Urgency of reassessment of role of obesity indices for metabolic risks

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Abstract

The definition of metabolic syndrome places emphasis on health care for persons at risk. However, whether an obesity index should be a mandatory component of the definition and whether obesity indices can identify metabolic risks satisfactorily require further exploration. Therefore, we investigated the effectiveness of various anthropometric obesity indices in identifying the clustering of 2 or more American Heart Association (AHA)/National Heart, Lung, and Blood Institute (NHLBI)/International Diabetes Federation (IDF)–defined metabolic risk factors (hypertension, hyperglycemia, hypertriglyceridemia, and low high-density lipoprotein cholesterol) for metabolic syndrome and those of other metabolic risk factors (high low-density lipoprotein cholesterol, hyperuricemia, high γ-glutamyltransferase, fatty liver) in 6141 men and 2137 women. The anthropometric indices were the following: (1) for both sexes—various levels of waist-to-height ratio (WHtR) including 0.5 and body mass index (BMI) of 23 and 25 kg/m²; (2) for men and women individually—waist circumference (W) 90/80 cm (AHA/NHLBI/IDF for ethnic groups), W 85/90 cm (Japan Society for the Study of Obesity), and combined W and BMI: W 85/90 cm and/or BMI 25 kg/m² (Japanese government). The results showed the following: (1) The optimal value for WHtR was 0.5 for AHA/NHLBI/IDF-defined risk factors and approximately 0.5 for other risk factors in both sexes. (2) The sensitivities of various proposed obesity indices for identifying clustering of defined and other risk factors varied between 74.4% (WHtR 0.5) and 36.3% (BMI 25) and between 80.5% (WHtR 0.5) and 43.7% (BMI 25) in men, and varied between 65.6% (WHtR 0.5) and 16.8% (W 90 cm) and between 82.3% (WHtR 0.5) and 28.2% (W 90 cm) in women. Because the sensitivities of many anthropometric indices were very low, a reassessment of the effectiveness of obesity indices in evaluating metabolic risks and especially their suitability as a single mandatory component of metabolic syndrome is urgently needed. However, WHtR 0.5 provides a very useful algorithm for screening persons at risk.

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1. Introduction

Body mass index (BMI), which was defined by the World Health Organization (WHO), has been used for many years as a global index for assessing obesity [1,2]. More recently, identifying metabolic syndrome has become more important than the simple assessment of obesity. In 2001, the Adult Treatment Panel III (ATP III) proposed a definition for metabolic syndrome as the presence of 3 or more of 5 metabolic risk factors, including large waist circumference [3]. In 2005, the International Diabetes Federation (IDF) also proposed a definition of metabolic syndrome, with large waist circumference as the single mandatory component. However, the cutoff values for waist circumference also varied for sexes, ethnic groups, and even countries [3,4]. In the same year, the American Heart Association (AHA)/National Heart, Lung, and Blood Institute (NHLBI) made a statement after minor revision of the definition of ATP III for the fasting glucose value [5]. In 2006, the IDF revised the cutoff value for the waist circumference of Japanese people from 85 to 90 cm in men and from 90 to 80 cm in women [6]; these were the same as those for South Asians, Chinese, and Asian Americans defined by AHA/NHLBI. However, the Japan Society for the Study of Obesity (JASSO) insists that waist circumferences of 85 cm in men and 90 cm in women...
(corresponding to a visceral fat area of 100 cm²) should continue to be used as the single essential component of metabolic syndrome for Japanese [7]. Recently, the Ministry of Health, Labour, and Welfare of Japan established special health checkups and interventions for metabolic syndrome that took effect in April 2008, with the combined criteria of waist circumferences and BMI as the single mandatory component of metabolic syndrome [8].

In 1995 and 1996, another anthropometric index, waist-to-height ratio (WHtR), was shown to be better associated with metabolic risk factors [9-12]. As an advantage of this index, the same cutoff value (0.5) can be applied to both men and women [9,10]. In the last few years, there has been an exponential increase in evidence from other investigators showing the superiority of WHR as a predictor of metabolic risks, stroke, and chronic kidney disease based on studies in both adults and children [13-29]. We have previously proposed WHtR of 0.5 or greater as a more effective index than the various indices of BMI and waist circumference for screening defined metabolic risk factors of metabolic syndrome using the former definition by the ATP III [30]. However, we have not yet reported sensitivity and specificity for various levels of WHR and their comparison with other proposed anthropometric indices including the recent proposal by the Japanese government in screening both defined and undefined metabolic risk factors of the recent definition of metabolic syndrome by AHA/NHLBI/IDF. Therefore, this index merits further evaluation.

