Field Study

Two New Criteria of the Metabolic Syndrome: Prevalence and the Association with Brachial-Ankle Pulse Wave Velocity in Japanese Male Workers

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Abstract: Two New Criteria of the Metabolic Syndrome: Prevalence and the Association with Brachial-Ankle Pulse Wave Velocity in Japanese Male Workers: Koichi MIYAKI, *et al.* Department of Preventive Medicine and Public Health, School of Medicine, Keio University—In 1998 and 2001, The World Health Organization and the National Cholesterol Education Program Adult Treatment Panel III proposed working criteria for the metabolic syndrome (MS), but they are not perfect for use in diverse ethnicities. In 2005, the International Diabetes Federation (IDF) and eight societies in Japan respectively proposed new criteria. However, there has been no report regarding the application of these new criteria in Japanese workplaces. We conducted a cross-sectional study of 377 healthy Japanese men aged 20–64 yr who worked in a chemical factory in Kanagawa, Japan. Participants completed a self-reported questionnaire, underwent a physical examination including waist measurements and brachial-ankle pulse wave velocity (baPWV), and provided overnight fasting blood samples. The prevalence of MS in Japanese men was 17.0% and 13.5% according to the new IDF and Japanese criteria respectively. In both of the new criteria, baPWV was significantly higher in those with MS than those without MS ($1,563 \pm 264.2$ vs $1,362 \pm 204.6$ cm/sec, $p < 0.001$ in the new IDF criterion; $1,574 \pm 265.2$ vs $1,368 \pm 209.1$ cm/sec, $p < 0.001$ in the Japanese criterion). In the analysis of the 5 or 6 subgroups stratified according to the number of MS components, baPWV increased significantly with increasing number of MS components

(p for trend < 0.01 in both criteria). The new IDF and Japanese criterion are both good for diagnosing MS among Japanese because a linear increase in baPWV occurred with increasing MS components after adjustment for potential confounding factors. Further studies are expected using these new criteria. (*J Occup Health* 2006; 48: 134–140)

Key words: Metabolic syndrome, baPWV, New criteria, Japan

Metabolic syndrome (MS) is a cluster of metabolic disorders including central obesity, glucose intolerance, hypertension, and dyslipidemia^{1,2}. These traits occur simultaneously to a greater degree than would be expected by chance alone^{3,4}. Although the contribution of an individual trait may be small, multiple traits may act together and exert an even greater influence than any one trait alone⁵.

The concept of MS has become well established, and several studies have suggested that subjects with MS are at an increased risk for type 2 diabetes^{6,7} and cardiovascular disease^{8–12}. However, there has been no uniform case definition for MS.

In 1998 and 2001, the World Health Organization (WHO)¹³ and the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)¹⁴ each proposed working criteria for MS. The NCEP ATP III report recommended the use of five variables for diagnosis of MS, including waist circumference, triglyceride level, HDL cholesterol level, blood pressure, and fasting glucose level. Subjects meeting three of these five criteria are classified as having MS. The WHO criteria are more complex because they take account of microalbuminuria and plasma insulin levels.

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According to the NCEP ATP III and WHO criteria, several studies of the prevalence and characteristics of MS have been conducted among diverse ethnicities^{15–23}. Some studies showed ethnic variation in the prevalence of MS^{15, 16, 23} and some studies which conducted in Asia suggested that the definition of central obesity recommended by the NCEP ATP III was inappropriate for Asian populations which are generally of smaller build than Caucasians because the criterion had been based on data from Caucasian cohorts^{16, 17, 21}.

In consideration of the ethnic differences in prevalence and characteristics of MS, the International Diabetes Federation (IDF) proposed the worldwide MS criteria that includes a criterion for Japanese in April 2005²⁴. According to the new IDF criteria, a person defined as having MS must have central obesity plus any two of the following four factors: 1) raised triglyceride level; 2) reduced HDL cholesterol; 3) raised blood pressure; 4) raised fasting plasma glucose. With regard to the definition of central obesity, ethnic specific values for waist circumference are used.

