then declined in males or females, respectively.

Fig. 4A shows the secular change in the prevalence rate of metabolic syndrome defined by two different criteria from 1989 to 2004 from age younger than 40 years through age 70 years and older at 10-year intervals. In ATPIII-BMI25 criteria in females except for younger than 40 and 70 years and older age groups the prevalence rate of metabolic syndrome decreased (trends: 40–49 years, $P<0.01$; 50–59 and 60–69 years, $P<0.0001$). In males aged 40–49 and 50–59 years the

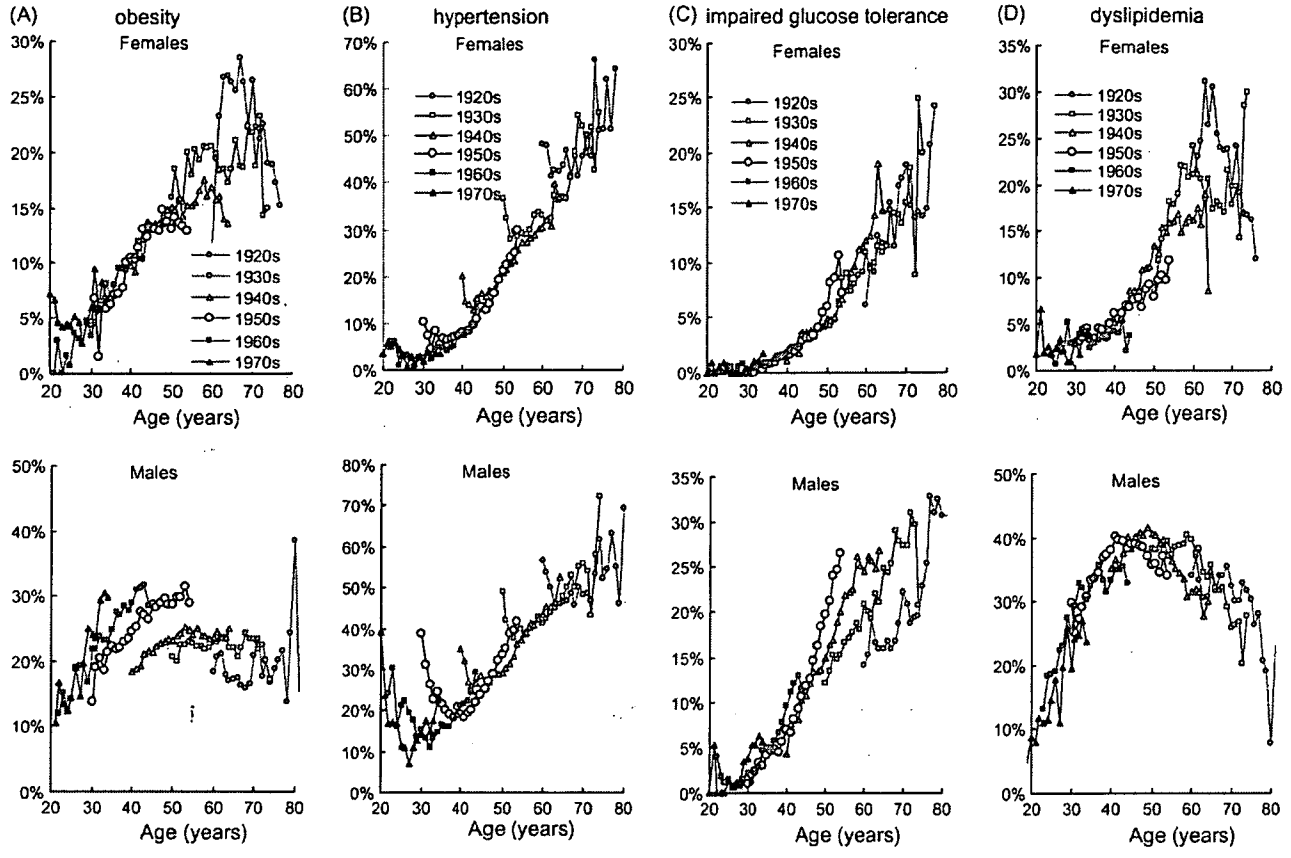

Fig. 2. Prevalence rates of individual component of metabolic syndrome in the modified Japanese criteria.

prevalence increased during study periods (trends, $P < 0.001$). According to the modified Japanese definition, the prevalence of metabolic syndrome decreased in females aged 50–59 and 60–69 years during study periods (trends, $P < 0.01$ and 0.001, respectively), and increased in males of youngest group, aged 40–49 and 50–59 years. Fig. 4B shows the trends in age-adjusted prevalence rate of metabolic syndrome defined by two criteria. The data were estimated age at 50 years. In both criteria the prevalence rate of metabolic syndrome decreased in females and increased in males, respectively.

