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Original article

# Prevalence of the metabolic syndrome in elderly and middle-aged Japanese

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## ABSTRACT

*Background/Purpose:* Diagnosis and management of the metabolic syndrome (MetS) are beneficial for successful aging. In spite of several criteria for MetS, there is little information on cardiometabolic risk clustering in elderly Japanese. The purpose of this study was, therefore, to determine the relationship between age-associated changes in obesity and metabolic components in the Japanese.

*Methods:* We analyzed data from the nationwide survey conducted in 2000. Using Adult Treatment Panel III (ATP III) and Japanese diagnostic criteria for MetS, we analyzed 2366 people aged from 40 to 79 years (men, 1425 and women, 941) from the total participants.

*Results:* The prevalence of MetS was almost three fold higher by modified ATP III, International Diabetes Federation, and Japanese criteria, in elderly women than in middle-aged women, whereas no difference was found between middle-aged and elderly men by the three criteria. A marked increase in the prevalence of MetS was found by modified ATP III and International Diabetes Federation criteria compared with that by the Japanese criteria in women. Among the risk factors, the prevalence of central obesity and dyslipidemia increased only in women and that of high fasting glucose and high blood pressure increased in both genders with aging. Among the MetS subjects who fulfilled the modified ATP III criteria, more clustering of risk was observed in elderly than in middle-aged subjects, especially in women. Blood pressure increased and triglyceride decreased in both genders, and non-high-density-lipoprotein cholesterol decreased in elderly men. The prevalence of dyslipidemia decreased in elderly men.

*Conclusion:* Aging is an important factor that affects the metabolic abnormality, and aging of the population would lead to increase in the prevalence of MetS. Therefore, the development of better approaches to the prevention and management of MetS is necessary for successful aging in our society. Copyright © 2010, Asia Pacific League of Clinical Gerontology & Geriatrics. Published by Elsevier Taiwan LLC. Open access under CC BY-NC-ND license.

## 1. Introduction

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In the developed countries, life expectancy has shown a continuous increase in the last decades, especially in Japan, along with an increase in age-associated diseases and disabilities.

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Because of the westernization of our lifestyle, this aging population will endure more chronic medical conditions, such as cardiovascular disease, dyslipidemia, diabetes mellitus, chronic kidney disease, and the metabolic syndrome (MetS). MetS is a constellation of multiple risk factors, such as central obesity, dyslipidemia, elevated glucose, and elevated blood pressure, in which insulin resistance is the main underlying disorder.<sup>1</sup> Because the degree of insulin resistance increases with age, elderly are at a higher risk to develop cardiometabolic disorders.<sup>2</sup> At the same time, elderly with MetS are supposed to have a higher risk of cardiovascular disease.<sup>3</sup> In elderly, the diagnosis of MetS is also related to a more pronounced cognitive decline and, thus, disability.<sup>4</sup> Therefore, the identification and treatment of patients with MetS would be an important approach to reduce morbidity and impairment in elderly.

In 2000, we conducted lipid survey in various districts in Japan.<sup>5</sup> In this survey, we found that the level of triglyceride increased in middle-aged men along with the increased body mass index (BMI) compared with the data in 1990.<sup>6</sup> However, the BMI did not change in the elderly population in spite of a small increase in triglyceride levels. Although MetS is a risk factor for cardiovascular disease in middle-aged and elderly people and, therefore, a public health problem, it is still unknown whether the same diagnostic criteria can be applied to both groups.

In the last few years, several expert groups have attempted to set forth simple diagnostic criteria to be used in clinical practice to identify patients with MetS. The committee of International Diabetes Federation (IDF) adopted waist circumference as the surrogate marker for central obesity as an essential component of this syndrome,<sup>7</sup> whereas the National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria required no single factor for diagnosis, but instead, required the presence of at least three out of five components for the diagnosis.<sup>1</sup> In Japan, the committee has established the diagnostic criteria under the same principle as the IDF criteria, except the cutoff for high glucose as 110 mg/dL instead of 100 mg/dL.<sup>8</sup> The cutoff of waist circumference for central obesity was adopted as 85 cm or greater in men and 90 cm or greater in women in Japanese criteria, although the Asian cutoff of waist circumference is 90 cm or greater in men and 80 cm or greater in women. Recently, several groups have shown that the Asian cutoff for the waist circumference is better than that of the Japanese.<sup>9–12</sup> Furthermore, Hata et al.<sup>13</sup> have shown that MetS defined by the Japanese criteria, with the modification of a waist circumference of 90 cm or greater in men and 80 cm or greater in women, is a better predictor of each ischemic stroke subtype in the Japanese population. Therefore, modification of the Japanese criteria for MetS might be necessary in the future.

