Body mass index and waist circumference both contribute to differences in insulin-mediated glucose disposal in nondiabetic adults

Helke MF Farin, Fahim Abbasi, and Gerald M Reaven

ABSTRACT

Background: Overweight and obese individuals are more likely to be insulin resistant and at increased risk of adverse clinical outcomes. Questions remain as to whether waist circumference (WC) or body mass index (BMI) most effectively identifies insulin-resistant individuals.

Objective: This study quantified insulin-mediated glucose uptake (IMGU) in 330 apparently healthy volunteers and compared the relation between this value and measurements of WC and BMI.

Design: IMGU was quantified via determination of the steady-state plasma glucose (SSPG) concentration during the insulin-suppression test. Differences in SSPG concentrations due to variations in WC within a given BMI category, as well as those due to differences in BMI within a given WC classification, were then compared.

Results: BMI and WC correlated with each other ($r = 0.78, P < 0.001$) and equally with SSPG concentrations ($r = 0.58$ and $0.57$, respectively; $P < 0.001$). When stratified by BMI, abdominally obese subjects within the overweight BMI category had higher SSPG concentrations than did those with a normal WC ($P < 0.05$). When classified by WC, subjects in the overweight BMI category had greater SSPG concentrations than did subjects in the normal BMI category within the normal WC category ($P < 0.01$), as did subjects in the obese BMI category in comparison with subjects in the overweight BMI category within the obese WC category ($P < 0.01$).

Conclusions: The more overweight or obese a person, the greater the degree of insulin resistance; differences in adiposity accounted for approximately one-third of the variation in IMGU, irrespective of the index used. Furthermore, there was no difference in the relation between the degree of insulin resistance and either index of adiposity.

KEY WORDS Obesity indexes, insulin resistance, abdominal obesity, overall obesity, body mass index, waist circumference

INTRODUCTION

The prevalence of obesity is rapidly increasing and is projected to soon become the leading cause of death in the United States (1). Although the link between obesity and cardiovascular disease (CVD) is already well recognized (2, 3), it has been further highlighted by the inclusion of abdominal obesity as one of the criteria selected by the Adult Treatment Panel III to diagnose the metabolic syndrome (4). The decision to use waist circumference (WC) for this purpose stems from the notion that it is the best predictor of obesity-related adverse clinical outcomes. There is certainly support for this belief (5–10), but evidence also shows that body mass index (BMI) may be as effective as WC in the prediction of diseases such as CVD, type 2 diabetes, and hypertension (11–16). Furthermore, measurements made in $\approx 15,000$ participants in the National Health and Nutrition Examination Survey (NHANES) showed that the correlation coefficient between BMI and WC was $>0.9$, irrespective of the age, sex, and ethnicity of the groups evaluated (17). Despite this very close relation between BMI and WC, there is evidence that, when stratified by BMI, those subjects with the highest WC values are at greatest risk to develop a series of negative outcomes (10, 18, 19). Although these data are often cited to support the superiority of WC over BMI in identifying insulin-resistant individuals at increased risk of CVD, type 2 diabetes, and hypertension, we are unaware of studies in which individuals were stratified on the basis of WC to see what effect differences in BMI might present. The current study has addressed this possibility by comparing the effect on insulin sensitivity of differences in BMI within a given classification of WC with that of variations in WC within a defined BMI category.

SUBJECTS AND METHODS

The study population consisted of 330 individuals ($n = 191$ women and 139 men) who had responded to print advertisements describing our studies on the role of insulin resistance in human disease. The Stanford Human Subjects Committee deemed all study procedures ethical and approved the study protocol. All subjects gave informed consent. Participants were apparently healthy, had normal results from physical examinations and liver and kidney function tests, had normal medical histories, were nondiabetic (fasting plasma glucose concentration $<126$ mg/dL as defined by the American Diabetes Association criteria; 20),...
and had normal blood counts. Studies were performed at the General Clinical Research Center of the Stanford University Medical Center.

Height and weight were measured while the subjects were wearing light clothing and no shoes, and BMI was calculated as weight (in kg)/height squared (in m). WC (cm) was quantified by placing a measuring tape around the waist at the upper point of the iliac crest and determined during minimal inspiration (21). Individuals were considered to be of normal weight, overweight, or obese on the basis of a BMI of <25, 25 to <30, or ≥30, respectively (22). Participants were deemed abdominally obese if their WC was >88 cm for women and >102 cm for men (4).

Insulin-mediated glucose uptake (IMGU) was quantified by using a modified version of the insulin-suppression test as described and validated by our research group (23–25). After the subjects fasted overnight, an intravenous catheter was placed in each arm of the subjects—one for the simultaneous 3-h infusion of octreotide (0.27 μg · m⁻² · min⁻¹), insulin (32 mU · m⁻² · min⁻¹), and glucose (267 mg · m⁻² · min⁻¹) and the other for the collection of blood samples every 10 min during the 150–180-min time period to measure plasma glucose and insulin concentrations. The values of the specimens obtained during these last 30 min were then averaged to determine steady-state plasma glucose (SSPG) and insulin (SSPI) concentrations. Because the glucose infusion rate per body surface area is identical in all subjects, and it has been shown (23–25) that under these conditions the SSPI concentrations do not differ from person to person, the resultant SSPG concentration provides a direct measure of the ability of insulin to mediate the disposal of a given glucose load, ie, the higher the SSPG, the more insulin resistant the individual.