3. Discussion

The cross-sectional observations suggested similar age-specific changes of the prevalence of metabolic syndrome with two different metabolic syndrome definitions. In addition, our results agree with the previous cross-sectional observations of age-specific prevalence of metabolic syndrome from other countries and ethnicities. The Third National Health and Nutrition Survey indicated that the prevalence of metabolic syndrome increased from 20–29 to 60–69 years [16]. A survey in Iran suggested that the prevalence increased with age, with the lowest prevalence at 20–29 years and the highest at 60–69 years in both genders [18]. A cross-sectional survey in China demonstrated that the prevalence of metabolic syndrome increased among men and women until age 65 years, when the prevalence decreased slightly among men and remained constant among women [17]. Although there are some differences in the peak age of the prevalence in males, it was surprising to find that there is a similarity of age-specific changes in the prevalence rate of metabolic syndrome among different ethnic groups and in different countries, which have different cultures, lifestyles, food habits, and longevity. This consistency may suggest that the aging effect highly regulates the prevalence of metabolic syndrome even if genetic and environmental influences may exist.

We clearly showed that the prevalence rate of metabolic syndrome was much higher in both genders as well as in all age groups with the ATPIII-BMI25 definition than with the modified Japanese definition. This is not surprising, since there are several noteworthy differences. The Japanese definition requires the presence of obesity [15]. In contrast, the NCEP definition makes obesity one of the five equally weighted criteria [12]. Furthermore, the thresholds for HDL-cholesterol levels under the modified Japanese definition are <40 mg/dl in both genders, but those under the NCEP definition are different between genders: men, <40 mg/dl; women, <50 mg/dl.

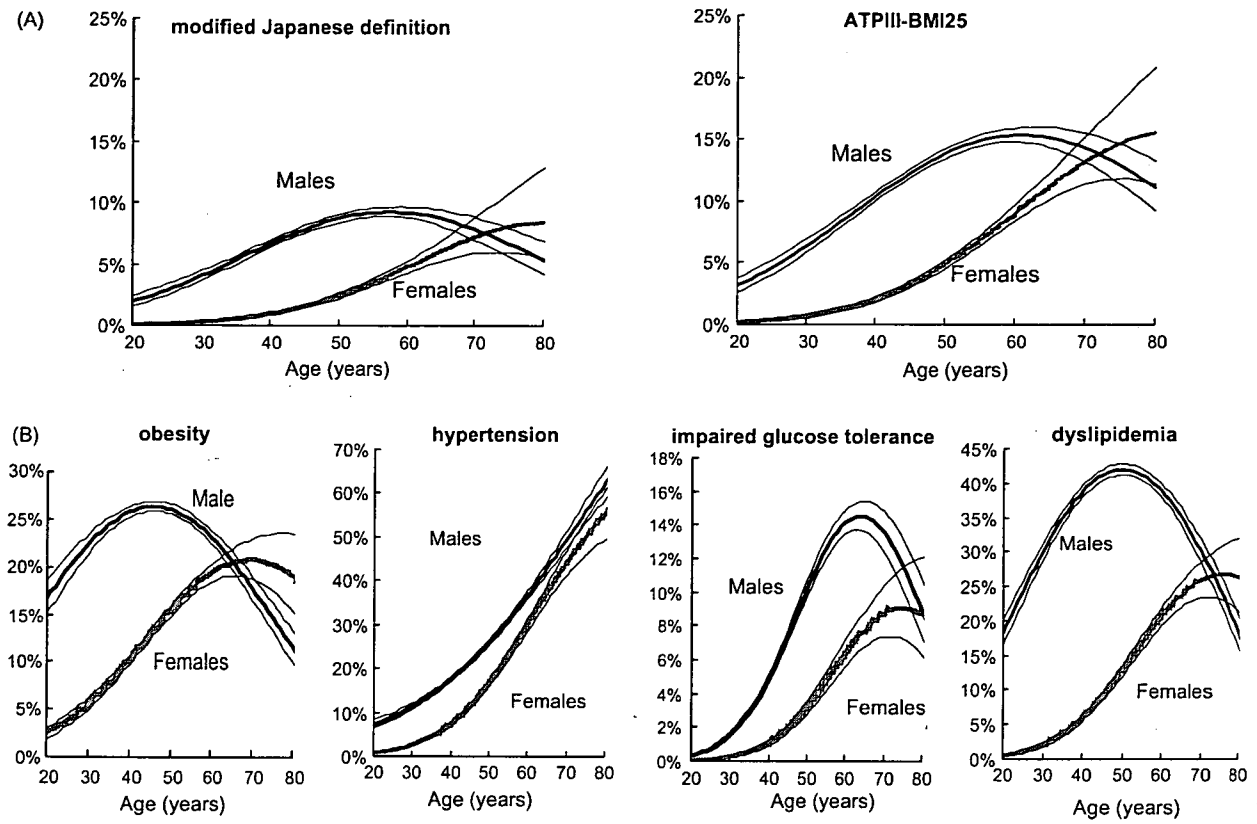

Fig. 3. (A) Estimated prevalence rate of metabolic syndrome at individual age according to the two different criteria after adjusting for examination year (estimation at 1997). (B) Estimated prevalence rate of each component of metabolic syndrome defined by the modified Japanese criteria at individual age after adjusting for examination year (estimation at 1997). Dotted curves indicate 95% CI.