At almost the same time, in April of 2005, eight societies in Japan, the Japan Society for the Study of Obesity, the Japan Atherosclerosis Society, the Japan Diabetes Society, the Japanese Society of Hypertension, the Japanese Circulation Society, the Japanese Society of Nephrology, the Japanese Society on Thrombosis and Hemostasis, and the Japanese Society of Internal Medicine, proposed a new criterion of MS for Japanese²⁵. According to the criterion, subjects are defined as having MS if they have central obesity plus any two of the following three factors: 1) dyslipidemia (raised TG level and/or reduced HDL cholesterol); 2) raised blood pressure; 3) raised fasting plasma glucose. To our knowledge no assessment of these new criteria has been performed among Japanese workers.

Pulse wave velocity (PWV) is an index of arterial stiffness^{26, 27}, and is regarded as a non-invasive marker of vascular damage^{28–30}. Previous studies have demonstrated that PWV is a marker of the severity of cardiovascular disease³¹ and a predictor of future events^{32–34}. As well, it is applicable as a screening tool for cardiovascular risk in a general population^{29, 35}. Recently, a simple device for measuring brachial-ankle PWV (baPWV) has been developed and made available^{36, 37}.

MS is a predictor of cardiovascular mortality^{8–10} and many studies have focused on the association of cardiovascular disease and its risk factors with increased PWV^{31, 32, 34, 36–38}. However, there are almost no studies relating PWV to MS^{5, 39}, and no study to our knowledge has investigated the relationship between PWV and MS as defined by the new criteria.

The aims of this study were to assess the prevalence and characteristics of MS using the two new criteria, the new IDF criterion and the Japanese criterion, and to

investigate the association between baPWV and MS in middle-aged Japanese men.

Methods

We conducted a cross-sectional study of Japanese male workers who worked in a chemical factory in Kanagawa, Japan. Of the 438 male workers, 377 (86.1%) aged 20–64 yr participated in the study. We divided the subjects into two subgroups according to the kind of occupation, office workers and laborers. Office workers were 176 (46.7%) and laborers were 201 (53.3%).

Of 377 subjects, 43 (11.4%), 4 (1.1%), and 7 (1.9%) were taking medication for hypertension, dyslipidemia, and diabetes, respectively. Although there were the potential effects of medications on metabolic values, we did not exclude the above-mentioned subjects because they should be included in each criterion of MS and for the purpose of reflecting the workplace population as it is without selection bias.

Participants completed a self-reported questionnaire (including medical history, medication use and smoking status), underwent a physical examination (including height, weight, waist circumference, blood pressure, and baPWV measurements), and provided overnight fasting blood samples. Body mass index (BMI) was calculated by kg/m². baPWV was measured by well-trained nurses on the left and right sides using the PWV/ABI device (Nippon Colin, Aichi, Japan) which was approved by the US Food and Drug Administration (FDA) as VP-2000/1000. We used the mean value of the right and left baPWV values. Of 377 subjects, 67 (17.8%) showed $\geq 1,600$ cm/sec baPWV and were diagnosed as having abnormally high PWV values. In this study, past smokers and those who had never smoked were combined and compared with current smokers. All subjects in the study gave their informed consent for the use of personal information for analysis. The Ethics Committee of the Keio University School of Medicine, Tokyo, Japan, approved the study protocol.

Definition of metabolic syndrome

According to the new IDF criterion, the characteristics of MS in Japan are defined by the following cutoff limits and the subjects are defined as having MS if they have central obesity plus two or more of the other components: 1) central obesity (waist circumference ≥ 85 cm in men); 2) raised triglyceride level (triglyceride ≥ 150 mg/dl) or specific treatment for this lipid abnormality; 3) reduced HDL cholesterol (HDL cholesterol < 40 mg/dl) or specific treatment for this lipid abnormality; 4) raised blood pressure (systolic blood pressure ≥ 130 mmHg or/and diastolic blood pressure ≥ 85 mmHg) or treatment of previously diagnosed hypertension; 5) raised fasting plasma glucose (fasting plasma glucose ≥ 100 mg/dl) or previously diagnosed type 2 diabetes.