The purpose of this study was to examine the prevalence of MetS in the Japanese elderly population and to compare the prevalence of MetS and comorbidities with those in the middleaged population. We also compared the prevalence of MetS by modified ATP III, IDF, and Japanese diagnostic criteria.

## 2. Methods

## 2.1. Designs and data collection

The Research Group on Serum Lipid Level Survey 2000 in Japan asked the members of 36 institutes from various areas around Japan to join this survey. The project was designed to produce representative data of serum lipid levels in the civilian Japanese population. The subjects were people receiving annual health examinations in general community, companies, and schools, and not those visiting hospitals. Among the total number of 12,839 participants, we measured the waist circumferences of 3264 people aged 20–79 years (men, 1917 and women, 1357). In this study, we examined the prevalence of MetS in subjects aged 40–79 years (men, 1425 and women, 941) and compared the prevalence of MetS along with each metabolic abnormality according to the Japanese and ATP III criteria. The Ethics Committee in Kyoto University School of Medicine approved this study. Oral informed consent was obtained from all the participants.

## 2.2. Laboratory methods

All serum and plasma samples were obtained in the fasting state. All lipid and other analyses were conducted on venous blood samples within 1 week of collection at Bio Medical Laboratories (BML) (Saitama, Japan). Serum cholesterol and triglyceride levels were measured by enzymatic assay. High-density-lipoprotein (HDL) and low-density-lipoprotein cholesterols were measured enzymatically by a kit from Daiichi Kagaku Co. Ltd. (Tokyo, Japan). The results of lipid analyses in the four surveys were indirectly standardized according to the criteria of the Centers for Disease Control and Prevention (CDC) Lipid Standardization Program.<sup>14</sup> Thus, the cholesterol levels in these five surveys appear to be comparable. Plasma glucose was determined enzymatically, and hemoglobin A1c (HbA1c) was determined by a kit from Kvowa Medex Co. Ltd. (Tokyo, Japan). Serum insulin was determined by immunoradiometric assay (Abbott Diagnostics Division, Abbot Park, IL). Waist circumference at the umbilical level was measured in the late exhalation phase in standing position.

## 2.3. Definition of MetS

According to the definition released by ATP III, published in 2008, we analyzed the prevalence of MetS. We modified the criteria by using the Asian cutoff of waist circumference (90 cm for men and 80 cm for women). Other differences are fasting glucose greater than or equal to 100 mg/dL and HDL cholesterol less than 50 mg/dL in women. MetS of modified ATP III criteria was defined as the presence of at least three abnormalities among central obesity, hypertriglyceridemia, low HDL cholesterolemia, high blood pressure, and fasting high glucose. We also analyzed using the Japanese diagnostic criteria of the MetS in 2005, defining MetS as the presence of two or more abnormalities in the presence of central obesity (waist circumference: 85 cm or more in men and 90 cm or more in women). Three abnormalities are as follows: (1) triglycerides greater than or equal to 150 mg/dL and/or HDL cholesterol less than 40 mg/dL or under treatment for this type of dyslipidemia; (2) systolic blood pressure greater than or equal to 130 mmHg and/or diastolic blood pressure greater than or equal to 85 mmHg, or under treatment for high blood pressure; (3) fasting glucose greater than or equal to 110 mg/dL or under treatment for diabetes (Table 1). Furthermore, we used modified IDF criteria for comparison. People treated with lipid-lowering drugs who had normal triglyceride and HDL cholesterol in this study were excluded, because we could not obtain data whether they were treated for hypercholesterolemia or hypertriglyceridemia.