Longitudinal observations demonstrated that there is a birth cohort effect on the prevalence rate of metabolic syndrome as well as the each of the components of metabolic syndrome in a large Japanese cohort. The estimated prevalence of metabolic syndrome increased from 20 up to 80 years in females both with the modified Japanese and ATPIII-BMI25 definitions. In males, the prevalence of metabolic syndrome gradually increased from 20 up to 50–59 years or up to 60–69 years followed by a decline at 70 years and older with the modified Japanese or ATPIII-BMI25 definition, respectively. It is obvious that the increasing trend of metabolic syndrome with age can be attributed to a similar age-related trend in each of the components of metabolic syndrome. The similar age-specific change of the prevalence rate was observed in obesity, impaired glucose tolerance, and dyslipidemia in males. The difference of the peak ages of the prevalence rate of metabolic syndrome in the ATPIII-BMI25 and modified Japanese criteria in males may be due to the requirement of obesity in the modified Japanese criteria, since the prevalence of obesity decreased after 50 years of age in males. In contrast to males, consistent age-specific changes of each component of the metabolic syndrome in females showed a consistent increase in the prevalence rate with age.

We showed the age-specific secular trends of the prevalence of metabolic syndrome in both genders from 1989 through 2004. In both definitions a similar trends of the prevalence of metabolic syndrome were demonstrated in both genders during study periods. The prevalence of metabolic syndrome decreased in females aged 50–69 years, and increased in males aged 40–59 years. Consistently the age-adjusted trends estimated at 50 years based on the longitudinal analysis decreased in females and increased in males in both criteria during study periods. Only a few reports regarding secular trends in the prevalence of metabolic syndrome are available. From two national surveys: the National Health and Nutrition Examination Survey (NHANES) III and NHANES 1999–2000, it has been demonstrated that the prevalence of metabolic syndrome increased significantly in females from 1988–1994 through 1999–2000 in US but increased much smaller without statistical significance in males [23]. The recent the Mexico City Diabetes Study, a population-based study, revealed that the prevalence of the metabolic syndrome has not increased in both genders between 1990–1992 and 1997–1999 [24]. These taken together with our findings suggest the secular trends of metabolic syndrome are dependent on each country or ethnicity which has differences in genetic background, social status, and diet. Two important determinants of the metabolic syndrome are obesity and physical activity. In our cohort the secular trends of the prevalence of obe-