According to the Japanese criterion, the characteristics of MS are defined by the following cutoff limits and the subjects are defined as having MS if they have central obesity plus two or more of the other components: 1) central obesity (waist circumference ≥ 85 cm in men); 2) dyslipidemia (triglyceride ≥ 150 mg/dl or/and HDL cholesterol < 40 mg/dl) or medication for dyslipidemia; 3) raised blood pressure (systolic blood pressure ≥ 130 mmHg or/and diastolic blood pressure ≥ 85 mmHg) or medication for hypertension; 4) raised fasting plasma glucose (fasting plasma glucose ≥ 110 mg/dl) or medication for diabetes.

According to the NCEP ATP III criterion¹⁴⁾, the characteristics of MS in men are defined by the following cutoff limits and subjects having three or more of the components are defined as having MS: 1) waist circumference > 102 cm; 2) triglyceride ≥ 150 mg/dl; 3) HDL cholesterol < 40 mg/dl; 4) systolic blood pressure ≥ 130 mmHg or/and diastolic blood pressure ≥ 85 mmHg or known treatment for hypertension; 5) fasting plasma glucose ≥ 110 mg/dl or known treatment for diabetes.

Statistical analysis

All log-normally distributed variables (fasting plasma glucose, triglyceride, and HDL cholesterol) were log-transformed before statistical analysis and back-transformed for reporting. Differences in metabolic, anthropometric, and numerical demographic variables between individuals with and without MS were assessed using independent samples *t* testing. The χ^2 test was used to determine whether frequencies for categorical variables differed between these two groups of subjects. Age-, BMI-, systolic blood pressure (SBP)-, and smoking status-adjusted Pearson correlations were calculated to investigate the relationship between baPWV and MS as well as other metabolic and anthropometric variables. Multivariate logistic regression analysis was used to assess the relationship between risk of increased baPWV and each feature of MS. All analyses were performed with the SPSS statistical package for Windows version 12.0. All reported *p*-values were two-sided, and *p* < 0.05 was considered statistically significant.

Table 1. Clinical and biochemical characteristics of all the subjects and the subjects with or without metabolic syndrome by the Japanese criterion and the new IDF criterion