### 2.4. Data analysis

The results were expressed as mean value  $\pm$  standard deviation. Differences in means were evaluated by unpaired *t* test, Mann–Whitney test, or analysis of variance, when appropriate. The categorical variables were compared by chi-square test. The analysis was performed by the Statistical Package for Social Sciences (ver. 11.5; SPSS Japan Inc., Tokyo, Japan). A *p* value of 0.05 or less was considered to indicate a statistically significant difference.

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Com	parison among	lapanese.	modified I	IDF. and	modified .	ATP III	criteria f	for metabol	ic syndrome
		1							

Definition of metabolic syndrome	Japanese (1) + any 2 or more of (2)–(4)	Modified ATP III for Asians 3 or more of (1)–(5)	Modified IDF for Asians (1) + any 2 or more of (2)–(5)
Components			
Central obesity (waist circumference)	(1) $\geq$ 85 cm (men), $\geq$ 90 cm (women)	(1) $\geq$ 90 cm (men), $\geq$ 80 cm (women)	(1) $\geq$ 90 cm (men), $\geq$ 80 cm (women)
High blood pressure	$(2) \ge 130/85$ mmHg and/or antihypertensive medication	(2) $\geq$ 130/85 mmHg and/or antihypertensive medication	(2) ≥130/85 mmHg and/or antihypertensive medication
Fasting high glucose	(3) ≥110 mg/dL and/or antidiabetic medication	(3) $\geq$ 100 mg/dL and/or antidiabetic medication	(3) ≥100 mg/dL and/or antidiabetic medication
Dyslipidemia	(4) Triglyceride ≥150 mg/dL and/or HDL-C <40 mg/dL	(4) Triglyceride $\geq$ 150 mg/dL	(4) Triglyceride $\geq$ 150 mg/dL
		(5) HDL-C <40 mg/dL (men), <50 mg/dL (women)	(5) HDL-C <40 mg/dL (men), <50 mg/dL (women)

IDF = International Diabetes Federation; ATP III = Adult Treatment Panel III; HDL-C = high-density-lipoprotein cholesterol.

# 3. Results

Table 2 shows the prevalence of MetS in Japanese middle-aged and elderly men and women according to the Japanese and modified ATP III and IDF criteria. According to the Japanese criteria, the prevalence of MetS was higher in both elderly men and women (13.3% vs. 18.9% in men and 1.5% vs. 4.8% in women). In women, the prevalence of MetS was almost three fold higher in the elderly than that in the middle-aged group (p < 0.01 by chi-square test). When we apply the modified ATP III and IDF criteria, the prevalence of MetS was also increased in women of each group (p < 0.01 in ATP III and IDF criteria by chi-square test), and the three fold increase in MetS in elderly women was consistent among the three criteria. The increase of MetS prevalence in women by modified ATP III and IDF criteria compared with that by the Japanese criteria was also statistically significant (p < 0.01). Intriguingly, when we used modified IDF criteria, the prevalence of MetS in middle-aged and elderly men was similar to that using the Japanese criteria. However, the prevalence of MetS in women by modified IDF criteria was similar to that by modified ATP III criteria.

To assess the effect of aging on each metabolic component, we compared the prevalence of central obesity, dyslipidemia, high blood pressure, high fasting glucose, and MetS in each age group according to the Japanese and modified ATP III criteria. In men, the prevalence of MetS was similar in each age group; yet, more people satisfied the modified ATP III criteria than the Japanese criteria (Table 3). In women, the prevalence of MetS was about 5% in the elderly, and almost no subjects were diagnosed with MetS less than 65 years old by the Japanese criteria. According to the modified ATP III criteria, the prevalence of MetS in women also increased in their 60s and was almost the same as that of men older than 65 years. We found a big difference in the prevalence of central obesity diagnosed by Japanese and Asian criteria for waist circumference in both genders. Thus, it is critical which cutoff is used to diagnose MetS.