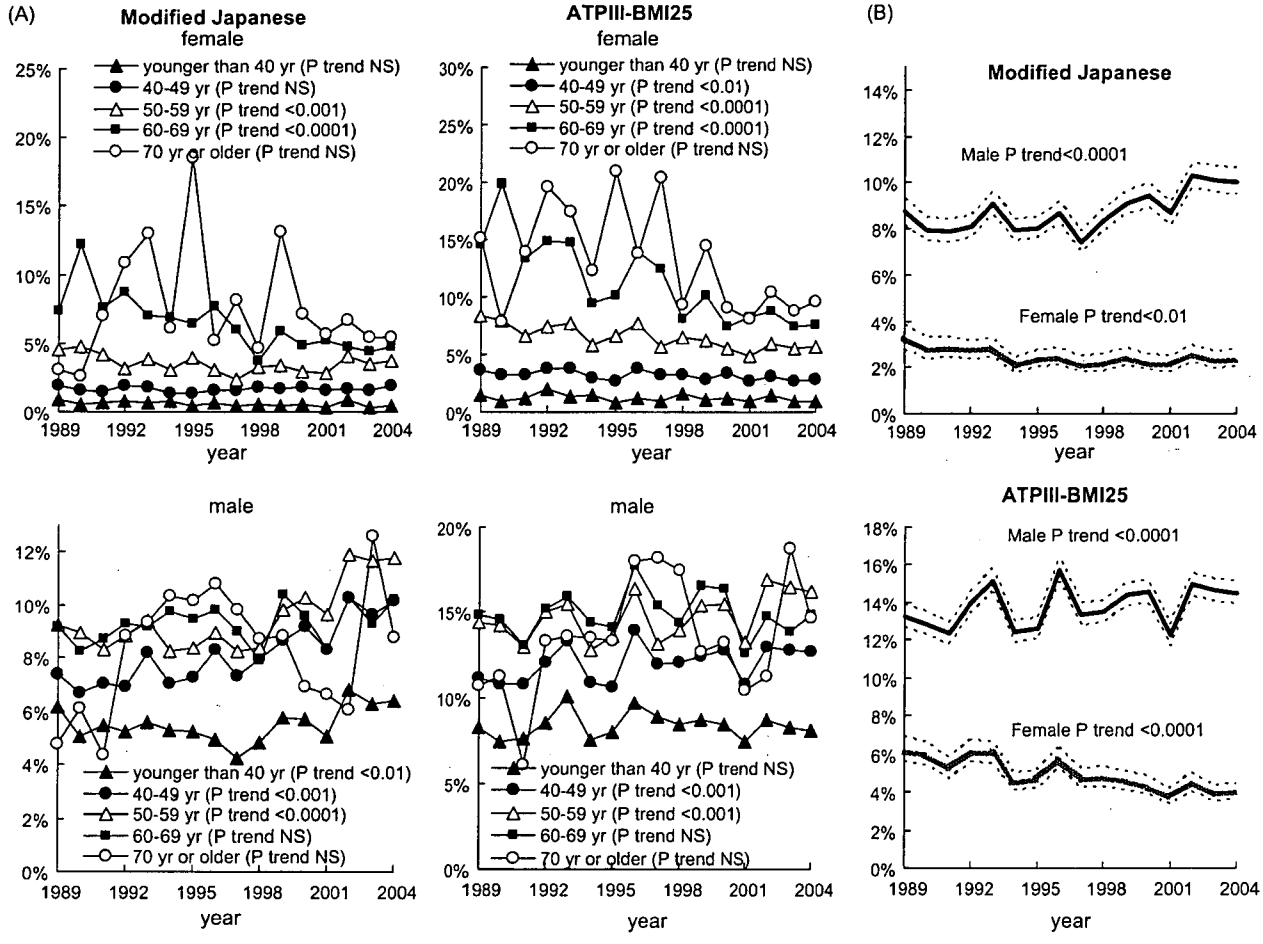

Fig. 4. (A) Secular change in the prevalence rate of metabolic syndrome defined by two different criteria from 1989 to 2004 from age younger than 40 years through age 70 years and older at 10-year intervals. (B) Trends in age-adjusted prevalence rate of metabolic syndrome defined by two criteria. The data were estimated age at 50 years.

sity decreased in females and increased in males in most of age groups during study periods (data not shown). This seems to affect the trends of metabolic syndrome in our cohorts. The data of physical activity in the participants are unavailable.

There are several limitations in the present study. The BMI was used as an index of obesity instead of waist circumference. This substitution appears to affect the prevalence rate of metabolic syndrome, although it has been reported that BMI may be useful in making comparisons pertaining to metabolic syndrome in the Japanese as the index of visceral obesity, rather than waist circumference, and that the ATPIII-BMI25 definition is suitable for the determination of metabolic syndrome for the Japanese [25]. Some selection bias such as a healthy worker bias may exist in our study, since most of the subjects were healthy office workers. In addition, the subjects may have been aware of the impact of body weight, blood pressure, glucose and lipid levels on their health, since they had been receiving annual examinations at a health examination center.

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研究論文●28

加齢とメタボリックシンドローム
—年齢別にみたメタボリックシンドロームのウエスト基準値の妥当性—

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研究論文●28

加齢とメタボリックシンドローム
—年齢別にみたメタボリックシンドロームのウエスト基準値の妥当性—

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大藏　倫博[3)]

1. 背景および目的

日本肥満学会などでは日本独自のメタボリックシンドロームの基準値を定めたが[1,2)]，腹部CTでの内臓脂肪面積などをもとにした高齢者での基準値の妥当性の検討はほとんどなされていない。本研究では，ウエスト基準値の妥当性を年齢別・性別に検討するために，無作為抽出された中高年地域住民を対象に，肥満度(BMI)や腹部CTでの内臓脂肪量との関連を年齢別・性別に解析した。

2. 方法

1．対象

対象は，「国立長寿医療センター研究所・老化に関する長期縦断疫学研究(NILS-LSA)」[3,4)]第3次調査(2004～2006年)に参加した40～84歳の中高年地域住民2,378名(男性1,204名，女性1,174名，平均年齢±SD：59.9±11.8歳)である。調査参加者は，愛知県大府市および知多郡東浦町の住民から年齢別・性別に層化無作為抽出されて選ばれている。

2．測定項目

1）身体計測

身長および体重を計測し，体重(kg)を身長(m)の2乗で割って求めたBMIを肥満度とした。空腹時の立位で計測した肋骨弓下縁と腸骨稜上縁の中間地点での胴周囲長をウエスト周囲長とした。

2）血液生化学検査

12時間以上の絶食後の朝9時前後の静脈採血により，HDLコレステロール，トリグリセライドおよび血糖の測定を行った。絶食が確認されなかった対象は解析から除外した。

3）血圧測定

少なくとも15分の臥位安静後に，自動血圧測定装置(Colin BP-203RV-Ⅱ)により血圧の測定を行った。

4）内臓脂肪量の計測

腹部CT(Shimazu SCT-6800TX)により，臥位での臍レベルでの断面を撮影し，FatScan N2 systemにより，皮下脂肪領域面積および腹腔内脂肪面積(内臓脂肪面積)を計測した[5)]。

