**Proposed Cutoff Level of Waist Circumference in Japanese Men: Evaluation by Homeostasis Model Assessment of Insulin Resistance Levels**

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**Abstract**

**Objective** The aim of this study is to propose the cutoff level of waist circumference (WC) on the basis of homeostasis model assessment of insulin resistance (HOMA-IR) levels in order to diagnose metabolic syndrome (MetS).

**Methods** We examined a total of 798 non-diabetic men (40-65 years of age) by using a receiver operating characteristic (ROC) curve to determine the cutoff level that yielded the maximum sensitivity plus specificity. According to the criteria proposed by the International Diabetes Federation (IDF), and the Japanese Society of Internal Medicine (JSIM), subjects with ≥2 metabolic components other than abdominal obesity, were considered to have MetS.

**Results** The overall prevalence rates of IDF- and JSIM-MetS were 17.4% (n=139) and 15.5% (n=124), respectively. The median levels of WC and HOMA-IR were 83.1 [interquartile range (IQR): 78.5-88.4] cm and 0.84 (IQR: 0.61-1.19), respectively. HOMA-IR was highly correlated with each metabolic parameter (each p<0.05), and in addition, multiple linear regression analysis of HOMA-IR (adjusted R²=0.459) showed that WC level was the strongest independent predictors of HOMA-IR level (F=141.1, p<0.05). According to ROC curve analysis, the cutoff level of HOMA-IR for predicting IDF- and JSIM-MetS was 0.92 for both (sensitivity: 79.9% and 78.2%, specificity: 64.9% and 63.6%). Based on the HOMA-IR level, the proposed WC cutoff level was 82.7 cm (sensitivity: 75.4%, specificity: 63.8%).

**Conclusion** This study suggests that WC level should be more strictly managed than current criteria, for preventing the development of MetS in non-diabetic middle-aged Japanese men.

**Key words:** waist circumference, cutoff level, metabolic syndrome, homeostasis model assessment of insulin resistance, Japanese men

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**Introduction**

Metabolic syndrome (MetS) is closely associated with abdominal obesity and is a possible cause of type 2 diabetes and cardiovascular disease worldwide (1, 2). This syndrome consists of various pathological conditions such as atherogenic dyslipidemia, elevated blood pressure, increased glucose levels, and prothrombotic and proinflammatory states (3, 4). MetS can be clinically diagnosed using a clustering of simple measurements, including waist circumference (WC), triglyceride, high-density lipoprotein (HDL) cholesterol, blood pressure, and fasting glucose. The diagnostic criteria proposed by 6 major world organizations, in-
Evaluation of MetS

In this study, MetS was defined according to the criteria proposed by the IDF, and the JSIM, excluding that for abdominal obesity. The IDF criteria are as follows: subjects with 2 and more of the following components were considered to have IDF-MetS: (i) elevated triglyceride defined as triglyceride ≥150 mg/dL or self-report of taking lipid-lowering medications; (ii) reduced HDL cholesterol defined as HDL cholesterol <40 mg/dL; (iii) elevated blood pressure defined as blood pressure ≥130/85 mmHg or self-report of taking antihypertensive drugs; (iv) elevated glucose defined as 100 mg/dL ≤ fasting glucose <110 mg/dL. The JSIM criteria are as follows: subjects with 2 or more of the following components were considered to have JSIM-MetS: (i) dyslipidemia defined as triglyceride ≥150 mg/dL, HDL cholesterol <40 mg/dL, or self-report of taking lipid-lowering medications; (ii) elevated blood pressure defined as blood pressure ≥130/85 mmHg or self-report of taking antihypertensive drugs; (iii) elevated glucose defined as 100 mg/dL ≤ fasting glucose <110 mg/dL.

Evaluation of WC cutoff level

First, we plotted the receiver operating characteristic (ROC) curve to determine the cutoff levels of HOMA-IR for predicting MetS. According to previous studies (13, 14), the level was set to obtain the maximum sensitivity plus specificity. Next, we examined the WC cutoff level for predicting the HOMA-IR levels by the same method. The WC level was also set to have the maximum sensitivity plus specificity.

Statistical analysis

Continuous data are expressed as median with interquartile range (IQR), because the values are not normally distributed. All of the continuous data were log-transformed to approximately normalize the distribution for the subsequent analyses. Categorical data are presented as absolute values and percentages. Analysis of variance was used for multiple comparisons of continuous variables, followed by the Tukey-Kramer post hoc test. Comparison of categorical variables was evaluated by the chi-square test. A simple regression analysis and multivariate linear regression analysis ad-
The characteristics of the study subjects [n=798, 49 (IQR: 44-55) years] are shown in Table 1. The overall prevalence rates of IDF- and JSIM-MetS were 17.4% (n=139) and 15.5% (n=124), respectively. The frequencies of elevated triglyceride, reduced HDL cholesterol, elevated blood pressure, elevated fasting glucose, dyslipidemia, elevated triacylglycerol, reduced HDL cholesterol, and hypertension were 27.4% (n=219), 2.9% (n=23), 42.1% (n=336), 7.6% (n=61), and 27.9% (n=223), respectively. The median levels of WC and HOMA-IR were 83.1 (IQR: 78.5-88.4) cm and 0.84 (IQR: 0.61-1.19), respectively. Study participants received medications for hyperlipidemia (n=57, 7.1%) and hypertension (n=88, 11.0%). Current smokers and drinkers comprised 23.6% (n=188) and 44.7% (n=357) of the study population, respectively.

