Sensitivity and Specificity of Body Mass Index as a Definition of the Obesity Component of Metabolic Syndrome

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ABSTRACT

Metabolic syndrome (MS) is a combination of risk factors that are associated with several chronic diseases. Its components (obesity, dyslipidemia, carbohydrate intolerance, hypertension, microalbuminemia) are diverse, whose thresholds vary in different definitions of MS. For example, a World Health Organization (WHO) panel defined the obesity component of MS based on waist-hip ratio, or body mass index (BMI), while the National Cholesterol Education Program (NCEP) defined the obesity component of MS by waist circumference. Since BMI is the common measure of obesity in most epidemiological studies, this research addressed how accurately the obesity component of MS is captured by BMI alone. Data presented showed that in a population with high prevalence of obesity, the specificity of detecting the obesity component of MS by BMI alone is almost 100%, but the sensitivity is low (e.g., <50%). Individuals with high BMI generally have large waist-hip ratio and wide waist circumference, but the converse is not necessarily true. Consequently, centralized obesity (a risk factor for several chronic diseases) is not always captured by a high BMI alone.

Key words: metabolic syndrome, body mass index, centralized obesity, sensitivity, specificity

Introduction

Recent reviews indicate that frequent co-morbidity of obesity, diabetes, hypertension, and hyperlipidemia in individuals was first noted in late 1960s, which was subsequently called «metabolic syndrome» (MS) in late 1970s\(^3\). Though at first MS was thought to be associated with atherosclerosis, its additional connection with insulin resistance lead to the terminology of «insulin resistance syndrome», also called «syndrome X»\(^5,6\). Subsequent studies indicate that, irrespective of the term used (Syndrome X, Insulin resistance syndrome, or metabolic syndrome), the phenomenon of concern is a clustering of risk factors, whose major components are: obesity, dyslipidemia, carbohydrate intolerance, hypertension, and microalbuminemia that are, in aggregate, closely associated with atherosclerosis, coronary heart disease, hyperglycemia, and insulin resistance.

As these diseases are generally classified as metabolic disorders, the term metabolic syndrome (MS) has become the most commonly used description of these clustered co-morbid risk factors. However, not until the attempts of the experts' panel of the World Health Organization (WHO) in 1998, and that of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) in 2001, criteria for defining MS in adults were established formally\(^7,8\). Though the WHO definition was subsequently modified in 1999 in conjunction with the European Group for the Study of Insulin Resistance (EGIR)\(^9\), there are important differences of case definition and prognostic ability in using the criteria of WHO versus that of NCEP-ATP III\(^10\).

As a consequence, studies on the prevalence of MS, judged by both WHO and NCEP-ATP III definitions, often produce conflicting results. For example, an almost 2-fold increased prevalence of MS according to the NCEP-ATP III definition, as compared to that of the WHO definition has been reported in Mexico (age-ad-
justed rate 26.6% versus 13.6%\textsuperscript{12}, while in the San Antonio Heart study cohort, the crude rates of MS by both definitions were almost the same (25%)\textsuperscript{13}. Almost equal prevalence of MS by these two definitions (crude rate of 81% by the NCEP-ATP III, versus 78% by the WHO criteria) were also seen in a series of type 2 diabetes patients in Italy\textsuperscript{14} but among the Arab-Americans a reverse trend; namely, a lower rate of MS (23% age adjusted) with the NCEP-ATP III criteria in comparison to the age-adjusted rate of 28% by the WHO definition, has been noted\textsuperscript{15}. Such a reverse trend was also noted in a study of adolescents of Greater Cincinnati region, where the crude prevalence of WHO-defined MS was exactly double (8.4%) of that defined by the NCEP-ATP III criteria (4.2%)\textsuperscript{16}. Though this study was conducted in a population of mixed ethnic origin (consisting of Black, White, and Hispanic school children, 7th through 12th grades), their NCEP-ATP III criteria based prevalence rate of MS agrees fairly with that of the adolescent study from the third NHANES survey\textsuperscript{17}. In addition, regardless of prevalence rates, the congruence of classifying individuals as having MS or not by these two definitions has been at best modest (e.g., the $\kappa$-statistic has been reported in the range of 0.41–0.50\textsuperscript{12,16}).

These discrepancies prompted some researchers to conclude that MS, as defined by these two guidelines, may not be caused by a common etiologic mechanism\textsuperscript{16}. However, ethnic variations of MS in general, and more so of its individual components\textsuperscript{5}, argue that such criticisms may not be totally valid, since the sensitivity and specificity of detection of MS may be dependent on the measures of each component of MS and their cut-off values.

