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Body mass index and waist circumference correlate to the same degree with insulin-mediated glucose uptake☆

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Abstract

To compare the relationship between insulin-mediated glucose uptake (IMGU) and excess adiposity as determined by measurement of either body mass index (BMI) or waist circumference (WC), IMGU was quantified by determining the steady-state plasma glucose (SSPG) concentration with the insulin suppression test and the relationship between the SSPG concentration and BMI or WC evaluated in a study of 208 healthy individuals (128 women/80 men). The results indicated that BMI and WC were correlated ($P < .001$) to a similar degree in both men ($r = 0.90$) and women ($r = 0.86$). Steady-state plasma glucose and both indices of excess adiposity were also significantly correlated ($P < .001$) to an essentially identical extent in men (r values of 0.71 vs 0.70) and women (r values of 0.54 vs 0.53). When the population was divided into tertiles on the basis of SSPG concentrations, 96% of those in the most insulin-resistant tertile were identified as being overweight/obese by BMI criteria and 84% as abdominally obese by WC criteria. However, a substantial number of those in the most insulin-sensitive tertile also demonstrated excess adiposity as defined by either BMI (45%) or WC (33%). To summarize, (1) BMI and WC correlate closely within an individual and equally well with IMGU, and (2) BMI is as effective as WC in identifying insulin-resistant individuals.

1. Introduction

Evidence was published 30 years ago that resistance to insulin-mediated glucose uptake (IMGU) was increased in obese nondiabetic individuals, and that this resistance would diminish with weight loss [1]. These initial observations have been confirmed innumerable times [2-5], with a shift in emphasis now to the importance of differences in regional fat distribution as compared with overall obesity [6-9] in modulation of IMGU. However, we are unaware of data derived from a substantial number of apparently healthy individuals comparing the relationship between a specific measure of IMGU and waist circumference (WC) with that between IMGU and body mass index (BMI). This seems important in view of the results of measurements obtained from approximately 15 000 participants in the National Health and Nutrition Examination Survey, showing that the correlation coefficient between BMI and WC was greater than 0.9 irrespective of the age, sex, and ethnicity of groups evaluated [10]. Consequently, we compared the magnitude of the relationship between a specific estimate of IMGU and both BMI and WC in 208 healthy nondiabetic individuals.

2. Materials and methods

The study population consisted of 208 nondiabetic apparently healthy individuals who had responded to print advertisements describing our studies of the role of insulin resistance in human disease. The Stanford Human Subjects Committee had approved the protocols, and all subjects gave informed consent. Participants were in relatively good health with normal physical examinations and medical histories, nondiabetic as defined by the American Diabetes Association criteria [11], with normal liver/kidney function, and no anemia. All studies were performed at the General Clinical Research Center of the Stanford University Medical Center, Stanford, Calif.

With the subject in light clothing and no shoes, height and weight were measured, and BMI was calculated

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(kilograms per square meter). Waist circumference (centimeters) was determined as described previously [12]. Individuals were considered to be overweight/obese if they had a BMI 25.0 kg/m^2 or greater, and abdominally obese if their WC was greater than 88 cm for women and greater than 102 cm for men [13,14].

Insulin-mediated glucose uptake was quantified by a modified version of the insulin suppression test as described and validated by our research group [15-17]. After an overnight fast, an intravenous catheter was placed in each arm of the subject, one for the simultaneous 3-hour infusion of octreotide (0.27 μg/m^2 per minute), insulin (32 mU/m^2 per minute), and glucose (267 mg/m^2 per minute), and the other for the collection of blood samples every 10 minutes during the 150- to 180-minute period to measure plasma glucose and insulin concentrations. The values obtained during these last 30 minutes were then averaged to determine the steady-state plasma glucose (SSPG) and steady-state plasma insulin concentrations. Because steady-state plasma insulin concentrations are comparable in all individuals, and glucose infusion is identical, the resultant SSPG concentration provides a direct measure of the ability of insulin to mediate the disposal of a given glucose load; that is, the higher the SSPG, the more insulin resistant (IR) the individual.

Values for SSPG concentrations vary more than 6-fold in an apparently healthy population [18], and because they are distributed continuously, there is no objective way to classify an individual as being either IR or insulin sensitive (IS). On the basis of 2 prospective studies, we have shown that the upper third of an apparently healthy population is sufficiently IR to develop adverse clinical outcomes, whereas they do not occur in the lower third [19,20]. Consequently, in this study, we have defined the subjects in the tertile with the highest SSPG concentrations as IR, whereas those in the lowest tertile were considered to be IS. Steady-state plasma glucose concentrations used to separate the 2 experimental groups were 197 mg/dL or greater (IR) and 95 mg/dL or less (IS), values similar to cut-points obtained from a prior study of 490 healthy volunteers for the IR and IS tertiles, respectively [18].