3．解析方法

性別および10歳ごとの年齢群別に分け，日本肥満学会などの基準値[1)]に基づいて，メタボリックシンドロームの有病率およびウエストが基準値以上の者の割合を求めた。これらの年齢によるトレンドの検定は，Cochran-Mantel-Haenszelの統計量を用いて行った。

一般線形モデル(GLM)にてウエストを目的変数とし，内臓脂肪面積，年齢および年齢と内臓脂肪面積の交互作用を説明変数とするモデルを作り，メタボリックシンドロームのカットオフポイント[2)]とされる内臓脂肪面積

1）国立長寿医療センター研究所疫学研究部　2）中京女子大学健康科学部栄養科学科　3）筑波大学大学院人間総合科学研究科

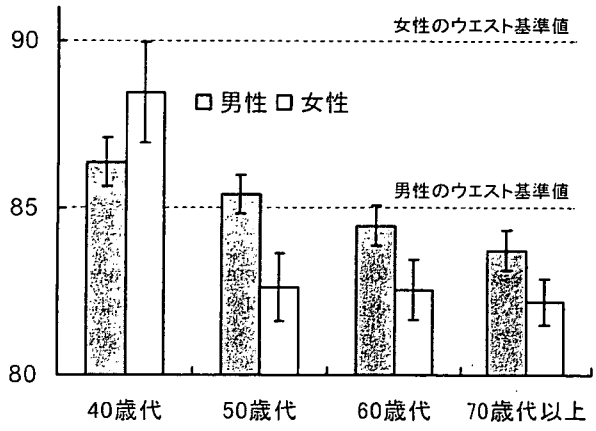

図1　性別・年齢別にみた腹部CTでの内臓脂肪面積正常上限100 cm²に相当するウエストの推定値と95%信頼区間
点線は日本肥満学会などによるウエストの基準値を示す。

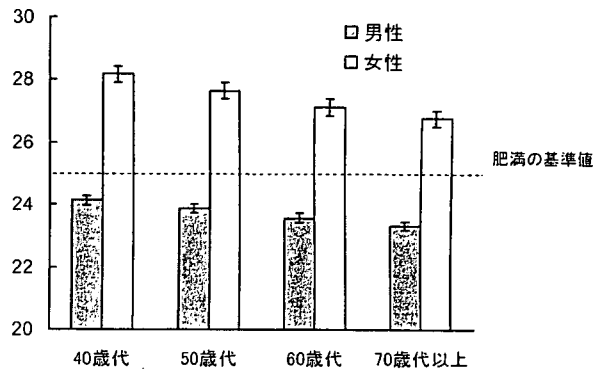

図2　性別・年齢別にみたウエストが基準値であるときのBMIの推定値と95%信頼区間
点線は日本肥満学会による肥満の基準値を示す。

100 cm²に相当するウエストの大きさを性別・年齢群別に推定し，Tukey-Kramer法による多重比較を行うとともに，推定値の年齢によるトレンドの検定を行った。

同様にBMIを目的変数とし，ウエスト，年齢および年齢とウエストの相互作用を説明変数とするモデルを作り，メタボリックシンドロームのカットオフポイントである男女のウエスト値でのBMIの大きさを性別・年齢群別に推定し，推定値の年齢によるトレンドの検定を行った。解析にはSASリリース8.2を用いた[6]。

3. 結果

メタボリックシンドロームは男性の14.4%，女性の2.6%にあり，男女とも年齢による有意なトレンドはなかった。

ウエストの大きさは男性の40.5%，女性の7.0%でメタボリックシンドロームの基準値を上回っていた。男性では60歳代で基準値を超える者の割合が高くなっていたが，年齢によるトレンドはなかった。女性では70歳以降でその割合が高くなっており，年齢による有意なトレンドが認められた(p＝0.001)。

腹部CTでの内臓脂肪面積正常上限である100 cm²に相当するウエストの推定値は，50歳以降の女性では基準値を大きく下回っていた(図1)。40歳代と比較すると，50歳以降のすべての年代で有意に低値であった(p＜0.0001)が，50歳以降の年代間には有意差はなかった。男性では，加齢とともにウエストの推定値は低下していた(p＜0.0001)。

ウエストが基準値である場合の推定BMIは男性全体で23.7，女性全体で27.3であり，男性では肥満の基準値を下回っていた。また，図2に示すように，男女とも加齢によりBMIの推定値は有意に低下していた(p＜0.0001)。

4. 考察

国際的に用いられているメタボリックシンドローム診断基準であるNCEP ATP-Ⅲでは，ウエストの基準値は男性では102 cm，女性では88 cmである[7]。これに比べると，日本における基準値は男性に極めて厳しい値となっている。