	All subjects	Metabolic syndrome			
		by the Japanese criterion		by the new IDF criterion	
		No	Yes	No	Yes
n	377	326	51	313	64
Age (yr)	45.6 $\pm$ 11.6	44.3 $\pm$ 11.9	51.8 $\pm$ 6.34*	44.6 $\pm$ 11.9	50.8 $\pm$ 8.21*
Height (cm)	168.6 $\pm$ 6.37	168.6 $\pm$ 6.44	168.5 $\pm$ 5.93	168.6 $\pm$ 6.25	168.7 $\pm$ 6.97
Weight (kg)	65.8 $\pm$ 10.3	64.4 $\pm$ 9.69	74.6 $\pm$ 9.64*	64.1 $\pm$ 9.31	74.1 $\pm$ 10.8*
BMI (kg/m ²)	23.1 $\pm$ 3.26	22.6 $\pm$ 3.06	26.2 $\pm$ 2.80*	22.5 $\pm$ 3.00	26.0 $\pm$ 2.97*
Waist circumference (cm)	83.2 $\pm$ 9.20	81.7 $\pm$ 8.74	92.8 $\pm$ 5.65*	81.3 $\pm$ 8.55	92.4 $\pm$ 6.32*
Systolic blood pressure (mmHg)	134.0 $\pm$ 17.3	131.6 $\pm$ 16.3	149.4 $\pm$ 15.5*	131.5 $\pm$ 16.3	146.4 $\pm$ 16.9*
Diastolic blood pressure (mmHg)	81.4 $\pm$ 12.4	79.7 $\pm$ 11.9	92.2 $\pm$ 9.99*	79.5 $\pm$ 11.8	90.3 $\pm$ 11.5*
Fasting plasma glucose (mg/dL)	96.3[1.24]	93.4[1.20]	116.7[1.37]*	92.7[1.19]	115.7[1.36]*
Total cholesterol (mg/dL)	205.8 $\pm$ 37.0	203.0 $\pm$ 35.6	223.9 $\pm$ 40.5†	202.6 $\pm$ 35.8	221.5 $\pm$ 38.9†
Triglyceride (mg/dL)	112.9[1.74]	103.7[1.67]	195.0[1.64]*	102.5[1.66]	181.0[1.71]*
HDL cholesterol (mg/dL)	54.1[1.28]	55.4[1.27]	46.6[1.31]*	55.7[1.27]	47.1[1.30]*
baPWV (cm/sec)	1,396 $\pm$ 228.3	1,368 $\pm$ 209.1	1,574 $\pm$ 265.2*	1,362 $\pm$ 204.6	1,563 $\pm$ 264.2*
Current smoking (%)	58.6	58.9	56.9	58.5	59.4
Waist circumference ≥ 85 (cm) (%)	43.5	34.7	100*	31.9	100*
SBP ≥ 130 or DBP ≥ 85 (mmHg) (%)	38.5	30.7	88.2*	30	79.7*
Fasting plasma glucose ≥ 100 (mg/dL) (%)	30	—	—	21.7	70.3*
Fasting plasma glucose ≥ 110 (mg/dL) (%)	18.8	13.5	54.0*	—	—
Dyslipidemia† (%)	31.3	23.2	84.0*	—	—
Triglyceride ≥ 150 (mg/dL) (%)	28.4	—	—	19.5	71.9*
HDL cholesterol < 40 (mg/dL) (%)	9.3	—	—	6.4	23.4*

Data are means $\pm$ SD and % for normally distributed variables, and geometric means [GSD] for non-normally distributed variables.

**p* < 0.001 ; †*p* = 0.001 for the *t* test of differences in means or the χ^2 test of differences in proportions for continuous and categorical variables, respectively, in comparisons between subjects with or without metabolic syndrome.

†Triglyceride ≥ 150 (mg/dL) or/and HDL cholesterol < 40 (mg/dL).

Fig. 1. The relation between baPWV values and metabolic syndrome by the Japanese criterion and the new IDF criterion. * $p < 0.001$ for the t test of differences in means in comparisons between subjects with or without metabolic syndrome.

Fig. 2. The relation between baPWV values and the number of components of metabolic syndrome by the Japanese criterion and the new IDF criterion. * $p < 0.001$; † $p < 0.01$ for Tukey's multiple comparison test. ‡ $p < 0.01$ for linear trend test adjusted for age, BMI, SBP and smoking status.

Table 2. Multivariate logistic regression analysis with baPWV* as a dependent variable and metabolic syndrome as an independent variable in the Japanese criterion and the new IDF criterion

	OR (95% CI) [†]	<i>p</i>
Metabolic syndrome by the Japanese criterion	2.08 (0.90–4.81)	0.087
Metabolic syndrome by the new IDF criterion	2.88 (1.30–6.37)	0.009

*High baPWV was defined as $\geq 1,600$ cm/sec, †Adjusted for age, BMI, Systolic blood pressure (SBP), and smoking status.

Results

Table 1 shows the clinical and biochemical characteristics of all the subjects and the subjects with or without MS by the new IDF criterion and the Japanese criterion. The prevalence of MS was 17.0% ($n=64$) in the new IDF criterion and 13.5% ($n=51$) in the Japanese criterion. Using the NCEP ATP III criterion, the prevalence of MS was 5.84% (data not shown).