Because obesity indices have been used as a single mandatory component of metabolic syndrome by the IDF and other institutions, individuals who have clustering of metabolic risk factors but whose anthropometric values do not exceed the cutoffs of obesity indices are underevaluated and may not receive the needed consultation. This is particularly a problem in light of government legislation requiring intervention for patients with metabolic syndrome [8]. In addition, the use of anthropometric indices and proposed cutoff values for the definition of metabolic syndrome is very complicated; and recommendations may even differ within the same country. We believe that both the care of persons at risk and the cost-effectiveness of such medical care can be substantially improved by a further exploration of the role of various obesity indices in screening of metabolic risks. Therefore, we evaluated the effectiveness of various anthropometric indices in screening defined and other metabolic risk factors, and considered whether the anthropometric index should be a mandatory or optional component of metabolic syndrome.

2. Methods

2.1. Study population

Routine health checkups are common in Japan because the Japanese government and companies encourage people to receive periodic examinations. The subjects in this study were 6141 men (49.5 ± 8.9 years old [mean ± SD], BMI from 14.7-37.5 kg/m²) and 2137 women (51.9 ± 9.0 years old, BMI from 13.9-43.3 kg/m²) who underwent such health checkups at the Medical Center of Health Science, Toranomon Hospital, Tokyo [13]. The research was approved by the institutional review committee for non-invasive study of human use.

2.2. Procedure and measurement

After an overnight fast, height and weight were measured. Waist circumference (W) was measured by the physician at the umbilical level with the subjects standing and breathing normally during physical examination [9,10]. Blood pressure was measured by hospital staff with the subjects in a sitting position. Plasma glucose, serum triglyceride, high-density lipoprotein (HDL) cholesterol, uric acid, and γ-glutamyltransferase were measured by enzymatic methods using autoanalyzer (Labospect; Hitachi, Tokyo, Japan). Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation, but excluding subjects with serum triglyceride of 400 mg/dL or greater [31]. Abdominal ultrasonography was performed using the SAA-250A device (Toshiba, Tokyo, Japan) by the experienced technician during the same morning, and the result was diagnosed later by the physician (specialist in ultrasonography). A total of 6061 men and 2073 women received this examination at the subject’s option. The current histories of subjects receiving medication for metabolic risks were obtained at the time of examination.

2.3. Anthropometric indices

2.3.1. Classification of WHR levels

For this study, WHR values were classified arbitrarily around our previous proposed value, 0.5 [9,10], into the 5 following groups, considering simplicity and the ease of effective calculation: at least 0.44, at least 0.46, at least 0.48, at least 0.5, and at least 0.52 [9,10]. These groups were studied to determine the optimal cutoff value.

2.3.2. Definition of obesity-related anthropometric cutoff values used for metabolic syndrome

2.3.2.1. Men. (1) W at least 90 cm (AHA/NHLBI for Asian Americans [5] and IDF for South Asians, Chinese, and Japanese [6]), (2) W at least 85 cm (JASSO [7]), and (3) W at least 85 cm and/or BMI at least 25 kg/m² (Ministry of Health, Labour, and Welfare of Japan [8]).

2.3.2.2. Women. (1) W at least 80 cm (AHA/NHLBI for Asian Americans [5] and IDF for South Asians, Chinese, and Japanese [6]), (2) W at least 90 cm (JASSO [7]), and (3) W at least 90 cm and/or BMI at least 25 kg/m² (Ministry of Health, Labour, and Welfare of Japan [8]).
2.3.2.3. Both men and women. (1) WHtR at least 0.5 (our proposal [9,10]), (2) BMI at least 23 kg/m² (WHO for Asians [2]), and (3) BMI at least 25 kg/m² (WHO [1]).