The prevalence of central obesity in men was almost constant according to the Japanese or Asian criteria of waist circumference, although the prevalence seemed to be decreased in their 70s. The prevalence of central obesity in women increased toward menopause and remained almost the same after their 50s. However, when we used the Asian criteria, the prevalence of central obesity in women further increased in their 70s. The prevalence of dyslipidemia was almost constant in men among each age group and increased toward menopause in women. However, the prevalence reached a plateau after 55 years of age. As expected, the prevalence of dyslipidemia was higher in women according to the ATP III criteria than that by the Japanese criteria. The prevalence of high blood pressure increased with age both in men and in women. Intriguingly, the prevalence of high blood pressure did not show further increase after 60 years of age in both genders. The prevalence of high fasting glucose increased after 50 years of age in men and after 65 years of age in women. Thus, the prevalence of MetS and related components are associated with age, especially with menopause in women. We also compared the number of the MetS traits by dividing the cohort into three groups: from 40 to 49 years (young middle age); from 50 to 64 years (old middle age); and from 65 to 79 years (elderly). As shown in Figure 1, the prevalence of the subjects with indicated numbers of MetS components according to the modified ATP III criteria is guite similar in men of all age groups. However, in older women, the number of MetS components increased, which is consistent with the data in Table 2.

Next, we compared the demographic characteristics of men and women diagnosed with MetS by the modified ATP III criteria. As shown in Table 4, age and total, HDL, and low-density-lipoprotein cholesterol were higher, and waist circumference, triglyceride, diastolic blood pressure, remnant-like particle (RLP) cholesterol, and fasting glucose were lower in women than in men.

We then compared the demographic characteristics of elderly and middle-aged men and women with MetS by modified ATP III criteria. As shown in Table 5, systolic blood pressure was higher in older-middle-aged and elderly than in younger-middle-aged group, and diastolic blood pressure was higher in older middle-aged group in both genders. HDL cholesterol was lower in younger-middleaged men and non-HDL cholesterol was lower in elderly men. Triglyceride was lower in elderly men and women. Insulin levels decreased according to age in men. There were no statistical differences in the other components.

#### Table 2

Tuble 2			
Prevalence of met	abolic syndrome in r	niddle-aged and	elderly Japanes

%	Male (1425)	р	p Female (941)			
	40–64 yr (1266)	65–79 yr (159)		40–64 yr (732)	65–79 yr (209)	
Japanese criteria	13.3	18.9	NS	1.5	4.8	<0.01
Modified Adult Treatment Panel III	19.0	21.4	NS	9.0	26.8	< 0.01
Modified International Diabetes Federation	14.0	14.8	NS	8.2	23.9	< 0.01

The numbers in parentheses indicate the number of subjects in each group. p Value, 40–64 yr vs. 65–79 yr. NS = not significant.

## Table 3

Prevalence of metabolic syndrome and metabolic components according to the Japanese and modified ATP III criteria in each age group in the Japanese population (%)

	Sex															
Criteria and metabolic components	Male (age group, yr), %							Female (age group, yr), %								
F	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75–79	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79
n	291	289	359	191	136	67	62	30	171	123	185	108	145	93	75	41
Japanese criteria																
Central obesity	49.1	56.4	54.0	57.1	55.1	61.2	48.4	43.3	5.3	11.4	16.8	16.7	11.7	16.1	14.7	17.1
Hypertriglyceridemia	33.7	43.6	31.2	28.8	33.1	25.4	25.8	13.3	6.4	7.3	15.1	22.2	20.7	20.4	18.7	14.6
Low HDL	11.3	14.2	12.3	13.1	12.5	9.0	9.7	13.3	1.8	4.1	2.2	2.8	2.8	6.5	2.7	4.9
cholesterolemia																
Dyslipidemia	36.4	46.0	34.5	33.5	36.0	31.3	30.6	20.0	7.6	8.9	15.1	22.2	22.1	21.5	20.0	19.5
High blood pressure	16.2	20.8	28.7	27.2	49.3	41.8	43.5	40.0	8.8	8.9	17.8	19.4	49.7	49.5	40.0	43.9
High fasting glucose	11.3	15.6	19.5	23.6	22.8	22.4	25.8	16.7	1.8	4.9	3.8	10.2	9.7	15.1	16.0	14.6
Metabolic syndrome	9.6	15.2	14.2	12.0	16.2	22.4	17.7	13.3	0.0	0.8	2.2	3.7	1.4	5.4	4.0	4.9
Modified ATP III criteria																
Central obesity	23.7	34.6	30.1	26.7	30.9	38.8	22.6	23.3	18.7	32.5	31.4	47.2	36.6	48.4	60.0	63.4
Hypertriglyceridemia	33.7	43.6	31.2	28.8	33.1	25.4	25.8	13.3	6.4	7.3	15.1	22.2	20.7	20.4	18.7	14.6
Low HDL	11.3	14.2	12.3	13.1	12.5	9.0	9.7	13.3	8.2	15.4	15.7	12.0	17.9	23.7	24.0	19.5
cholesterolemia																
Dyslipidemia	36.4	46.0	34.5	33.5	36.0	31.3	30.6	20.0	12.9	17.9	22.7	26.9	29.7	33.3	32.0	31.7
High blood pressure	16.2	20.8	28.7	27.2	49.3	41.8	43.5	40.0	8.8	8.9	17.8	19.4	49.7	49.5	40.0	43.9
High fasting glucose	34.7	38.4	43.2	44.0	39.7	41.8	40.3	36.7	8.8	15.4	14.6	18.5	24.8	29.0	33.3	26.8
Metabolic syndrome	14.1	22.8	19.2	16.2	25.0	22.4	19.4	23.3	1.8	5.7	9.2	13.9	16.6	26.9	30.7	19.5