In both the new criteria, subjects with MS were significantly older, and had higher BMI, waist circumference, SBP, DBP, fasting plasma glucose, triglyceride, and baPWV but smaller HDL cholesterol than the subjects without MS. Height and percentage of current smoking subjects did not differ between the two groups in both the criteria.

In the analysis of two subgroups, laborers and office workers, the prevalences of MS were not significantly different in both the new IDF and Japanese criteria ($p=0.083$ in the IDF criterion; $p=0.111$ in the Japanese criterion) (data not shown).

baPWV was significantly higher in those with MS than those without MS in both the criteria ($1,563 \pm 264.2$ vs

$1,362 \pm 204.6$ cm/sec, $p < 0.001$ in the new IDF criterion; $1,574 \pm 265.2$ vs $1,368 \pm 209.1$ cm/sec, $p < 0.001$ in the Japanese criterion) (Fig. 1). After adjustment for age, BMI, SBP, and smoking status, baPWV was still significantly higher in those with MS than those without MS ($p=0.001$ in the new IDF criterion; $p=0.045$ in the Japanese criterion). In the two subgroups, laborers and office workers, baPWV was also significantly higher in those with MS than those without MS in both the criteria ($p < 0.001$ in both the criteria in both subgroups) (data not shown).

Subjects with different numbers of components of MS were placed in 6 and 5 subgroups, respectively, in the new IDF criterion and the Japanese criterion (graded from 0 through 5 and 4, respectively). Following stratification into the 6 and 5 subgroups, age-, BMI-, SBP-, and smoking status-adjusted baPWV significantly increased with increasing numbers of components of MS ($1,257 \pm 172.2$, $1,371 \pm 158.0$, $1,438 \pm 231.5$, $1,648 \pm 246.8$, $1,669 \pm 344.7$ cm/sec, p for trend < 0.01 in the new IDF criterion; $1,264 \pm 171.1$, $1,364 \pm 169.9$, $1,465 \pm 235.4$, $1,553 \pm 236.9$, $1,689 \pm 281.1$ cm/sec, p for trend < 0.01 in the Japanese criterion) (Fig. 2). The subjects with 1, 2, 3,

and 4 components of MS had significantly higher baPWV than those without MS in both of the criteria ($p < 0.001$ for all). It was also shown in the two subgroups, laborers and office workers, that baPWV increased with increasing number of components of MS after controlling for age, BMI, SBP, and smoking status (p for trend < 0.01 in both criteria for laborers; p for trend < 0.05 in both criteria for office workers) (data not shown).

To assess the utility of the two new criteria of MS to identify individuals with increased baPWV, we analyzed the risk of increased baPWV in relation to MS in the two criteria by a multiple logistic regression analysis. After controlling for age, BMI, SBP, and smoking status, the odds ratios for increased baPWV in subjects with MS were 2.07 (95%CI=0.90–4.81) in the Japanese criterion and 2.88 (1.30–6.36) in the new IDF criterion compared with those without MS (Table 2).

Discussion

In the present study, only 1.6% of all subjects were classified as having central obesity using the NCEP ATP III criterion of central obesity (data not shown) and the prevalence of MS by the NCEP ATP III criteria was 5.84% which is a quarter of the prevalence of 24.0% reported in the U.S. using the NCEP ATP III criteria⁴⁰. Because the NCEP ATP III criteria are based on data from Caucasian cohorts, the great difference of the prevalence of MS may reflect not only the prevalence itself but also the build between races and, thus, the NCEP ATP III criteria may not be appropriate for Japanese.

On the other hand, the prevalences of MS by the new IDF and Japanese criteria were 17.0% and 13.5%, respectively, in middle-aged Japanese men. Because the new criteria use ethnic specific values for waist circumference, the difference of MS prevalence between Japan (17.0% by the new IDF criterion; 13.5% by the new IDF criterion) and the U.S. (24.0% by the NCEP ATP III criterion) may reflect the true value of the difference of MS prevalence. Thus, the new two criteria may be better for diagnosis of MS than the NCEP ATP III criterion, although we understand that the present data cannot be simply compared with previous data obtained using the other criterion of MS.