2.4. Definition of metabolic risk factors

2.4.1. AHA/NHLBI/IDF-defined metabolic risk components of metabolic syndrome [5,6]

(1) Hypertension: systolic blood pressure at least 130 mm Hg and/or diastolic blood pressure at least 85 mm Hg and/or currently receiving medication for hypertension. (2) Hyperglycemia: fasting plasma glucose at least 100 mg/dL and/or currently receiving medication for hyperglycemia. (3) Hypertriglyceridemia: serum triglyceride at least 150 mg/dL and/or currently receiving medication for hypertriglyceridemia. (4) Low HDL cholesterol: serum HDL cholesterol less than 40 mg/dL for men and less than 50 mg/dL for women.

2.4.2. Other metabolic risk factors

(1) High LDL cholesterol: serum LDL-cholesterol at least 140 mg/dL and/or currently receiving medication for hypercholesterolemia. (2) Hyperuricemia: serum uric acid greater than 7 mg/dL and/or currently receiving medication for hyperuricemia. (3) High \( \gamma \)-glutamyltransferase: serum \( \gamma \)-glutamyltransferase greater than 109 IU/L. (4) Fatty liver: bright liver, increased liver echotexture compared with kidneys, vascular blurring, and deep attenuation as shown by ultrasonography [32].

2.5. Data analysis

Sensitivity was calculated as true positives over the sum of true positives and false negatives. Specificity was calculated as true negatives over the sum of true negatives and false positives. The optimal cutoff value was determined by the value that had the largest sum of sensitivity and specificity [17]. JMP software (SAS Institute, Cary, NC) was used in this analysis.

3. Results

3.1. Sensitivity and specificity for identification of 1 or more and 2 or more AHA/NHLBI/IDF-defined metabolic risk factors by various levels of WHtR in men and women

In men, the optimal cutoff value of WHtR for the identification of both 1 or more and 2 or more AHA/NHLBI/IDF-defined metabolic risk factors was 0.5. In women, the optimal value for the identification of 1 or more metabolic risk factors was 0.48; and that for the identification of clustering of 2 or more AHA/NHLBI/IDF-defined metabolic risk factors was 0.5 (Table 1).

3.2. Sensitivity and specificity for identification of 1 or more and 2 or more other metabolic risk factors by various levels of WHtR in men and women

In men, the optimal value of WHtR for the identification of 1 or more other metabolic risk factors was 0.5; and that for the identification of clustering of 2 or more other metabolic risk factors was 0.5 to 0.52 (sum of sensitivity and specificity, 132.3–133). In women, the optimal value for the identification of 1 or more other metabolic risk factors was 0.48; and that for the identification of clustering of 2 or more other metabolic risk factors was 0.5 to 0.52 (sum of sensitivity and specificity, 152.6–152.8) (Table 2).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Sensitivity and specificity for identification of 1 or more and 2 or more AHA/NHLBI/IDF-defined metabolic risk factors by various levels of WHtR</th>
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3.3. Sensitivity and specificity for identification of 1 or more and 2 or more AHA/NHLBI/IDF-defined metabolic risk factors by various proposed anthropometric indices in men

The optimal index for identification of both 1 or more and 2 or more AHA/NHLBI/IDF-defined metabolic risk factors among the various proposed indices was WHR 0.5 in men. Waist-to-height ratio of 0.5 also showed the highest sensitivity (65.4 for 1 or more risk factors, 74.4 for 2 or more risk factors). Waist circumference of 85 cm and BMI 23 kg/m² had a slightly lower sensitivity (62.6 and 62.3 for 1 or more risk factors, 71.5 and 69.5 for 2 or more risk factors). The combined index of “W 85 cm and/or BMI 25 kg/m²” was not much more sensitive than W 85 cm alone (63.1 for 1 or more risk factors, 72.0 for 2 or more risk factors). The sensitivities were much lower for both W 90 cm and BMI 25 kg/m² (34.3 and 29.7 for 1 or more risk factors, 41.7 and 36.3 for 2 or more risk factors) (Table 3).