ATP III = Adult Treatment Panel III; HDL = high-density lipoprotein.





Finally, we compared the prevalence of central obesity and other components among the people who satisfied the modified ATP III criteria according to their age in both genders. As shown in Table 6, the prevalence of hypertriglyceridemia and dyslipidemia in men was lower in the elderly, whereas the prevalence of high blood pressure increased in older-middle-aged and elderly men. In women, there was a tendency that the prevalence of hypertriglyceridemia was lower in elderly and that of high blood pressure increased according to age.

# 4. Discussion

In this study, we compared the prevalence of MetS in the Japanese middle-aged and elderly population by the Japanese and

#### Table 4

Demographic characteristics of men and women with metabolic syndrome

	Male ( <i>n</i> = 467)		Female	( <i>n</i> = 201)	р
	Mean	SD	Mean	SD	
Age, yr	53.4	8.8	61.9	9.4	< 0.01
Body mass index	25.9	3.0	26.3	2.9	0.27
Waist circumference, cm	92.1	6.7	86.2	8.0	< 0.01
Systolic blood pressure, mmHg	136	18	135	18	0.69
Diastolic blood pressure, mmHg	84	12.6	81	9.9	0.02
T-Cho, mg/dL	214	35.4	224	33.6	0.01
TG, mg/dL	197	155, 268	159	115, 194	< 0.01
HDL-C, mg/dL	45.7	12.2	51.7	11.0	< 0.01
Low-density-lipoprotein cholesterol, mg/dL	126	34.0	140	30.0	<0.01
Non-HDL-C, mg/dL	168	35.8	173	32.5	0.24
RLP-C, mg/dL	6.6	4.2, 10.7	4.3	3.2, 8.5	0.02
HbA1c, %	5.3	0.77	5.4	0.82	0.15
FBS, mg/dL	108	26	100	18.4	0.01
Insulin, µU/mL	8.3	4.7	8.0	4.4	0.52

TG and RLP-C are expressed as median (interquartile range). The difference was analyzed by unpaired *t* test except for TG and RLP-C. Mann–Whitney test was used for TG and RLP-C.

SD = standard deviation; HDL-C = high-density-lipoprotein cholesterol; T-cho = total cholesterol; TG = triglyceride; RLP-C = remnant-like particle cholesterol; HbA1c = hemoglobin A1c; FBS = fasting blood sugar.