As central adiposity has been shown to determine the prevalence differences of MS\textsuperscript{18}, and weight loss has a significant impact on the syndrome itself\textsuperscript{19}, the purpose of this research is to examine how a specific measure of obesity, an important component of MS, impacts the sensitivity and specificity of the detection of the obesity component of the MS. In particular, using data on a random sample of 992 Mexican American men and women, aged 15 through 75 years of age, as described in earlier research\textsuperscript{20–22}, we show that the most popular measure of obesity; namely, the body mass index (BMI = Weight / Height\textsuperscript{2}, with weight measured in kilograms, and height in meters) determines the obesity component of MS by both WHO and NCEP-ATP III definitions of MS with almost perfect (100%) specificity, but sensitivity is at best modest (28.3 to 45.9% for the WHO definition, and 43.2 to 77.1% for the NCEP-ATP III definition, depending upon age and gender). Thus, we argue that for defining MS, BMI alone is not an adequate indicator of obesity; it must be supplemented by measures of centralized obesity, such as the waist circumference, or the waist-hip ratio. This is so, because individuals with low or moderate BMI generally have low waist-hip ratio (WHR) and waist circumference (WC), but in contrast obesity may be due to higher WHR and/or wide WC (i.e., centralized obesity) without BMI being high (i.e., without being obese in general).

### Materials and Methods

#### Definition of MS and its obesity component

The definition of MS, according to the WHO criteria has two components. First, for an individual to be classified as having MS, the person must have hyperinsulinemia (defined as the upper quartile of the nondiabetic population), a post-2-hour glucose load $\geq$140 mg/dL, a fasting plasma glucose $\geq$110 mg/dL, or taking medication for diabetes. In addition, the person must have at least two of the following abnormalities; general or abdominal obesity (i.e., either BMI $\geq$30 kg/m\textsuperscript{2}, or a waist-hip ratio (WHR) $>0.90$ in men, or $>0.85$ for females), dyslipidemia (i.e., triglycerides $\geq$150 mg/dL, and/or HDL cholesterol $<35$ mg/dL in men, or $<39$ mg/dL in women), high blood pressure (i.e., $\geq$140/90 mm Hg), or microalbuminuria (i.e., urinary albumin excretion rate $\geq$20 mg/min, or albumin/creatinine ratio $\geq$30 mg/g). Thus, the WHO-definition of MS is somewhat complex, as it consists of insulin resistance as the essential element, and the obesity component is either general (determined by high BMI), or centralized adiposity (e.g., with large WHR)\textsuperscript{7}.

In contrast, the NCEP-ATP III criteria of MS are simpler. According to this, individuals who has 3 or more of the following abnormalities would be called having MS: hyperglycemia (i.e., fasting glucose $\geq$110 mg/dL), abdominal obesity (i.e., waist circumference, WC $>102$ cm in men, or $>88$ cm for women), triglycerides $\geq$150 mg/dL, low HDL cholesterol (i.e., HDL $<40$ mg/dL in men, or $<50$ mg/dL in women), high blood pressure (HBP $\geq$130/$\geq$85 mm Hg)\textsuperscript{8}. Thus, the two definitions of MS differ with respect to the components (e.g., albumin abnormality is included in the WHO definition, but not in NCEP ATP III; hyperglycemia and/or diabetes is essential for the WHO definition, but not a necessary condition for the NCEP ATP III; and obesity pattern can be either general or centralized according to the WHO definition, but only needs to be centralized according to the NCEP ATP III criteria). Further differences are in the cut-off values for several components (e.g., the designations of HBP and low HDL are different). In addition, even the measure used to define centralized adiposity is different between them (WHR versus WC). Numerous studies showed ethnic as well as demographic differences of variation with respect to these different components of MS, and hence, it is not surprising that the prevalence of MS by these two definitions show a somewhat discrepant trend, depending upon age, gender, and ethnicity of the subjects studied.

For the analysis of the present study, we consider the three measures of obesity (e.g., BMI $\geq$30 kg/m\textsuperscript{2}; WHR $>0.90$ in men, or $>0.85$ for females; and WC $\geq$102 cm in men, or $>88$ cm for women). We address the question of sensitivity and specificity of determining the obesity component of the WHO- and NCEP ATP III-definitions of MS, by using the BMI criterion alone, since weight loss (i.e. reduction of BMI) appears to be the most popular suggested intervention modality for controlling MS in population-based studies\textsuperscript{18}. 