日本における基準は，臍部における腹部CTでの内臓脂肪面積が100 cm²以上で冠動脈疾患の危険因子蓄積が増加することから，この値を基準として内臓脂肪面積が100 cm²に相当するウエストの大きさをメタボリックシンドロームの基準としたが[2]，年齢を考慮した基準値ではない。

今回の結果では，内臓脂肪量からみると，特に50歳以降の女性ではウエストの基準値は高すぎると思われる。閉経による性ホルモンの急激な変化に伴う体脂肪分布の変化を考慮する必要があろう。

肥満度からみると，男性，特に高齢男性では，ウエストの基準値は低すぎると推測される。BMIが23程度の非肥満者でもウエストは基準値を超えてしまい，高齢者に不要な減量をさせてしまうことになりかねない危険がある。

死亡率や生活習慣病の罹患率が最も低くなる肥満度を理想的な肥満度といい，40歳代ではBMI 22くらいが，この理想的な肥満度であることが知られている[8,9]。米国で

の420万人のデータからの解析では，死亡率の最も低い理想的な肥満度は加齢とともに大きくなる。理想的なBMIの値は男女で大きな差はなく，年齢とともにほぼ直線的に大きくなっていく[10,11]。理想的な肥満度は70歳以降の高齢者では25を超えており，高齢者では肥満よりもむしろやせや低栄養が死亡のリスクとなる[12]。

また，椎間の狭小化，椎骨の圧迫骨折による脊椎前彎の増強などにより，身長が年齢とともに低くなっていく。このため，高齢者のBMIは本来あるべき値よりも大きくなっていることにも注意しなければならない[12]。

メタボリックシンドロームは生活習慣病の核をなす概念であり，その対応が急がれるが，一方で年齢を考慮しない一律の生活指導は，高齢者ではむしろ健康を害することになるかもしれないことに十分な注意を払うべきであろう。

5 結語

メタボリックシンドローム診断基準におけるウエスト基準値の妥当性を検討するために，無作為抽出された中高年地域住民を対象に，BMIや腹部CTでの内臓脂肪量との関連を年齢別・性別に解析した。

内臓脂肪量を基準にした検討では，50歳以降の女性ではウエストの基準値は高すぎ，また肥満度からの検討では男性，特に高齢男性ではウエストの基準値は低すぎると推測された。

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本研究の発表に際し，「国立長寿医療センター研究所・老化に関する長期縦断疫学研究(NILS-LSA)」にご参加いただいている愛知県大府市ならびに東浦町の住民の皆様，および調査スタッフに感謝いたします。この研究の一部は，厚生労働科学研究費補助金循環器等生活習慣病対策総合研究事業「内臓肥満の要因と動脈硬化促進に関する総合的研究」(H18-循環器等(生習)-一般-045)により行われました。

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研究論文●31

一般地域住民における腹部肥満感受性因子の網羅的検討

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研究論文●31

一般地域住民における腹部肥満感受性因子の網羅的検討

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1. 目的

肥満，特に腹部肥満はメタボリックシンドロームの源流にある病態として近年注目されている[1,2)]。メタボリックシンドロームに関連する病態(肥満，高脂血症，高血圧，耐糖能異常)はいずれも多因子疾患と考えられており，多くの遺伝子多型との関係が報告されている[3,4)]。従来このような高脂血症，高血圧，耐糖能異常との関連が報告されている遺伝子多型が，腹部肥満にも影響を及ぼしている可能性がある。

本研究では，腹部肥満指標(内臓脂肪面積およびウエスト周囲径)と126種の老化・老年病関連候補遺伝子多型との関係を網羅的に検討し，腹部肥満感受性遺伝子多型を抽出することを目的とした。

2. 対象および方法

対象は，「国立長寿医療センター研究所・老化に関する長期縦断疫学研究(NILS-LSA：National Institute for Longevity Sciences-Longitudinal Study of Aging)[5)]」の第一次調査(1997～2000年)，第二次調査(2000～2002年)にともに参加した地域在住中高年男女1,813人(第二次調査時42～82歳，平均年齢60.5±10.6歳，男性944人，女性869人)の中で，本研究に必要な調査項目を完遂した約1,750人である(遺伝子多型の判定が可能であった人数が遺伝子多型によって異なるため，解析人数は一定ではない)。

腹部肥満指標として臍位腹部CTスキャンにおける内臓脂肪面積(WCT)，および前日午後9時より欠食で午前中に測定したウエスト周囲径(WC)を用いた。腹部肥満の有無の判定には，わが国のメタボリックシンドローム診断基準(2005年)[6)]に基づき，内臓脂肪面積100 cm^2 (WCT-J)，ウエスト周囲径男性85 cm，女性90 cm (WC-J)をカットオフポイントとして用いた。