#### Table 5

Demographic data of subjects with metabolic syndrome in each age group

	Sex	40–49 yr (M, 195; F, 27)		50–64 yr (M, 223; F,	50–64 yr (M, 223; F, 102)		72)	р
		Mean	SD	Mean	SD	Mean	SD	
Body mass index	M	26.1	3.0	25.9	3.1	25.5	2.5	0.55
	F	26.7	2.1	26.3	3.1	26.1	2.7	0.78
Waist circumference, cm	М	92.2	7.0	91.9	6.8	92.2	5.8	0.96
	F	87.9	8.7	85.6	9.1	86.3	6.7	0.65
Systolic blood pressure, mmHg	М	130	17.6	138	18.1	143	17.7	< 0.01
	F	125	18.0	140	19.4	132	14.6	0.01
Diastolic blood pressure, mmHg	М	82	13.1	86	12.5	82	9.4	0.02
	F	80	11.2	84	10.9	79	7.8	0.04
T-Cho, mg/dL	М	219	34.9	212	35.6	203	33.6	0.06
	F	213	28.8	230	33.2	220	34.3	0.13
TG, mg/dL	М	272	154	234	242	171	71	0.03
	F	169	79.7	189	89.6	144	57.1	0.01
HDL-C, mg/dL	М	43.1	8.3	47.2	13.7	47.9	14.9	0.02
	F	48.3	9.6	52.9	11.5	51.4	10.7	0.38
Low-density-lipoprotein cholesterol, mg/dL	Μ	128	34.8	126	34.2	121	31.6	0.62
	F	131	26.2	142	28.9	140	31.1	0.51
Non-HDL-C, mg/dL	М	176	34.8	165	36.4	155	32.3	0.01
	F	165	33.5	178	31.0	169	33.6	0.26
HbA1c, %	М	5.1	0.7	5.4	0.9	5.4	0.6	0.14
	F	5.3	0.7	5.3	1.0	5.5	0.7	0.63
FBS, mg/dL	Μ	112	24.3	113	25.2	108	21.5	0.58
	F	100	13.6	106	22.5	106	19.7	0.61
Insulin, mU/mL	Μ	9.4	5.9	7.8	3.8	7.2	3.4	0.01
	F	7.9	2.0	8.1	3.6	8.0	5.6	0.98

p Value was analyzed by analysis of variance.

M = male; F = female; HDL-C = high-density-lipoprotein cholesterol; T-cho = total cholesterol; TG = triglyceride; RLP-C = remnant-like particle cholesterol; HbA1c = hemoglobin A1c; FBS = fasting blood sugar.

modified ATP III and IDF criteria. We showed that the prevalence of MetS was almost three fold higher by all the three criteria in elderly women than in middle-aged women, whereas there was almost no difference between middle-aged and elderly men. Consistent with our findings that the prevalence of MetS increased in elderly women compared with that in middle-aged population, other studies have also shown that the prevalence of MetS increases with increasing age.<sup>15</sup> Ford et al.<sup>15</sup> reported that the prevalence of MetS in subjects older than 60 years is approximately 40% in the Third Report of the National Cholesterol Education Program Expert Panel, in which they used the cutoff of 110 mg/dL for high fasting glucose and their criteria of waist circumference for central obesity. The prevalence of MetS in middle-aged population is approximately 25% in both genders, which is different from the result in our cohort. In Japan, Ishizaka et al.<sup>16</sup> and Aizawa et al.<sup>17</sup> have shown that the prevalence of MetS in men is approximately 20% in both middle-aged and elderly populations, whereas that in women is approximately 5% and 10% in

#### Table 6

Prevalence of each metabolic abnormality in each age group in the subjects with metabolic syndrome

	Sex	Age grou	Age group (yr)					
		40-49	50-64	65-79				
Central obesity	М	74.5	72.1	82.4	0.47			
	F	92.3	82.8	89.3	0.48			
Hypertriglyceridemia	Μ	92.5	72.9	58.8	< 0.01			
	F	61.5	69	48.2	0.08			
Low HDL cholesterolemia	Μ	39.6	34.3	32.4	0.61			
	F	69.2	46.6	55.4	0.29			
Dyslipidemia	Μ	94.3	77.9	73.5	< 0.01			
	F	76.9	79.3	71.4	0.62			
High blood pressure	М	50.9	70.0	85.3	< 0.01			
	F	46.2	67.2	76.8	0.09			
High fasting glucose	М	79.3	82.1	79.4	0.75			
	F	46.2	65.5	64.3	0.41			

The difference was analyzed by chi-square test.