Study population and data used

To examine the utility of BMI alone for detecting WHO- or NCEP ATP III-based criterion of the obesity component of MS, we use the data gathered in the gallbladder genetic epidemiology study among the Mexican Americans of Starr County, Texas20–22. Statistical features of different measures of body fat distribution in this sample have been reported earlier along with a study of the validity of the use of body silhouettes for distinguishing abdominal and lower body obesity and their relationship with type 2 diabetes and gallbladder disease22,23. This survey, over 1000 Mexican Americans from Starr County were randomly sampled to measure their body fat distribution and determine the prevalence of obesity, type-2 diabetes, and gallbladder disease. Of these, for 992 individuals, aged 15 to 75 years (296 males, and 696 females), measurements were available for waist and hip circumference, height, and weight, so that BMI, WHR, and WC could all be computed for the purpose of the present analyses. The survey design, description of the study population, and details of physical examination and measurement procedures were described earlier20–23. For the purpose of the present analyses, summary results are presented by classifying the sampled individuals by gender and two age groups (15–44 yrs, and 45–75 yrs.), although for some analyses (e.g., correlations between the different measures of body fat distribution) age-adjustment was done by considering the exact age of each individual. Table 1 shows the sample sizes of the data analyzed in the present study.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 – 44 yrs</td>
<td>193</td>
<td>426</td>
<td>619</td>
</tr>
<tr>
<td>45 – 75 yrs</td>
<td>103</td>
<td>270</td>
<td>373</td>
</tr>
<tr>
<td>Total</td>
<td>296</td>
<td>696</td>
<td>992</td>
</tr>
</tbody>
</table>

Statistical methods

Descriptive statistics of the three measures of body fat distribution (BMI = Weight/Height2, with weight measured in kg, and height in meters; WHR = Ratio of waist and hip circumference; and WC = Waist Circumference in cm) were computed to depict the general characteristics of body fat patterning in the sample. Age-adjusted (i.e., linear effect of age on each body fatness variable removed by regression analyses) values of BMI, WHR, and WC were used to compute their product-moment correlations. Using the cut-of values for the obesity component of MS according to the WHO definition (i.e., either BMI ≥ 30 kg/m², or a WHR > 0.90 in men, or > 0.85 for females), and by the NCEP ATP III definition (i.e., WC > 102 cm in men, or > 88 cm for women), the obesity component of metabolic syndrome (MS-obesity) was defined for each definition. Standard epidemiological definitions of sensitivity and specificity were used for detecting these two types of MS-obesity criteria by classifying individuals as obese by BMI testing alone (i.e., BMI ≥ 30 kg/m²)24. All analyses were done by using the respective modules of the SPSS-v.10 software.

Results

Descriptive statistics of obesity variables

Table 2 shows the descriptive statistics (mean and s.d.) of the three measures of body fatness, and age, for males and females separately. Roughly, the study sample consists of men and women, both approximately 40 years old, on average. On an average, both males and females in this sample are in the mid over-weight category (i.e., BMI between 25 to 30 kg/m²). Average WHR exceeds the WHO criteria of MS-obesity for both males and females. In other words, according to the WHO criteria of abdominal obesity, an average male or female of this sample would be called obese. In contrast, the mean WC exceeds the NCEP ATP III criterion of abdominal obesity for women, but not for the men. In other words, women of this sample are on an average MS-obese by the NCEP ATP III criterion, but not the men in general.

**TABLE 2** DESCRIPTIVE STATISTICS OF OBESITY-RELATED TRAITS IN THE SAMPLE

<table>
<thead>
<tr>
<th>Variable</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 – 44 yrs</td>
<td>39.75 (15.79)</td>
<td>40.41 (15.22)</td>
</tr>
<tr>
<td>45 – 75 yrs</td>
<td>27.28 (5.84)</td>
<td>27.59 (5.92)</td>
</tr>
<tr>
<td>Total</td>
<td>0.95 (0.07)</td>
<td>0.91 (0.09)</td>
</tr>
</tbody>
</table>

Age in years, WC = Waist circumference (in cm), BMI = Body Mass Index = Weight/Height

Inter-relationships between the obesity measures

Table 3 presents the age-adjusted product-moment correlations between the three obesity variables (BMI, WHR, and WC) for males and females, separately. It is clear that WHR is comparatively less correlated with BMI and WC, while in both men and women BMI and WC are more strongly correlated. The more modest correlation between BMI and WHR, in a sense justifies the inclusion of BMI- and/or WHR-based measures of the obesity component in the WHO definition of MS, since with this definition both general and centralized form of body fat distribution can be covered. Nonetheless, the correlation structure shown in the data of Table 3 is consistent with the common notion that BMI captures a general form of obesity, while WHR and WC are perhaps a better description of central obesity.
Sensitivity and specificity of BMI-based detection of the obesity component of MS