Statistical analyses were performed using Systat version 7.0 (SPSS Science, Chicago, Ill). Pearson correlation coefficients were calculated between SSPG and BMI, SSPG and WC, and BMI and WC. In addition, a 2 × 2 table was constructed to determine the ability of BMI and WC to classify subjects as being either IR or IS. χ^2 analysis was performed to asses the statistical significance of the identification of IR and IS individuals by BMI or WC measures. Multiple linear regression analyses were performed to evaluate the relative contributions of BMI and WC, as well as other variables, in the prediction of SSPG.

3. Results

The mean ± SD age of the population was 50 ± 11 years (range, 18 to 75 years), the population contained more women then men (62% vs 38%), and 74% of the subjects were Caucasian, with smaller numbers of Asians, Hispanics, and African Americans. A substantial proportion (72%) of the subjects were overweight/obese by BMI criteria, and cut-points for WC defined a large proportion of both men (49%) and women (59%) as being abdominally obese. Of note, the mean SSPG concentration of study population was 153 mg/dL comparable to the value (151 mg/dL) previously reported in a study of 490 healthy volunteers [18].

The relationship between BMI and WC is shown in Fig. 1. These data indicate that BMI and WC were highly correlated ($P < .001$) in both men ($r = 0.90$) and women ($r = 0.86$).

The relationship between SSPG concentration and either adiposity index was identical in the population considered as a whole ($r = 0.60$, $P < .001$). The results in Fig. 2 illustrate the relationships between the SSPG concentration and the 2 adiposity indices in men and women when considered separately. Although it is clear that the relationships between SSPG and either BMI or WC were essentially identical within each sex group, the magnitude of the

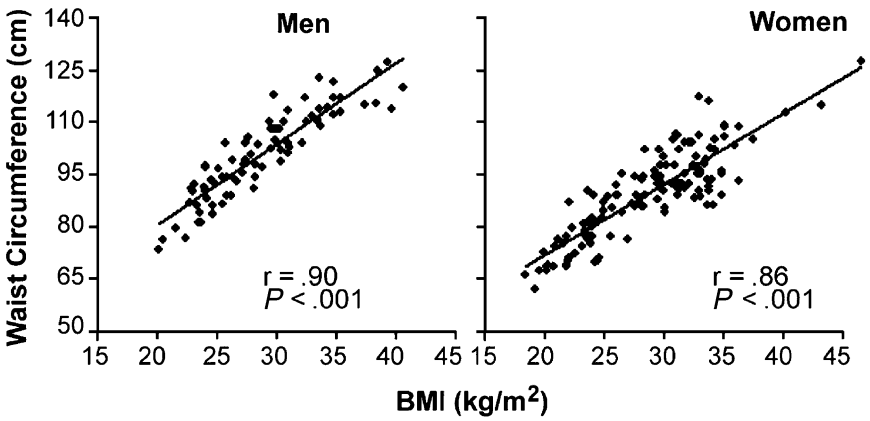

Fig. 1. Relationship between BMI and WC in the 208 study participants analyzed by sex.