The median levels of HOMA-IR according to the number of MetS component are shown in Figure 1. The levels in subjects with 0 (n=322), 1 (n=337), 2 (n=117), and 3 or 4 (n=22) components were 0.71 (IQR: 0.52-0.95), 0.83 (IQR: 0.60-1.21), 1.19 (IQR: 0.95-1.60), and 1.41 (IQR: 1.06-1.81), respectively. The levels in subjects with 2 and 3/4 components were comparable (p=0.09), and in contrast were significantly higher than those in subjects with 0 and 1 components (each p<0.05). The correlations between HOMA-IR and each MetS parameter are shown in Table 2. HOMA-IR was significantly correlated with each parameter (each p<0.05). In addition, multiple linear regression analysis of HOMA-IR (adjusted R²=0.459) showed that WC and the levels of triglyceride, HDL cholesterol, and fasting glucose were independent predictors of HOMA-IR, and that WC level was the strongest predictor of HOMA-IR level (F=141.1, p<0.05). Otherwise, the correlation between WC and HOMA-IR (R²=0.315, p<0.05) was stronger than that between body mass index and HOMA-IR (R²=0.293, p<0.05).

**WC cutoff level evaluated by HOMA-IR levels**

According to the ROC curve, the HOMA-IR cutoff level that yielded the maximum sensitivity plus specificity for predicting IDF-MetS was 0.92, whose sensitivity and specificity were 79.9% and 64.9%, respectively (Fig. 2A). This HOMA-IR level was the same even though using the JSIM criteria (sensitivity: 78.2%, specificity: 63.6%) (Fig. 2B). The proposed WC cutoff level for predicting the HOMA-IR value of 0.92 was 82.7 cm; the sensitivity and specificity were 75.4% and 63.8%, respectively (Fig. 2C). This WC level had a higher sensitivity compared to that in the IDF and JSIM criteria. Moreover, when plotting the ROC of WC levels for predicting IDF- and JSIM-MetS, the sensitivity plus specificity was similar in the WC cutoff level of 82.7 cm, 85.0 cm (JSIM criteria), and 90.0 cm (IDF criteria), whereas there were differences in the individual sensitivities (Fig. 3A, B). Otherwise, the frequencies of HOMA-IR ≥0.92 and WC ≥82.7 cm in the study subjects were 42.9% (n=342)
and 53.0% (n=423), respectively.

Next, we examined the influence of each WC cutoff value on IDF- and JSIM-MetS prevalence, and HOMA-IR levels (Table 3). The prevalence rates of IDF- and JSIM-MetS, and median levels of HOMA-IR were higher in subjects with WC of 82.7-84.9 cm, 85.0-89.9 cm, and ≥90.0 cm than in subjects with WC <82.7 cm. In addition, the data in subjects with WC of 82.7-84.9 cm and 85.0-89.9 cm were comparable, and were lower than that in subjects with WC of ≥90.0 cm.

**Discussion**

The incidences of type 2 diabetes and cardiovascular disease are increasing worldwide, resulting in an enormous burden to the society. The ultimate aim of MetS screening is to identify subjects at a high risk of developing such diseases (15). MetS can be clinically diagnosed by using a

<table>
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<th>Table 2. Univariate and Multivariate Analysis of HOMA-IR</th>
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<tr>
<td>MetS parameters</td>
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<tr>
<td>Waist circumference (cm)</td>
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<td>Triglyceride (mg/dL)</td>
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<tr>
<td>HDL cholesterol (mg/dL)</td>
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<td>Systolic blood pressure (mmHg)</td>
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<td>Diastolic blood pressure (mmHg)</td>
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<td>Fasting glucose (mg/dL)</td>
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<td>All data were log-transformed to achieve linearity. HOMA-IR: homeostasis model assessment of insulin resistance, MetS: metabolic syndrome, HDL: high-density lipoprotein</td>
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**Figure 2.** The ROC curve for HOMA-IR to predict IDF-MetS (A) and JSIM-MetS (B), and for WC to detect the HOMA-IR level of 0.92 (C). ○, cutoff level that yielded the maximum sensitivity plus specificity. ●, cutoff levels proposed by the Japanese Society of Internal Medicine (JSIM) and International Diabetes Federation (IDF) criteria (85.0 cm and 90.0 cm). AUC: area under the curve