The two new criteria are similar in that they regard central obesity as an indispensable item and include the criteria of dyslipidemia, hyperglycemia, and hypertension. However, there are two different points. First, the fasting plasma glucose threshold is higher in the Japanese criterion than in the new IDF criterion. If the cutoff value for the fasting plasma glucose in the Japanese criterion (≥ 110 mg/dL) is substituted with the cutoff value in the new IDF criterion (≥ 100 mg/dL), the number of subjects with MS increases by 9 to 60 (15.9%) which is almost the same number as that of the MS subjects by the new IDF criterion. Therefore, the difference in the prevalence

of MS between the new IDF criterion (17.0%) and the Japanese criterion (13.5%) was mainly the result of a difference in the fasting plasma glucose threshold. Second, while the new IDF criterion uses two items of dyslipidemia, i.e. HDL cholesterol and triglyceride, for the criteria of MS on equal terms with other criteria, the Japanese criterion put the two items together as dyslipidemia. Weighting each trait equally in the new IDF criterion may overweight the contribution of dyslipidemia to MS, though it is unlikely that each trait confers equivalent disease risk.

Of the 377 subjects, 14 (3.7%) satisfied the IDF criterion of MS but did not satisfy the Japanese criterion of MS. Their mean value of baPWV was $1,482.4 \pm 290.1$ and it was not significantly different from that of those who satisfied both criteria (baPWV = $1,585.8 \pm 255.0$, $p = 0.241$) or that of those who satisfied neither criteria (baPWV = $1,362.1 \pm 204.6$, $p = 0.148$). Therefore, we could not conclude which of the two criteria was good for Japanese men in terms of a predictor for high baPWV.

The present study demonstrated that MS was significantly associated with a risk of increased baPWV after adjustment for the potential confounding factor of aortic stiffness in both the new criteria. This assures that multiple risk factors act together and exert an even greater influence on future events than expected by each risk factor alone. Our data concurs with a previous study which reported that clustered features of MS are related to increased aortic PWV⁵. However, in the previous study, the characteristics of MS were not defined by any proposed criteria but by their original criterion because the aim of the study was to investigate the association between clusters features of MS and increased aortic PWV.

Although the present study also demonstrated that the new IDF criterion was a better predictor of increased baPWV than the Japanese criterion, further studies are expected to assess the utility of the two new criteria to identify individuals with increased cardiovascular risk, because baPWV is a surrogate marker of cardiovascular disease.

The present study has several limitations. First, the number of subjects was relatively small and the results of this study need to be assessed in larger sample size. However, there was a strong and positive association of MS components with the level of baPWV after adjustment for potential confounding factors in both of the new criteria, and the relationship between baPWV and MS was not associated with the kind of occupation according to the analysis of the subgroups of laborers and office workers. Therefore, we suggest that the two new criteria are good for diagnosing MS among Japanese men in large populations. Second, we used a surrogate measurement of arterial stiffness and therefore may not have identified its prevalence precisely. However, previous studies have

shown that PWV reflects vascular damage^{28–30}) and severity of cardiovascular disease³¹), and predicts future events^{32–34}); moreover, PWV is a non-invasive marker. Therefore, PWV may have been an appropriate marker for arterial stiffness in the present study. Finally, our cross-sectional study design lacks information on the time sequence of events and, thus, does not permit identification of causal relationships.

In conclusion, the new IDF criterion and the Japanese criterion are both good for diagnosing MS among Japanese men, because a linear increase in baPWV occurred with increasing MS components after adjustment for potential confounding factors in both the new criteria. Our study was a cross-sectional study, and further prospective studies are expected to follow.

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