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Waist Circumference can Predict the Occurrence of Multiple Metabolic Risk Factors in Middle-aged Japanese Subjects

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Abstract: Visceral obesity is associated with the clustering of metabolic risk factors and the incidence of cardiovascular events. However, the association between the waist circumference values and the metabolic risk factors has not been fully established in Japanese middle-aged subjects. We examined the data from 6,033 Japanese middle-aged subjects aged 40–59 yr (4,599 male and 1,434 female). Metabolic risk factors such as high blood pressure, dyslipidemia, and glucose intolerance were identified according to the diagnostic criteria for metabolic syndrome in Japan. Numbers of metabolic risk factors were significantly associated with the waist circumference values in both male and female subjects. The prevalence of subjects with multiple (two or more) metabolic risk factors was 29.7% and 7.4% in male and female, respectively. According to receiver operating characteristic analysis, the cut-off values of waist circumference with the maximal sensitivity plus specificity to predict the presence of multiple metabolic risk factors were 86 cm and 81 cm in male and female, respectively. These values were in agreement with the diagnostic criteria for metabolic syndrome in Japanese male, but not in female. In conclusion, the waist circumference values can predict the presence of multiple metabolic risk factors in Japanese middle-aged subjects.

Key words: Epidemiology, Waist circumference, Risk factor, Middle-aged subjects, Health examination

Introduction

Visceral obesity is associated with the accumulation of metabolic risk factors such as high blood pressure, dyslipidemia, and glucose intolerance, which may increase the risk of cardiovascular disease[1–4]. Visceral obesity can be evaluated by measuring waist circumference and body mass index (BMI), however, waist circumference has been shown to be a superior marker of abdominal and visceral fat than BMI[5, 6]. Asian populations had lower average BMI values and higher prevalence of body fat as a given BMI than Caucasians[7]. Thus, the measurement of the waist circumference is one of useful methods to evaluate visceral fat accumulation especially in Asian populations[8, 9]. The Committee of Japan Society for Study of Obesity (JASSO) and the committee of International Diabetes Federation (IDF) recommended visceral obesity as an essential criteria for the diagnosis of metabolic syndrome[10, 11]. However, the association between waist circumference values and the accumulation of metabolic risk factors has not been fully examined. Moreover, the association between waist circumference and metabolic risk factors was attenuated with advancing ages[12].

In this study, we examined the relation between the

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waist circumference values and the presence of metabolic risk factors in middle-aged subjects in Japan.

Methods

Study subjects

The present study included 6,296 Japanese subjects who had an annual health examination during the period from April 2008 to March 2009, aged from 40 to 59 yr old (51 ± 9 yr, mean , standard deviation (SD)). A total of 263 subjects (202 male, 61 female) were excluded due to prior coronary artery disease (CAD) or stroke. Thus, a total of 6,033 subjects remained in the present analysis. The study protocol was approved by the ethical committee of Hokkaido University School of Medicine and informed consent was obtained from all subjects.

Data collection

Blood samples were obtained from antecubital vein in the morning after overnight fasting and serum samples were separated after a centrifugation. High-density lipoprotein (HDL)-cholesterol was measured after precipitation of apo B-containing lipoproteins with a commercial reagent containing phosphotungstate and magnesium chloride (Daiichi Pure Chemicals, Tokyo, Japan). Triglyceride was measured enzymatically (Kyowa Medex, Tokyo, Japan). Fasting plasma glucose was enzymatically determined by the hexokinase method (Shino-Test, Tokyo, Japan). Blood pressure was measured by a trained nurse using a standard mercury sphygmomanometer with the study subjects in the sitting position after at least a 5-min rest. Body weight, body height, and waist circumference were measured in the morning in the fasting state. Waist circumference was measured around the abdomen at the level of the navel at the late expiratory phase by using a tape measure. BMI was calculated as body weight (kg) divided by squared height (m^2).

Outcome measures

Metabolic risk factors were defined based on the diagnostic criteria of metabolic syndrome by JASSO; 1). high blood pressure; systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg, 2). dyslipidemia; triglyceride ≥150 mg/dl and/or HDL-cholesterol <40 mg/dl, and 3). glucose intolerance; fasting plasma glucose ≥110 mg/dl. Each factor was considered to be present when the subjects were under medications. Two or more risk factors were defined as "multiple".