遺伝子多型は，NILS-LSAで2005年度までに測定された老化・老年病関連候補遺伝子多型145種の中で，解析に必要な多型の分布が得られた126種である(詳細割愛)。各遺伝子多型について頻度の高いalleleを野生型，頻度の低いalleleを変異型とし，ホモ野生型/ヘテロ・ホモ変異型間で腹部肥満指標を比較した。解析は性別，女性ではさらに閉経の有無別で行い，年齢で調整した一般線形モデルで内臓脂肪面積，ウエスト周囲径と遺伝子多型との関係を検討した後，関係が有意であった遺伝子多型について，腹部肥満の有無との関係を年齢を調整した多重ロジスティック回帰分析を用いて検討した。統計解析にはSAS 8.2を用い，$p<0.05$を統計的有意とした。

3. 結果

126種の候補遺伝子多型中，24種の遺伝子多型で，多型により内臓脂肪面積(WCT)，ウエスト周囲径(WC)が有意に異なっていた(表1)。これらの遺伝子多型の中で8種の遺伝子多型では，年齢を調整した多重ロジスティック回帰分析で検討した結果，腹部肥満のリスクが遺伝子

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表1　内臓肥満と遺伝子多型

遺伝子多型		性	閉経の有無	従属変数	遺伝子多型間の有意差 (p value)
略　号	名称(多型部位) (rs No.)			腹腔内脂肪面積(WCT)/ウエスト周囲径(WC)	
ADR	Androgen receptor (CAG repeat) (rs4045402)	女性	未閉経	WCT	0.022
CAL	Calcitonin receptor (C1377T) (rs1801197)	女性	未閉経	WCT	0.047
CP10	Calpain10 (G-43A) (rs3792267)	女性	閉経	WCT	0.021
CYP17	Cytochrome P450, family 17, subfamily A, polypeptide 1 (T-34C) (rs743572)	女性	閉経	WC	0.029
DRD2	Dopamine receptor D_2 CG (Ser311Cys) (rs1801028)	女性	未閉経	WC	0.046
EDN1	Endothelin-1 (Lys198Asn)	女性	未閉経	WC	0.041
		女性	未閉経	WCT	0.048
GNB	Guanine nucleotide-binding protein β3 (C825T) (rs5443)	女性	閉経	WC	0.045
GP1BA	Glycoprotein I bα (C1018(Thr145Met)) (rs6065)	男性		WC	0.018
		男性		WCT	0.008
IRAK1	Interleukin-1 receptor-associated kinase 1 (T587C(F196S)) (rs1059702)	女性		WCT	0.043
		女性	閉経	WC	0.031
		女性	閉経	WCT	0.029
KLOT	Klotho (G-395A) (rs1207568)	男性		WC	0.047
		男性		WCT	0.045
MMP12	Matrix metalloproteinase-12 (A-82G) (rs2276109)	男性		WC	0.019
		男性		WCT	0.010
MAOB	Monoamine oxidase B {GA(intron13/exon14)} (rs1799836)	女性	未閉経	WC	0.021
		女性	未閉経	WCT	0.027
Mt15497	MT15497 (G/A)	女性		WC	0.013
		女性		WCT	0.019
		女性	閉経	WC	0.009
		女性	閉経	WCT	0.016
Mt15524	MT15524 (A/G)	女性	閉経	WC	0.049
		女性	閉経	WCT	0.034
NOSID	Nitric oxide synthase 3 (ID)	男性		WCT	0.010
PAI	Plasminogen activator inhibitor 1 (4G/5G) (rs1799889)	男性		WC	0.025
PRC	24 kDa protein of complex I (Ala29Val) (rs906807)	女性	閉経	WC	0.035
RAGE1	Receptor of advanced glycation end products (AGER) (1704G/T) (rs184003)	男性		WCT	0.029
RIL	Reversion-induced LIM (T-333C) (rs453602)	男性		WC	0.041
		男性		WCT	0.007
TNF	Tumor necrosis factor α (C-863A) (rs1800630)	男性		WCT	0.030
TOM40	TOM40 polymorphism SNP988 (T5328C) (rs157581)	女性		WC	0.009
		女性		WCT	0.020
		女性	閉経	WC	0.001
		女性	閉経	WCT	0.003
UCP1	Uncoupling protein 1 (A-3826G) (rs1800592)	男性		WC	0.013
VDR1	Vitamin D receptor (T2C)	女性	閉経	WC	0.049
VEGF4	Vascular endothelial growth factor (G-1154A) (rs1570360)	男性		WC	0.008
		男性		WCT	0.048