3.4. Sensitivity and specificity for identification of 1 or more and 2 or more other metabolic risk factors by various proposed anthropometric indices in men

The optimal index for identification of 1 or more other risk factors was WHR 0.5. The sum of sensitivity and specificity for identification of 2 or more other risk factors was very close for the combined index of “W 85 cm and/or BMI 25 kg/m²,” W 85 cm, and WHR 0.5 (132.5–132.3), indicating that these would be the optimal indices for identification of 2 or more other risk factors in men. On the other hand, among various proposed indices, the sensitivities for identification of both 1 or more and 2 or more other metabolic risk factors were highest for WHR 0.5 in men (69.2 for 1 or more risk factors, 80.5 for 2 or more risk factors), followed by “W 85 cm and/or BMI 25 kg/m²” and W 85 cm (67 and 66.4 for 1 or more risk factors, 78.9 and 78.3 for 2 or more risk factors). The sensitivities were much lower for both W 90 cm and BMI 25 kg/m² (37.1 and 32.8 for 1 or more risk factors, 49.8 and 43.7 for 2 or more risk factors) (Table 4).

3.5. Sensitivity and specificity for identification of 1 or more and 2 or more AHA/NHLBI/IDF-defined metabolic risk factors by various proposed anthropometric indices in women

The optimal index for identification of both 1 or more and clustering of 2 or more AHA/NHLBI/IDF-defined metabolic risk factors among the various proposed indices was WHR 0.5 in women. In addition, WHR 0.5 also showed the highest sensitivity (48.8 for 1 or more risk factors, 65.6 for clustering of 2 or more risk factors). Both W 80 cm and BMI 23 kg/m² showed lower sensitivity (39.1 and 39.1 for 1 or more risk factors, 54.7 and 54 for 2 or more risk factors). The sensitivities were much lower for both W 90 cm and BMI 25 kg/m² (10.2 and 20.2 for 1 or more risk factors, 16.8 and 32.7 for 2 or more risk factors). The combined index of “W 90 cm and/or BMI 25 kg/m²” was not much more sensitive than BMI 25 kg/m² alone (21.4 for 1 or more risk factors, 33.9 for 2 or more risk factors) (Table 5).

### Table 3

<table>
<thead>
<tr>
<th>Risk factors</th>
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<th>AHA/NHLBI for Asian Americans and IDF for South Asians, Chinese, and Japanese</th>
<th>JASSO ≥85 cm</th>
<th>WHO for Asians</th>
<th>The Ministry of Health, Labour, and Welfare of Japan ≥85 cm</th>
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### Table 4

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3.6. Sensitivity and specificity for identification of 1 or more and 2 or more other metabolic risk factors by various proposed anthropometric indices in women

The optimal index for the identification of both 1 or more and clustering of 2 or more other metabolic risk factors among the various proposed indices was WHtR 0.5 in women. In addition, WHR 0.5 also showed highest sensitivity (50.1 for 1 or more risk factors, 82.3 for clustering of 2 or more risk factors). Both W 80 cm and BMI 23 kg/m² showed lower sensitivity (39.1 and 39.7 for 1 or more risk factors, 72.4 and 68.0 for 2 or more risk factors). The sensitivities were much lower for either W 90 cm or BMI 25 kg/m² (10.0 and 21.1 for 1 or more risk factors, 28.2 and 46.4 for 2 or more risk factors). The combined index of “W 90 cm and/or BMI 25 kg/m²” was not much more sensitive than BMI 25 kg/m² alone (22.3 for 1 or more risk factors, 48.1 for 2 or more risk factors) (Table 6).

4. Discussion

In this study, the sensitivities of some of the proposed anthropometric indices in identification of clustering of both defined and other metabolic risk factors were very low (<50; BMI 25 for both men and women; AHA/NHLBI/IDF for men; JASSO and the Ministry of Health, Labour, and Welfare of Japan for women). Therefore, their suitability as a component of metabolic syndrome requires further study.

The optimal WHtR for identification of 2 or more AHA/NHLBI/IDF-defined and other metabolic risk factors in our current study was approximate 0.5 in both men and women, based on combined sensitivity, specificity, and simplicity. We found that, among various proposed indices of abdominal obesity, only WHR 0.5 could identify more people with clustering of metabolic risk factors in both men and women, considering sensitivity and specificity. Our optimal WHtR value is very similar to those in other reports from Japan (0.49 for men) [11], Taiwan (0.48 for men and 0.45 for women) [14], Hong Kong (0.48 for both sexes [17], and the United Kingdom (0.5 for children) [21] for identifying any or more metabolic risk factors under various definitions in their populations. Indeed, a recent meta-analysis has shown that WHR may be a better indicator of metabolic risks than BMI, waist circumference, or waist-to-hip ratio [33].