**Figure 3.** The ROC curve for WC to predict IDF-MetS (A) and JSIM-MetS (B). ○, cutoff level proposed by this study (82.7 cm). ●, cutoff levels proposed by the Japanese Society of Internal Medicine (JSIM) and International Diabetes Federation (IDF) criteria (85.0 cm and 90.0 cm). AUC: area under the curve
cluster of simple measurements, including WC, triglyceride, HDL cholesterol, blood pressure, and fasting glucose. However, different organizations have varying definitions of MetS. In this regard, one of the most serious issues for the Japanese population is the differences in WC criteria proposed by the IDF and JSIM: these differences highly influence the diagnosis of MetS, and consequently, subjects with a high risk for type 2 diabetes and cardiovascular disease may be overlooked. The criterion proposed by the JSIM, i.e., cutoff levels of 85 cm in men and 90 cm in women were determined using the 100 cm² of intra-abdominal visceral fat area (16), but the validity of these cutoff levels remains controversial (17-19). Thus, it is strongly recommended in the Japanese population that further evidence should be accumulated to establish suitable cutoff levels of WC measurements for clinical use. WC measurement, which is convenient and inexpensive, is useful for evaluating visceral fat accumulation in the Asian population (20, 21). The INTERHEART study confirmed the importance of such accumulation, as a potent risk factor for myocardial infarction (22). It is well known that visceral fat is closely related to increased insulin resistance, which is the pathophysiological basis for MetS. On the basis of this information, this study was designed to determine the WC cutoff level corresponding to HOMA-IR levels that are used to diagnose MetS.

Several important findings were obtained in this study. First, the WC cutoff level corresponding to the estimate of HOMA-IR levels for predicting a cluster of metabolic abnormalities was 82.7 cm in non-diabetic middle-aged Japanese men. This value had a similar utility for predicting subjects with a cluster of metabolic abnormalities compared to those mentioned in the IDF and JSIM criteria. In addition, the HOMA-IR levels were significantly higher in subjects with WC ≥82.7 cm than in those with WC <82.7 cm. These findings suggest the validity of the WC cutoff level in this study. In MetS screening, early detection in subjects at a high risk of developing type 2 diabetes and cardiovascular disease is very important. Even if the specificity is considerably decreased, it indicates the need for aggressive lifestyle management, including weight reduction, smoking cessation, increased physical activity, and diet modification. Additionally, if MetS criteria similar to the JSIM criteria include WC as an essential component, the WC cutoff values should have higher sensitivities for detecting subjects with a cluster of metabolic abnormalities. Large clinical studies have shown that WC has significant predictive power for type 2 diabetes and cardiovascular disease (23, 24), indicating that strict management of WC levels has a role in preventing the development of such diseases. Second, HOMA-IR was correlated with each metabolic parameter, and in addition, WC levels were most strongly predictive of HOMA-IR levels. Also, HOMA-IR showed a stronger correlation to WC than to body mass index. These results support the significance of using HOMA-IR levels in order to determine the WC cutoff level for diagnosing MetS, and indicate that WC is a valuable marker for HOMA-IR and thus WC levels should be measured on a regular basis. In this study, the HOMA-IR level that yielded the maximum sensitivity plus specificity for predicting subjects having a cluster of metabolic abnormalities was 0.92 in both IDF and JSIM criteria, although there was a limitation in the JSIM criteria because its MetS included only the subjects with dyslipidemia (TG ≥150 mg/dL or HDL-C <40 mg/dL) and elevated blood pressure (≥130/85 mmHg). This value was much lower than a HOMA-IR level of 1.73 previously reported as indicative of insulin resistance (25). The discrepancy in HOMA-IR cutoff levels may be derived from differences in characteristics of study subjects. In particular, we excluded subjects with fasting glucose ≥110 mg/dL to diminish the possibility of inaccurate evaluations of HOMA-IR. There is still no clear cutoff for the definition of insulin resistance based on HOMA-IR, and Japanese subjects have lower levels of HOMA-IR and lower insulin secretion than Western subjects (26, 27). A recent prospective study showed that even minimal increases in HOMA-IR levels predicted subsequent cardiovascular events in non-diabetic Japanese men (28). These findings suggest that the HOMA-IR cutoff value proposed by this study may have clinical implications for type 2 diabetes and cardiovascular disease.

This study has some limitations. First, our study was limited to a single institution, and extensive investigations will be necessary to validate these findings. Second, a similar study should be performed in other institutions because these study subjects may not be representative of all Japanese men. Third, we could not investigate whether the WC cutoff levels proposed in this study actually have a role in the prevention of MetS, type 2 diabetes, and/or cardiovascular disease. Interestingly, a large prospective study has shown that an increased weight in adolescence constitutes a
substantial risk factor for obesity-related disorders in midlife (29). Further studies will be necessary to examine the clinical implications of WC level.

In conclusion, we showed that the WC cutoff level for diagnosing MetS, evaluated by HOMA-IR levels, was 82.7 cm in non-diabetic middle-aged Japanese men. This study suggests that WC levels should be more highly considered and strictly managed than the current criteria, for preventing the development of MetS in Japanese men.

The authors state that they have no Conflict of Interest (COI).

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