Statistical analysis

All analyses were performed separately according to male and female. The clinical and biochemical data of the study subjects were expressed as means ± SD, a median (and interquartile range) for variables with a skewed distribution, and percentages. The differences between two groups were examined by the Student unpaired *t* test for variables distributed normally, or by the Wilcoxon rank-sum test for triglyceride, and by the χ^2-test for the categorical variables. A one-way analysis of variance (ANOVA) was used to calculate the differences in continuous variables among the multiple groups. Receiver operating characteristic curve (ROC) analysis was used to determine the appropriate waist circumference according to male and female. We calculated the maximal sensitivity and specificity between waist circumference and multiple risk factors. According to the ROC curve, the optimal point was defined as the closest point on the ROC curves to the point at 1-specificity of 0 and sensitivity of 100%. A *p* value of less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed by using the Statistical Package for Social Science (version 11.0).

Results

Table 1 shows the clinical characteristics of the study subjects. Male subjects were older and had greater waist circumference, BMI, systolic and diastolic blood pressure, triglyceride, fasting plasma glucose, and lower HDL-cholesterol than female subjects. The mean waist circumference values of male and female subjects were 85 ± 9 and 78 ± 9 cm, respectively. The prevalence of

Table 1. Clinical characteristics of the study subjects

	Male (n=4,599)	Female (n=1,434)
Age (yr)	53 ± 8	50 ± 7*
Waist circumference (cm)	85 ± 9	78 ± 9*
Body mass index (kg/m^2)	23.9 ± 3.4	21.8 ± 3.5*
Systolic blood pressure (mmHg)	126 ± 19	117 ± 18*
Diastolic blood pressure (mmHg)	79 ± 12	71 ± 12*
Triglyceride (mg/dl)	112 (78–166)	73 (53–101)*
HDL-cholesterol (mg/dl)	55 ± 14	69 ± 16*
Fasting plasma glucose (mg/dl)	105 ± 33	92 ± 19*
Medical history		
Hypertension (%)	17.8	8.4*
Diabetes mellitus (%)	6.0	1.0*
Dyslipidemia (%)	2.2	2.6

HDL; high-density lipoprotein.
Values are presented as mean ± SD, median (interquartile range) for skewed variables, or percentage.
*p<0.05 vs. male.

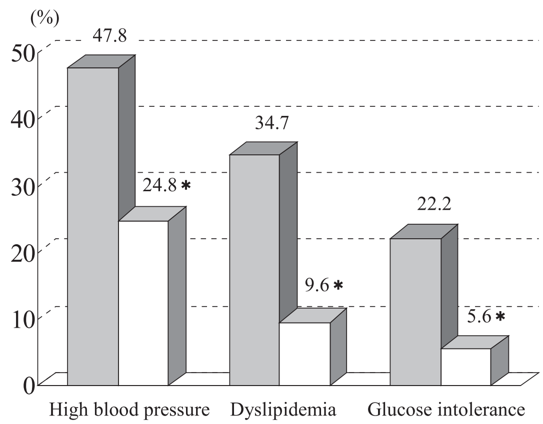

Fig. 1. The prevalence of metabolic risk factors in male (closed bars) and female (open bars) subjects.
*$p<0.05$ vs. male.

hypertension and diabetes mellitus was significantly greater in male than in female subjects.

Figure 1 shows the prevalence of metabolic risk factors in male and female subjects. The prevalence of the metabolic risk factor such as high blood pressure, dyslipidemia, and glucose intolerance was significantly higher in male than in female subjects.

Figure 2 shows the relation between waist circumference values and numbers of metabolic risk factors in the study subjects. The waist circumference values were significantly greater according to the increase in the numbers of metabolic risk factors in both male and female subjects. The prevalence of subjects who had multiple (two or more) risk factors was 29.7% and 7.4% in male and female, respectively. The waist circumference values of the study subjects who had multiple risk factors were 89 ± 9 cm and 88 ± 9 cm in male and female, respectively.