### Statistical analysis

Statistical analyses were performed by using SYSTAT version 7.0 and SPSS 12.0 for WINDOWS student version (SPSS Inc, Chicago, IL). Results are expressed as means ± SEMs. Pearson’s correlation coefficients were calculated between BMI and WC, SSPG and BMI, and SSPG and WC. These correlations were examined with a z test for the significance of the difference between 2 correlations. Means were compared by using Student’s t test and one-way analysis of variance followed by a post hoc pairwise comparison where appropriate. Multiple linear regression analyses were performed to evaluate the relative contributions of BMI and WC in the prediction of SSPG. Statistical significance was set at a P value <0.05.

### RESULTS

The study population had a mean (±SEM) age of 50 ± 1 y and was primarily white (74%); Asians, Hispanics, and African Americans accounted for 15%, 8%, and 3% of the population, respectively. The mean (±SEM) SSPG concentration of 147 ± 4 mg/dL (range: 45–333 mg/dL) was comparable with the mean value (151 mg/dL) previously reported in a study of 490 healthy volunteers (26). The mean (±SEM) BMI was 28.5 ± 4.7 (range: 18.5–46.6), with approximately one-third of the population in each BMI category, and WC measurements defined an estimated one-half of the participants as being abdominally obese.

The relation between the 2 indexes of adiposity in the 330 volunteers in this study is shown in Figure 1. It is apparent from these data that measurements of BMI and WC were significantly correlated with each other within a given individual (r = 0.78, P < 0.001).

The relation between the 2 indexes of obesity and the SSPG concentrations are illustrated in Figure 2. It is clear from these data that there was no difference in the magnitude of the correlation coefficient between BMI and SSPG (r = 0.58, P < 0.001) compared with that between WC and SSPG (r = 0.57, P < 0.001). Furthermore, the best-fit lines describing the relation between the specific adiposity measures and the SSPG concentrations were also not significantly different (P = 0.90). To discern any interaction between BMI and WC in their relation to the SSPG concentration, multiple linear regression analysis was performed, with an interaction term—defined as the cross product of BMI and WC—introduced into the model. The results...
indicate that there was a significant interaction ($\beta = 0.99$, $P = 0.03$) between BMI and WC in their relation to the SSPG concentration. The high degree of multicolinearity among the independent variables (BMI, WC, and the BMI-WC cross product) prevented us from drawing any additional conclusions from these analyses.

The effect of differences in WC classification on SSPG concentrations when participants are subdivided on the basis of BMI category (upper panel) and the effect of differences in BMI category on SSPG concentrations when subjects are stratified on the basis of WC category (lower panel) are shown in Figure 3. The data in Figure 3 show that 96% (81/84) of the subjects with a normal BMI also had a normal WC, and that 93% (114/123) of those within the obese BMI category were abdominally obese. Thus, a valid comparison of the effect of differences in WC on IMGU within a given BMI range was limited to those with a BMI between 25 and 29.9. The results showed that the abdominally obese subjects had significantly higher ($P < 0.05$) SSPG concentrations than did those with a normal WC (147 ± 9 compared with 123 ± 7 mg/dL).

The effect of differences in BMI category on the SSPG concentrations of subjects divided into the 2 WC groups is shown in Figure 3. Similar to the pattern of findings in Figure 3, only 6% (9/151) of those in the normal WC group were obese on the basis of BMI criteria, and only 3 of the 179 persons (2%) classified as abdominally obese had a normal BMI. Consequently, within the normal WC group, we could only compare the SSPG concentrations of subjects who were either normal or overweight on the basis of BMI criteria. Likewise, in the abdominally obese group, the comparison was limited to those who were classified as overweight or obese on the basis of BMI. The results in Figure 3 indicate that, irrespective of WC classification, the greater the BMI, the higher the SSPG concentration. Thus, in those with a normal WC, the mean SSPG concentration of overweight subjects (123 ± 7 mg/dL) was significantly greater ($P < 0.01$) than that of normal-weight (94 ± 5 mg/dL) subjects. The magnitude of the effect on IMGU due to differences in BMI was even greater in abdominally obese participants; SSPG concentrations were significantly higher ($P < 0.01$) in those with a BMI indicating obesity (197 ± 7 mg/dL) than in those with a BMI indicating overweight (147 ± 9 mg/dL).

**DISCUSSION**

Two facets of our results need to be discussed to put into perspective the relevance of the current findings to the relation between obesity and insulin action. At the simplest level, the results of this study again show that the more overweight or obese
an apparently healthy individual is, the more likely they are to be insulin resistant. At the same time, it is clear from Figure 2 that, irrespective of the index of adiposity used, either estimate can only account for approximately one-third of the variation in insulin action in the 330 individuals that we studied—a finding consistent with the results of earlier studies (27, 28). The level of physical activity is another lifestyle variable that adversely affects insulin action (29, 30), and when the levels of both physical fitness and adiposity were evaluated in a biracial population, each variable accounted for ≈25% of the variability in insulin action (29). On the basis of evidence that variations in the degree of insulin resistance indicate both familial clustering and powerful ethnic differences (31–33), it is likely that the remaining 50% of the variability in insulin action is related to genetic factors; however, no major genetic link has been recognized. Thus, although it is clinically useful to know which index of adiposity can help recognize individuals at increased risk of insulin resistance, it is important to realize that it is only one of the factors that modulate insulin action.