M = male; F = female.

middle-aged and elderly populations, respectively, although they used the original ATP III criteria and BMI instead of waist circumference. Tanaka et al.<sup>18</sup> also showed that the prevalence of MetS in Okinawa, a group of islands located in southwest of Japan, is approximately 30% in middle-aged and elderly men and 10% and 20% in middle-aged and elderly women, respectively, when they use ATP III criteria with the Japanese cutoff of waist circumference. Thus, the higher prevalence of MetS in middle-aged and elderly men than that in women is consistent in Japanese cohorts, although the prevalence is different with each diagnostic criterion.

Among the metabolic components, the prevalence of central obesity and dyslipidemia increased with aging only in women, and that of high fasting glucose and high blood pressure increased in both genders (Table 3). The prevalence of dyslipidemia decreased in elderly men. Thus, middle-aged men tend to be more dyslipidemic, whereas elderly population tends to have a higher prevalence of central obesity, impaired glucose metabolism, and high blood pressure. Among the subjects diagnosed with MetS by modified ATP III criteria, systolic blood pressure increased with aging in both genders, whereas triglyceride and insulin decreased with aging in both genders, and insulin levels decreased with aging only in men (Table 5). The increased prevalence of high blood pressure in older middle-aged and elderly population is also confirmed in Table 6, although the p value was not statistically significant in women. Thus, blood pressure seems to have the strongest association with aging in both genders. The prevalence of central obesity did not increase with aging in the female subjects with MetS (Tables 5 and 6), whereas the prevalence of central obesity increased in female general population, as shown in Table 3. Thus, central obesity in women seems to be affected by aging, which is consistent with the results of other studies in Japan.<sup>16,18</sup> In men, the insulin levels decreased in the elderly in spite of the fact that FBS and HbA1c were not changed among the three groups, suggesting impaired insulin secretion in elderly men with MetS.

In this study, we used the Japanese and modified ATP III and IDF definitions to determine MetS. However, there was a large difference in the prevalence of MetS among the three definitions. This difference

is because of the fact that the Japanese definition requires the central obesity for its diagnosis as in the modified IDF criteria and has more stringent criteria for high fasting glucose for both genders and for HDL cholesterol for women. As shown in this study, the prevalence of MetS in elderly women by the Japanese criteria was very low. This is the reason why we used various analyses using modified ATP III criteria in this cohort. However, the Japanese guideline for MetS was established to identify patients with central obesity, who can reduce the risks by weight loss, whereas the ATP III criteria try to identify patients with multiple risk factors. Therefore, the Japanese criteria should be used to identify obese patients who can have a benefit by weight loss in middle-aged and elderly populations. However, in terms of risk prediction, there have been several reports discussing the cutoff levels of MetS components. Hata et al.<sup>13</sup> have shown significant associations between MetS defined by various criteria and the risk of ischemic stroke in the Hisayama study. In the study, they found that MetS was an independent risk factor for ischemic stroke when they used the modified Japanese criteria with Asian definition of central obesity. Another study from the same group showed that the optimal cutoff level of waist circumference to predict cardiovascular disease was 90 cm in men and 80 cm in women,<sup>19</sup> as we used in modified ATP III definition in this study. Sone et al.<sup>11</sup> also proposed to use the Asian cutoff for waist circumference to define central obesity from the data of Japan Diabetes Complication Study. In terms of the appropriate cutoff level of HDL cholesterol for the definition of MetS in Japanese women, not so many analyses have been done. In our study, the prevalence of low HDL cholesterolemia with the cutoff of 40 mg/dL was less than 5% and was approximately 20% with the cutoff of 50 mg/dL in elderly women. We previously showed that central obesity was significantly associated with low HDL cholesterolemia only when we used the cutoff of 50 mg/dL for women.<sup>5</sup> Therefore, further study is necessary to determine the appropriate cutoff level of HDL cholesterol in women.

In summary, we have shown the prevalence of MetS in Japanese elderly and middle-aged population using Japanese and modified ATP III and IDF criteria, and found the effect of aging on the prevalence only in women with either criterion. We also showed the effect of aging on each metabolic component in this cohort. Thus, aging is an important factor that affects the metabolic abnormality, and aging of the population would lead to the increase in the prevalence of MetS. Therefore, the development of better approaches to the prevention and management of MetS is necessary for successful aging in our society.