Figure 3 shows the ROC curve to determine the appropriate waist circumference values for detecting the presence of multiple risk factors in male and female. In male subjects with the cut-off values of 86 cm, the sensitivity and specificity were 64% and 62%, respectively, which were found to be the maximal values. The area under the curves was 0.68. In female subjects with the cut-off values of 81 cm, the sensitivity and specificity were 75% and 70%, respectively, which were the maximal values. The area under the curves was 0.79. The sensitivity became as low as 40% and specificity was 90% when the waist circumference cut-off values of 90 cm were used in female subjects.

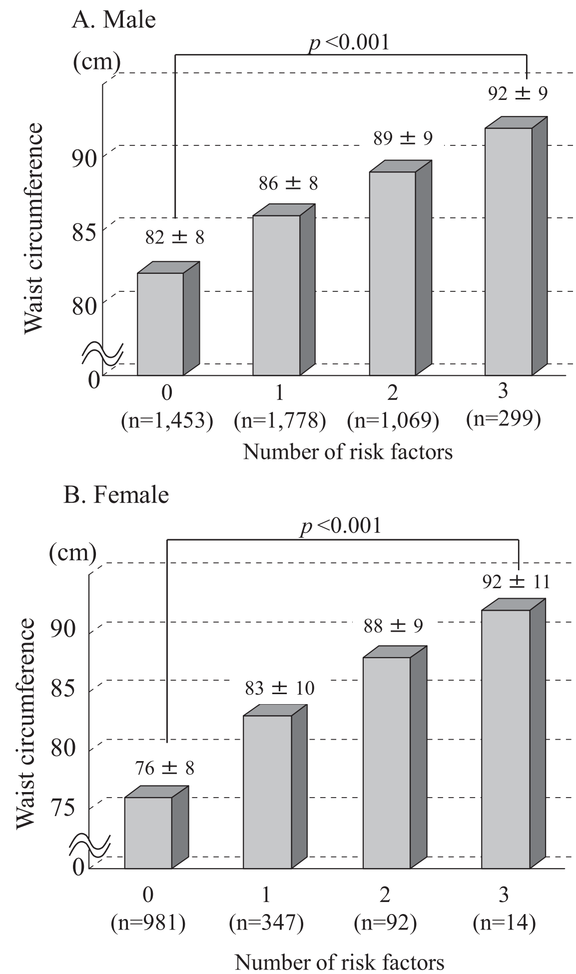

Fig. 2. Waist circumference values according to the numbers of metabolic risk factors in male (A) and female (B) subjects.
Values are presented as mean ± SD.

Discussion

The present study demonstrated that waist circumference values were significantly associated with the numbers of metabolic risk factors in middle-aged subjects and the cut-off values of waist circumference were 86 cm in male and 81 cm in female to predict multiple metabolic risk factors.

Visceral obesity was closely associated with insulin resistance[13]. Insulin resistance is the pathophysiological basis for the presence of metabolic risk factors such as high blood pressure, dyslipidemia, and glucose intolerance. Clustering of these risk factors is now recognized as an emerging risk for developing for CAD[14, 15]. Thus, the measurement of waist circumference is the simple and useful method to predict cardiovascular risk factors. Misra *et al*. reported that Asian Indians had relatively higher abdominal fat mass compared with Caucasians and African Americans, despite similar or lower average waist circumference[16]. These results may suggest that the measurement of waist circumference in Asians is more useful to predict the metabolic risk than Caucasians. Ohkubo *et al*. demonstrated that the opti-