A more complicated, and certainly more contentious issue, is whether BMI or WC is the best predictor of insulin resistance, and the results presented in Figures 2 and 3 suggest that their performance in this context is not different. For example, if we first focus on BMI categories, 96% of participants with a normal BMI also had a normal WC, and 93% of individuals within the obese BMI category were abdominally obese. Turning now to the WC classifications, only 6% of those in the normal WC group were obese by BMI criteria, and an even smaller proportion (2%) of those classified as abdominally obese, had a normal BMI. Thus, the most simplistic analysis indicates that it is exceedingly unlikely for a normal weight person by BMI criteria to be abdominally obese by WC classification, and that it is just as unlikely for an individual who is obese by BMI criteria to have a normal WC. Similarly, it is highly unlikely for an individual with a normal WC to have an obese BMI, or for an abdominally obese person by WC criteria to have a normal BMI.

The 2 indexes of adiposity also behave comparably when it comes to their ability to identify differences in insulin action. The categorization of participants on the basis of BMI (Figure 3) resulted in essentially equal numbers of subjects in the overweight group with either normal or abnormal WC values. Comparison of SSPG concentrations indicated that the values were 16% higher ($P < 0.05$) in the abdominally obese subset. These findings are consistent with previously published results from studies (10, 18, 19) that used several variables related to insulin resistance and showed the independent adverse effects of abdominal obesity within a given BMI category. For reasons unclear to us, these studies have not reversed the analysis and evaluated the effect of differences in BMI within a given WC classification. When we analyzed the data in this manner (Figure 3), the effect on SSPG concentrations of differences in BMI within the 2 WC classifications was highly statistically significant. Thus, the data in Figure 3 and 3B indicate that these 2 alternative ways of evaluating the effect of adiposity on insulin action provide information that is not different, and it is not clear from these measurements how it can be concluded that one index is more clinically useful than the other. The fact that the current results do not provide evidence of a clear-cut advantage for either index of obesity to predict insulin resistance is consistent with results of previous studies (11–16), which showed that BMI and WC provide comparable information regarding the presence of many adverse consequences related to insulin resistance.

Although the results of our study question the putative superiority of abdominal obesity in the identification of insulin-resistant individuals, it should be emphasized that approximately three-quarters of the participants in our study were white, and our results may not apply to other ethnicities. On the other hand, this may be less of an issue in light of the evidence from the NHANES database, which shows that the correlation coefficient between BMI and WC was $>0.9$, regardless of the age, sex, and ethnicity of the groups evaluated (17).

Finally, it is necessary to emphasize that measurements of WC do not distinguish between visceral fat and subcutaneous fat, and our conclusion that WC, an estimate of abdominal obesity, is no more closely linked to insulin action than is BMI, an estimate of overall obesity, does not necessarily speak to the notion of the crucial role of visceral fat in modulating insulin action. Indeed, there are ≥2 studies in which fat distribution has been quantified by imaging techniques, which indicates that the magnitude of the relation between insulin action and visceral fat is much greater than that with subcutaneous fat (34, 35). In contrast, on the basis of his review of the available literature, Garg (36) concluded that available data “do not indicate that variation in [intraperitoneal] or visceral fat has any unique effect on insulin sensitivity.” He further states that the data “support a role for excess sc [subcutaneous] truncal fat in causing insulin resistance in non-diabetic subjects as well as in patients with T2DM [type 2 diabetes mellitus]”. Notwithstanding the importance of this issue, it is not directly related to the goals of our study, and lack of a definitive answer to the relative roles played by different fat depots in modulation of insulin action does not detract from our conclusion that both BMI and WC are related to a specific measure of insulin action and, seemingly, to a comparable degree. Perhaps the findings most relevant to this issue are those of Janssen et al (37), who quantified fat distribution by magnetic resonance imaging in 341 subjects. On the basis of their results, they concluded that, “BMI and WC independently contribute to the prediction of total, non-abdominal, abdominal, subcutaneous, and visceral fat.” They also indicated that, “our findings provide further support for the notion that BMI and WC combined better predict metabolic risk than does either variable alone.”

In conclusion, the goal of this study was to compare the relations between measurements of BMI or WC and IMGU. The results indicate that there was no difference in insulin action irrespective of the adiposity index used and that the maximal yield of information comes from measurements of both. On the other hand, at a clinical level, it could be argued that measurement of either one alone will serve its purpose—helping health care providers to identify those individuals whose degree of obesity puts them at increased risk of insulin resistance.

HMFF, FA, and GMR were responsible for the study design, data collection and analysis, and writing of the manuscript.

REFERENCES