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### References

- Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120:1640–5.
- Facchini FS, Hua N, Abbasi F, Reaven GM. Insulin resistance as a predictor of age-related diseases. J Clin Endocrinol Metab 2001;86:3574–8.
- Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005;365:1415–28.
- Yaffe K. Metabolic syndrome and cognitive disorders: is the sum greater than its parts? Alzheimer Dis Assoc Disord 2007;21:167–71.
- Arai H, Yamamoto A, Matsuzawa Y, Saito Y, Yamada N, Oikawa S, et al. Prevalence of metabolic syndrome in the general Japanese population in 2000. J Atheroscler Thromb 2006;13:202–8.
- Yamamoto A, Horibe H, Mabuchi H, Kita T, Matsuzawa Y, Saito Y, et al. Analysis of serum lipid levels in Japanese men and women according to body mass index. Increase in risk of atherosclerosis in postmenopausal women. Research Group on Serum Lipid Survey 1990 in Japan. *Atherosclerosis* 1999; 143:55–73.
- Zimmet P, Magliano D, Matsuzawa Y, Alberti G, Shaw J. The metabolic syndrome: a global public health problem and a new definition. J Atheroscler Thromb 2005;12:295–300.
- Matsuzawa Y. Metabolic syndrome—definition and diagnostic criteria in Japan. J Atheroscler Thromb 2005;12:301.
- Oka R, Kobayashi J, Yagi K, Tanii H, Miyamoto S, Asano A, et al. Reassessment of the cutoff values of waist circumference and visceral fat area for identifying Japanese subjects at risk for the metabolic syndrome. *Diabetes Res Clin Pract* 2008;**79**:474–81.
- Sato A, Asayama K, Ohkubo T, Kikuya M, Obara T, Metoki H, et al. Optimal cutoff point of waist circumference and use of home blood pressure as a definition of metabolic syndrome: the Ohasama study. *Am J Hypertens* 2008;**21**:514–20.
- Sone H, Tanaka S, Iimuro S, Oida K, Yamasaki Y, Oikawa S, et al. Components of metabolic syndrome and their combinations as predictors of cardiovascular disease in Japanese patients with type 2 diabetes. Implications for improved definition. Analysis from Japan Diabetes Complications Study (JDCS). J Atheroscler Thromb 2009;16:380–7.
- Kashihara H, Lee JS, Kawakubo K, Tamura M, Akabayashi A. Criteria of waist circumference according to computed tomography—measured visceral fat area and the clustering of cardiovascular risk factors. *Circ J* 2009;**73**:1881–6.
- Hata J, Doi Y, Ninomiya T, Tanizaki Y, Yonemoto K, Fukuhara M, et al. The effect of metabolic syndrome defined by various criteria on the development of ischemic stroke subtypes in a general Japanese population. *Atherosclerosis* 2009;**210**:249–55.
- Johnson CL, Rifkind BM, Sempos CT, Carroll MD, Bachorik PS, Briefel RR, et al. Declining serum total cholesterol levels among US adults. The National Health and Nutrition Examination Surveys. JAMA 1993;269:3002–8.
- Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002;287:356–9.
- 16. Ishizaka N, Ishizaka Y, Toda E, Hashimoto H, Nagai R, Yamakado M. Hypertension is the most common component of metabolic syndrome and the greatest contributor to carotid arteriosclerosis in apparently healthy Japanese individuals. *Hypertens Res* 2005;28:27–34.
- Aizawa Y, Kamimura N, Watanabe H, Makiyama Y, Usuda Y, Watanabe T, et al. Cardiovascular risk factors are really linked in the metabolic syndrome: this phenomenon suggests clustering rather than coincidence. *Int J Cardiol* 2006;109:213–8.
- Tanaka H, Shimabukuro T, Shimabukuro M. High prevalence of metabolic syndrome among men in Okinawa. J Atheroscler Thromb 2005;12(5):284–8.
- Doi Y, Ninomiya T, Hata J, Yonemoto K, Arima H, Kubo M, et al. Proposed criteria for metabolic syndrome in Japanese based on prospective evidence: the Hisayama study. Stroke 2009;40:1187–94.