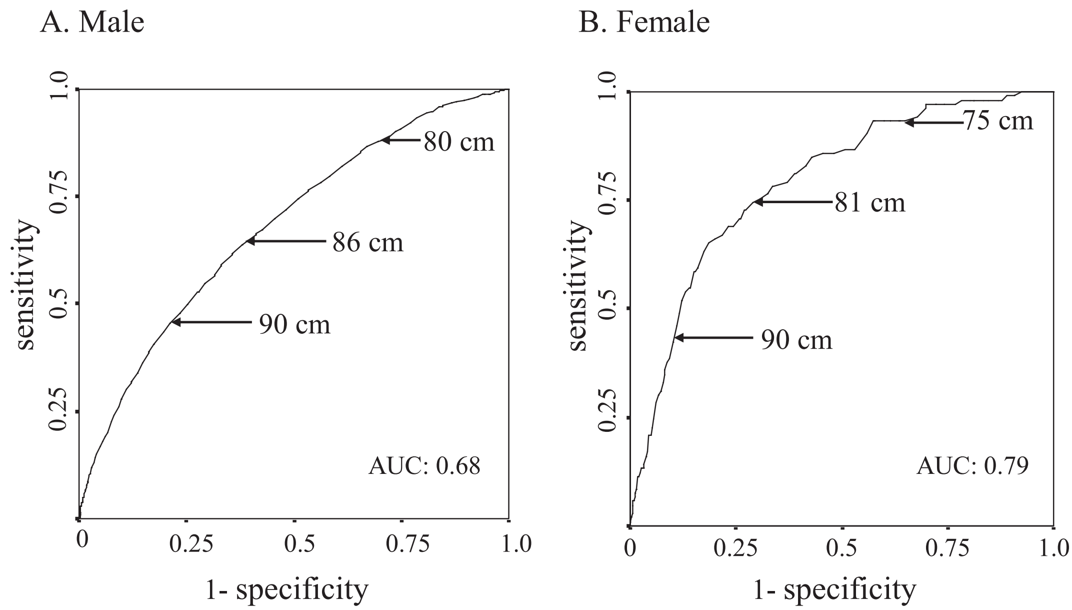

Fig. 3. The ROC (receiver operating characteristic) curve for the waist circumference to detect multiple metabolic risk factors in male (A) and female (B) subjects.
AUC, area under curve.

mal cut-off values of waist circumference for predicting the presence of insulin resistance was 83 cm in men and 75 cm in women in Japanese general population aged more than 35 yr in Ohasama study[17]. Janssen *et al*. demonstrated that the relationship between waist circumference and insulin resistance was weak according to advancing age[12]. Oda *et al*. also confirmed that the correlations between obesity and metabolic risk factors were stronger in younger men compared to older men in Japanese population[18]. Thus, the appropriate cut-off values of waist circumference to detect cardiovascular risk factors might differ among young, middle-aged, and older subjects.

Specific health examination has been newly started from 2008 in Japan, in which waist circumference is measured in all subjects aged from 40 to 74 yr. Middle-aged employees from 40 to 65 yr need to be particularly targeted in the industrial health. In our middle-aged subjects, the cut-off values of waist circumference to predict multiple metabolic risk factors were 86 cm in men and 81 cm in women. Hara *et al*. proposed that the optimal cut-off values of waist circumference to detect multiple risk components by using National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III) criteria were 85 cm in male and 78 cm in female among 692 healthy subjects (408 male and 284 female)[19]. Miyawaki *et al*. analyzed data from 3,574 employees of a telephone company and their family members (2,947 male and 627 female) obtained from health examinations and demonstrated the appropriate cut-off waist circumference values of 86 cm for male and of 77 cm for female to detect multiple risk components by using Japanese criteria based on their visceral-fat area cut-off levels of 100 cm^2 in male and 65 cm^2 in female[20]. However, in their study, waist circumference was measured only in a very limited numbers of study subjects (5.6% for male and 8.5% for female). In the present study, we measured waist circumference in all study subjects and investigated the relationship between waist circumference and the metabolic risk factors by using Japanese criteria, which differed from these previous studies.

There are several limitations that should be acknowledged in this study. First, our study subjects ranged from 40 to 59 yr old. Therefore, we have to be cautious in extending the present results to the general population. Second, even though visceral obesity is considered to be associated with CAD, we did not examine the relationship between waist circumference and the incidence of CAD. Further investigations are needed to evaluate the association between waist circumference and future occurrence of cardiovascular events to establish appropriate cut-off values of waist circumference.

Conclusions

The present study demonstrated that waist circumference values were significantly associated with the metabolic risk factors, and the appropriate value of waist circumference to detect multiple risk factors were

86 cm in male and 81 cm in female in middle-aged Japanese subjects. Based on these findings, maintaining appropriate waist circumference values by the lifestyle modification including diet and exercise may be one of important health instructions in occupational health promotion strategy.

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