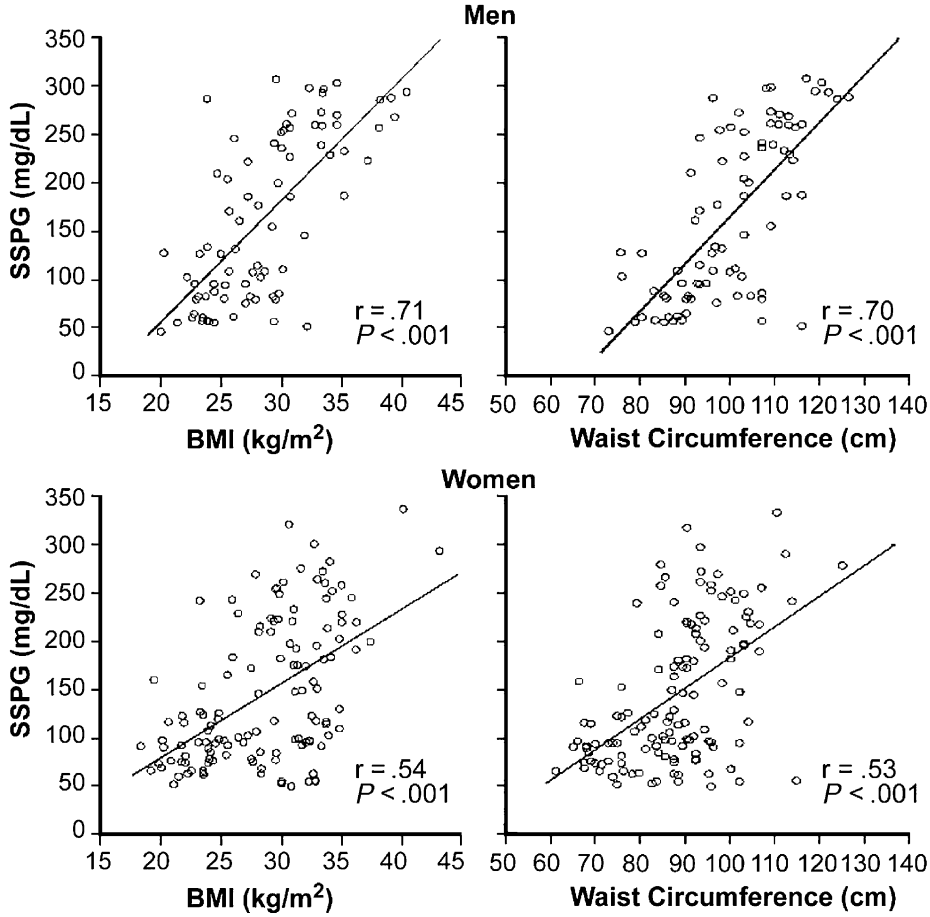

Fig. 2. Relationship between degree of insulin resistance (SSPG concentration) and BMI or WC in the 208 study participants analyzed by sex.

correlation with SSPG varied considerably. Specifically, in men, the *r* values between SSPG and BMI (0.71) or WC (0.70) were greater than in women in whom the same correlation coefficients were 0.54 and 0.53, respectively.

The results in Table 1 compare the relative ability of measurements of BMI or WC to identify individuals as being either IR or IS (see "Materials and methods" section for the definition of the 2 groups). It can be seen that a high BMI ($\geq$25.0 kg/m^2) identified 96% of the IR individuals, and a low BMI (<25.0 kg/m^2) identified 45% of the IS individuals (χ^2 = 42.5, P < .001). Similarly, a high WC correctly identified 84% of the IR subjects, and a low WC identified 33% of the IS individuals (χ^2 = 36.6, P < .001). These results show that both indices were effective and comparable in the classification of IR and IS individuals.

Table 1
Ability of BMI and WC to identify individuals as IR or IS

Classification	BMI <25	BMI ≥25	Nonobese WC[a]	Obese WC[b]
IR, N = 69	3 (4%)	66 (96%)	11 (16%)	58 (84%)
IS, N = 69	38 (55%)	31 (45%)	46 (67%)	23 (33%)

[a] ♀ ≤88 cm, ♂ ≤102 cm.
[b] ♀ >88 cm, ♂ >102 cm.

To assess the relative contributions of BMI and WC in the prediction of SSPG, we performed multiple linear regression analyses with SSPG concentration as the dependent variable, and age, sex, BMI, and WC as the independent variables. In addition, to evaluate any synergistic effect of BMI and WC in the prediction of SSPG, an interaction term was introduced into the model. The interaction term was defined as the cross product of BMI and WC. The results of these analyses indicated that when age, sex, BMI, and WC were entered in the regression model, both BMI and WC significantly predicted SSPG, however, with much reduced standardized regression coefficients (BMI, β = .34, P = .003; WC, β = .32, P = .01) as compared with their individual univariate relationships with the SSPG concentration (β = .60). When the interaction term was introduced into the above model, none of the independent variables were significant predictors of SSPG. These results indicate that both BMI and WC provide similar information in terms of the prediction of the SSPG, and the high degree of multi-colinearity among the independent variables (BMI, WC, and the BMI-WC cross product) prevents us from drawing any additional conclusions from these analyses.

4. Discussion

At the simplest level, the results in Fig. 1 are consistent with the observation by Ford et al [10] that BMI and WC are highly correlated in both men and women. Our findings extend this earlier observation by demonstrating in Fig. 2 that the magnitude of the relationships between the SSPG concentration and the 2 adiposity indices were identical. In other words, BMI and WC predicted insulin resistance to the same extent. However, as noted previously, the association between SSPG and either BMI or WC was much greater for men (r = 0.71 vs 0.70) than for women (r = 0.54 vs 0.53). Thus, it is obvious that excess adiposity, irrespective of the index used, can account for no more than 25% of the variability of IMGU in women, a finding that we are unaware has been previously described.