Using the definition of the obesity component of MS in the WHO and NCEP ATP III definitions, we determined the sensitivity and specificity indices when obesity is tested by BMI alone (i.e., BMI ≥30 kg/m²). The summary results are shown in Table 4. As the prevalence of MS and its components varies by age and gender, our sensitivity/specificity computations were done for each sex separately, with individuals grouped into two age groups (<45 yrs, and ≥45 yrs.) for each gender. In all age-sex groups, the specificity of detecting the obesity component of MS (for either definition) by BMI testing alone is very high (100% for the WHO definition, and exceeding 96% for the NCEP ATP III definition). However, the sensitivity is low or at best modest for either definition. In particular, for the WHO definition of the obesity-component of MS, BMI-testing alone has sensitivity below 46% in all sex-age categories. For the NCEP ATP III definition, the men have a somewhat higher sensitivity (77.1% in men of younger ages, and 60% for the older). In other words, these statistics indicate that the chance of false positive rate of detection of the obesity component of MS (in either definition) by BMI testing alone is very low, but a substantial proportion of WHO- and NCEP ATP III-based obesity component will be missed by BMI testing alone (as sensitivity is never larger than 77.1%). (Table 4 approximately here)

Discussion and Conclusion

The data presented here show that while BMI (a measure of generalized obesity) is significantly correlated with WC and WHR (traditionally regarded as indicators of centralized adiposity), the poorer correlations of BMI with WC and WHR indicate that a high value of BMI may not necessarily capture abdominal obesity (determined by cut-of values of WHR and/or WC). In particular, the low (but significant) correlation of BMI with WHR in both men and women is reflected in the lowest sensitivity of detecting the obesity component of MS by BMI alone, when the WHO-definition of MS-obesity is used (Table 4). Before generalizing the high specificity of BMI-based obesity detection, shown here, we recall that the Mexican Americans of Starr County, Texas have a very high prevalence of diabetes, gallbladder disease, as well as obesity19,20. Thus, in such a high-risk population, the low false detection rate of abdominal obesity (i.e., high specificity) by using an index of generalized obesity (such as BMI) is not unexpected. The lack of sensitivity of detection of abdominal obesity (the focus of the obesity component of MS in both WHO and NCEP ATP III definitions), through the index of general obesity (BMI), however, raises concern, in particular when the disease risk is mainly contributed by abdominal body fat distribution. Substantial evidence exists suggesting that this is true for metabolic syndrome, as many studies show that centralized adiposity determines prevalence differences of MS, and its prognostic value for disease morbidity and mortality18,25.

In summation, data presented here provide an empirical support of the notion that individuals with normal or moderate BMI do generally have small waist-hip ratio and waist circumference (resulting in high specificity of detecting obesity by BMI measurement alone), but individuals can have high WC and/or WHR without having high BMI (yielding missing substantial proportions of centrally obese individuals by BMI testing alone). This is caused by the fact that centralized obesity is not necessarily captured by a high BMI alone. In contrast, simple and non-invasive measures of both general and abdominal obesity (such as BMI, WHR, and WC) exist, and these may even be adequately assessed by self-reported data26,27. Thus, large-scale epidemiologic studies should use both forms of obesity measures to capture the different dimensions of obesity-related disease risks, such as the ones signified by metabolic syndrome.

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OSJETLJIVOST I SPECIFIČNOST INDEKSA TJELESNE MASE KAO DEFINICIJA PRETILOSTI, KOMPONENTE METABOLI^KOG SINDROMA

S A Ž E T A K

Metabolički sindrom (MS) je kombinacija rizičnih faktora koji su povezani sa nekoliko kroničnih bolesti. Komponente MS-a (pretilost, dislipidemija, intolerancija prema karbohidratima, hipertenzija, mikrobuminera) su različite za razna tumačenja definicija MS-a. Npr., Svjetska zdravstvena organizacija (WHO) definira pretilost kao glavnu komponentu MS-a, omjerom struk-bedra ili indeksom tjelesne mase (BMI), dok za razliku od njih Nacionalni centar za edukaciju o kolesterolu (NCEP) definira omjer opseg struka. Od kada je indeks tjelesne mase postao uobičajena mjera u epidemiološkim studijama, ova studija pokazuje može li se pretilost mjeriti visokim indeksom tjelesne mase. Podaci su pokazali kako je u populaciji sa visokom prevalencijom pretilosti, indeks tjelesne mase bio dovoljan za detekciju u gotovo 100% slučajeva, ali sa malom osjetljivošću (<50%). Pojedinci sa visokim vrijednostima indeksa tjelesne mase, uobičajeno imaju veliki omjer struk-bedra ili širok opseg struka, dok obrnuto ne mora biti tako. Prema tome, centralizirana pretilost (rizik za neke kronične bolesti) nije uvijek mjerljiva visokim indeksom tjelesne mase.