Short people may have higher metabolic risks than taller people with a similar waist circumference [34]. We can speculate on the following 3 possible reasons for the better sensitivity of WHtR in identifying metabolic risk factors in both men and women: (1) The relative amount of central fat may be more closely associated with metabolic risks than the absolute amount of central fat, especially for people with moderate BMI. (2) Waist circumference adjusted by height may better reflect the different risk experienced by older and younger people. In particular, in Japan, younger people are generally taller than older people because of the improved nutritional environment in recent years. Thus, using the same cutoff value for waist circumference for all ages may overestimate the metabolic risk for younger people and underestimate the metabolic risk for older people. (3) Waist circumference

Table 5
Sensitivity and specificity for identification of 1 or more and 2 or more AHA/NHLBI/IDF-defined metabolic risk factors by various proposed anthropometric indices in women

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<th>Risk factors</th>
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Table 6
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adjusted by height may better reflect the combined metabolic risks due to stature and girth. For example, shorter persons may be prone to metabolic risks and/or cardiovascular disease because of their poor nutritional state in intrauterine life or childhood.

The AHA/NHLBI/IDF initially defined metabolic syndrome using limited data. However, it has been reported that the recommendations issued in the ACC/AHA’s current clinical practical guidelines were largely developed based on low levels of evidence or expert opinion. These findings highlight the need to improve the process of writing guidelines and to expand the evidence base from which clinical practical guidelines are derived [35]. The definitions of metabolic syndrome made by AHA/NHLBI/IDF; JASSO; and the Ministry of Health, Labour, and Welfare of Japan are other examples of this problem.

Because none of the presently proposed indices perfectly identifies people with clustering of metabolic risk factors, a reassessment of the effectiveness of the present indices and definitions in enhancing health promotion is urgently required. There may be individual differences in susceptibility to metabolic risks due to hereditary or other reasons that are not necessarily related to these anthropometric indices. From this viewpoint, we suggest that an anthropometric index should not be a mandatory component of metabolic syndrome; and we also support the use of the obesity index as one of the optional components of metabolic syndrome as proposed by AHA/NHLBI in recommending consultation to individuals who have clustering of metabolic risk factors but an anthropometric index less than the cutoff value because dietary treatment such as salt restriction, low cholesterol, low-purine diets, and appropriate alcohol and calorie intake in combination with exercise may be also effective. On the other hand, the sensitivities and specificities of some anthropometric indices for identifying clustering of metabolic risks were very close. The significance of differences requires further study.

However, in addition to other anthropometric indices, the potential of WHtR 0.5 as an optional component of metabolic syndrome and its global utilization as an obesity index in public health should not be neglected, considering its simplicity and effectiveness in screening both men and women with metabolic risk factors [36].

5. Issue for future research on role of obesity indices in metabolic syndrome and other health risks

(1) Why should the same cutoff value of BMI be used as a global obesity index for both sexes, but not waist circumference? (2) Should individual differences in height be ignored for the sake of simplicity? (3) Which has a higher correlation with metabolic risk, total amount of visceral fat or relative amount of visceral fat to stature, especially in subjects with moderate BMI? (4) Do people with the same amount of abdominal fat have the same threshold for metabolic risks, irrespective of hereditary, environmental, and other factors? (5) Why do some people with anthropometric values of obesity less than the cutoff values still have clustering of metabolic risks? (6) Why should anthropometric index of obesity be a mandatory component of metabolic syndrome? (7) Are there any discrepancies between BMI and waist circumference as parameters of metabolic risks and other health risks? Is a 90-cm waist size a meaningful criterion for women, considering the fact that women with a waist circumference greater than 90 cm defined by JASSO and the Ministry of Health, Labour, and Welfare of Japan can almost always be identified as overweight or obese from appearance without measuring their waist circumferences? It should be noted that, when attempting to establish an anthropometric index for metabolic risks, it is desirable to use an index that can also contribute to preventing other complications of obesity, such as the effect of weight itself on the joints.

References