Because BMI and WC are highly correlated, and the relationship between BMI and SSPG is as strong as that between WC and SSPG, it could be postulated that BMI would be as useful as WC in the identification of IR individuals. To address this issue, we compared the ability of the 2 estimates of obesity to determine the most IR third of the population. The National Institutes of Health criteria [14] classify those individuals with a BMI 25 kg/m^2 or greater as overweight/obese. The WC criteria of the Adult Treatment Panel III [13] define abdominal obesity in men (>102 cm) and women (>88 cm). The results in Table 1 indicate that the 2 indices were successful to a comparable degree, identifying either 66/69 (BMI) or 58/69 (WC) of the most IR tertile population as being either overweight/obese (BMI) or abdominally obese (WC). In effect, this approach to evaluating the clinical utility of BMI and WC also supports the view that they are equally useful in identifying those individuals at increased risk for the adverse consequences linked to excess adiposity. The data in Table 1, in addition, illustrate that excess adiposity does not necessarily mean that an individual will be IR and demonstrate that a substantial number of individuals defined as having a high BMI (45%) or considered abdominally obese (33%) were actually IS (lowest SSPG tertile).

Although the results presented provide evidence that measurements of BMI and WC are comparable in their capability to identify IR individuals, at least 2 important qualifications need to be explicitly addressed. First, 74% of the participants in this study were of European ancestry, and it could be argued that our findings will only apply to this ethnic group. On the other hand, Ford et al [10], in their analysis of the NHANES database, determined that there was a highly significant correlation between WC and BMI ($\geq$0.9), independent of age, sex, or ethnicity. Furthermore, although there were relatively few Asian (14%), Hispanic (9%), and African American (3%) participants in our study, the correlation coefficients between SSPG and either BMI or WC in each of the individual ethnic groups were essentially identical to the values in the Caucasian volunteers. However, the fact that the relationship between BMI and WC, and that between SSPG and BMI or WC, was independent of ethnicity does not negate the evidence that the untoward impact of increases in either BMI or WC on insulin resistance and its consequences does vary with ethnicity [21,22]. Indeed, in light of these ethnic differences, it has been suggested that the BMI and WC cut-points used to identify overweight/obese individuals should be made ethnic specific [21]. The suggestion that the absolute values of BMI and WC with which to identify excess adiposity should be modified to take into account ethnic differences [21] does not diminish the fact that BMI and WC are both closely correlated with each other and to a comparable degree with a particular measure of IMGU.

Second, it is also necessary to emphasize that our findings do not imply that abdominal obesity is unrelated to insulin resistance, nor are they relevant to questions [7-9] concerning the relative roles of subcutaneous vs visceral obesity in contributing to the negative impact of abdominal obesity on IMGU. However, they do raise the possibility that measurement of abdominal obesity, as assessed by WC, may not provide information concerning IMGU that is any more clinically useful than simply measuring height and weight for BMI determination. This statement is not meant to ignore evidence suggesting that WC is more useful than BMI in predicting clinical syndromes related to insulin resistance [23-26]. However, even in this instance, the data are not unanimous. For example, in Pima Indians, increases in visceral obesity did not correlate with decreases in IMGU [27], and BMI was the estimate of adiposity with the highest hazard ratio in the prediction of type 2 diabetes [28]. Furthermore, adding WC to this study's model did not improve its predictive ability. In a prospective study of Mexican Americans, Haffner et al [29] reported somewhat similar results, illustrating that individuals with the highest baseline plasma glucose and insulin values were most likely to develop type 2 diabetes independently of differences in age, BMI, or central obesity. It has also been shown in studies of several ethnic groups that BMI is more strongly associated with blood pressure than is abdominal obesity [30-32]. A similar conclusion was reached concerning the presence of carotid atherosclerosis in Japanese men [33], and the clustering of dyslipidemia, hyperuricemia, diabetes, and hypertension described in both whites and African Americans was most strongly related to insulin concentration, although the magnitude decreased when adjusted for differences in BMI and abdominal obesity [34]. In this latter instance, it was concluded that all 3 variables—insulin concentration, abdominal girth, and BMI—contributed to the negative clinical issues related to insulin resistance. Thus, although WC may be a more powerful predictor of clinical outcomes linked to insulin resistance, there is also considerable evidence that overall

obesity, as estimated by BMI, not only contributes to insulin resistance, but also increases the likelihood that an individual will develop the clinical syndromes associated with the defect in insulin action.

In conclusion, the results presented demonstrate that the 2 estimates of excess adiposity commonly used to identify individuals likely to be IR are closely related and correlate to an essentially identical degree to a specific measure of IMGU. Consequently, it appears that simply measuring height and weight to calculate BMI provides a clinical index that may be as useful as measuring WC in identifying individuals at increased risk to be IR. Furthermore, as pointed out in a recent article [35], a review of the literature indicated that at least 14 different sites have been used to measure WC to relate differences in abdominal obesity to adverse outcomes, and even the 4 most commonly used sites yield quite different absolute values for WC. Thus, the putative superiority of WC as compared to BMI in documenting the presence of a clinically important degree of excess adiposity may be less important than the difficulty in both the widespread implementation of standardized methods to quantify WC and the agreement on what absolute values define an individual as being abdominally obese.

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