腹腔内脂肪面積(WCT)もしくはウエスト周囲径(WC)を従属変数，遺伝子多型を説明変数，年齢を調整変数とした，性別・閉経の有無別の一般線形モデルによる分析。

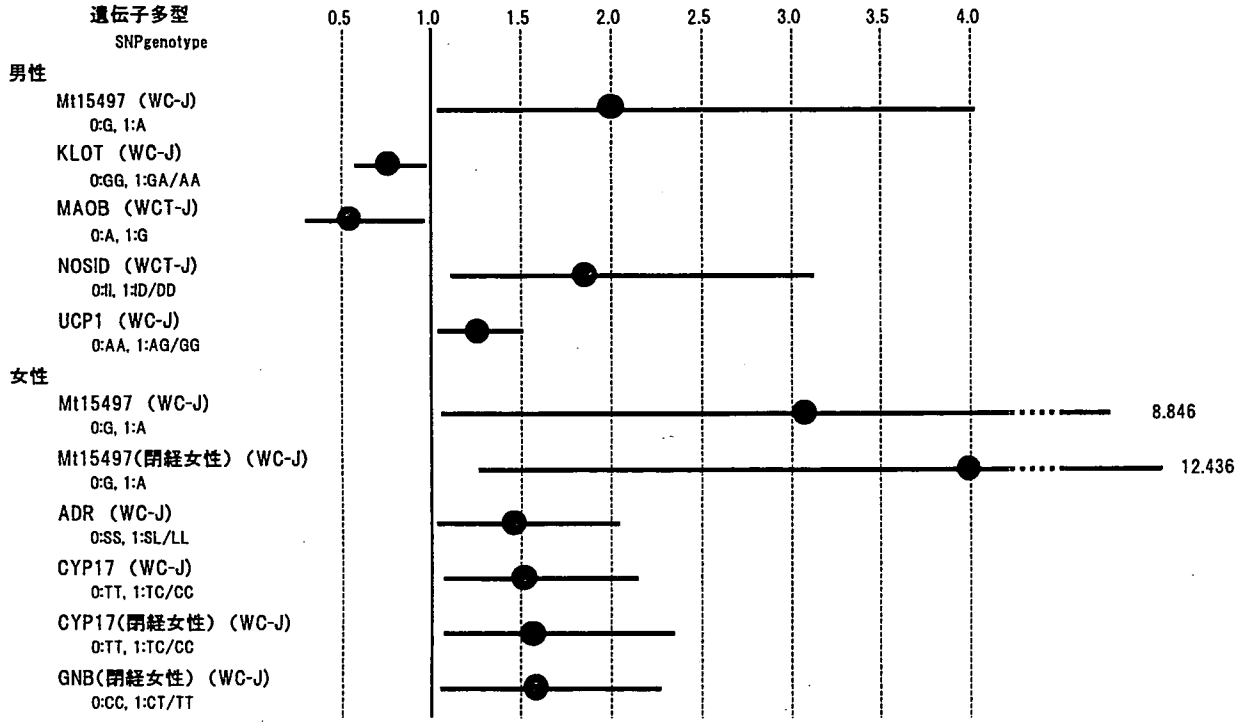

図1 ロジスティック解析(性別，閉経の有無別，年齢調整済み)
結果変数：腹部肥満(WC-JもしくはWCT-J) 無：0，有：1。

多型によって有意に増大することが示された(図1)。

呼吸・代謝に関連するミトコンドリアの遺伝子多型の1つであるMt15497のG alleleを有する者では，A alleleを有する者より，ウエスト周囲径で判定される腹部肥満を示す危険性が男性では約2倍，女性では約3倍，特に閉経女性では約4倍高かった。

そのほかに男性ではKLOT，MAOB，NOSID，UCP1，女性ではADR，CYP17，GNBの遺伝子多型で腹部肥満を示す危険性が異なる可能性が示された。

4 考察，結論

老化・老年病に関わる複数の遺伝子多型が中高年者の腹部肥満に関連していると考えられた。肥満のみならず，腹部肥満も多因子疾患であり，腹部肥満に影響を与える遺伝子多型は男女共通のものと，男性，女性にそれぞれ特異なものがあると考えられた。Mt15497と肥満との関係についてわれわれは既に一部報告しているが[7]，今回，わが国でのメタボリックシンドロームのカットオフポイントとの関連も明らかになった。しかし，腹部CTあるいはウエスト周囲径と遺伝子多型との関係と，わが国のメタボリックシンドローム腹部肥満診断基準と遺伝子多型との関係は，必ずしも一致していなかった。腹部肥満診断基準の妥当性については現在，論議されているところであり，個別の遺伝子多型が腹部肥満に与える影響のカットオフポイントがあるかどうかも検討すべきであろう。今後，これらの遺伝子多型の機能や腹部肥満への影響の性・年齢特異性，さらにはこれらの遺伝子多型の集簇により腹部肥満の危険性が増大するかどうかについて検討が必要である。

謝辞

本研究の発表に際し，「国立長寿医療センター研究所・老化に関する長期縦断疫学研究(NILS-LSA)」にご参加いただいている愛知県大府市ならびに東浦町の住民の皆様，および調査スタッフに感謝いたします。この研究の一部は，厚生労働科学研究費補助金循環器等生活習慣病対策総合研究事業「内臓肥満の要因と動脈硬化促進に関する総合的研究」(H18-循環器等(生習)-一般-045)により行われました。

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