Sagittal Abdominal Diameter Is a Strong Anthropometric Marker of Insulin Resistance and Hyperproinsulinemia in Obese Men

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OBJECTIVE — It is clinically important to find noninvasive markers of insulin resistance and hyperproinsulinemia because they both predict cardiovascular and diabetes risk. Sagittal abdominal diameter (SAD) or "supine abdominal height" is a simple anthropometric measure previously shown to predict mortality in men, but its association with insulin resistance and hyperproinsulinemia is unknown.

RESEARCH DESIGN AND METHODS — In a common high-risk group of 59 moderately obese men (aged 35–65 years, BMI 32.6 ± 2.3 kg/m^2), we determined anthropometry (SAD, BMI, waist girth, and waist-to-hip ratio [WHR]); insulin sensitivity (euglycemic-hyperinsulinemic clamp); and plasma concentrations of intact proinsulin, specific insulin, C-peptide, glucose, and serum IGF binding protein-1 (IGFBP-1). To compare SAD with other anthropometric measures, univariate and multiple regression analyses were used to determine correlations between anthropometric and metabolic variables.

RESULTS — SAD showed stronger correlations to all measured metabolic variables, including insulin sensitivity, than BMI, waist girth, and WHR. SAD explained the largest degree of variation in insulin sensitivity ($R^2 = 0.38$, $P < 0.0001$) compared with other anthropometric measures. In multiple regression analyses, including all anthropometric measures, SAD was the only independent anthropometric predictor of insulin resistance ($P < 0.001$) and hyperproinsulinemia ($P < 0.001$).

CONCLUSIONS — In obese men, SAD seems to be a better correlate of insulin resistance and hyperproinsulinemia (i.e., cardiovascular risk) than other anthropometric measures. In overweight and obese individuals, SAD could represent a simple, cheap, and noninvasive tool that could identify the most insulin resistant in both the clinic and clinical trials evaluating insulin sensitizers. These results need confirmation in larger studies that also include women and lean subjects.

Diabetes Care **27:2041–2046, 2004**

More than half of adult Americans are overweight or obese (1). Many, but far from all of those subjects, will suffer from obesity-related diseases. Insulin resistance may be the key factor in obesity that contributes to increased health risk, as the more insulin resistant an individual, the more likely they are to develop diabetes and cardiovascular disease (2–4). Therefore, identification of insulin resistance also is important in moderately obese subjects.

Recently, elevated intact proinsulin, reflecting both insulin resistance and β-cell dysfunction (5), has emerged as an independent predictor of type 2 diabetes (5–7) and cardiovascular mortality (8,9). However, a simple clinical surrogate marker for hyperproinsulinemia is still to be found.

McLaughlin and Reaven (10) recently highlighted the need for a useful tool to identify insulin resistance, as direct measures of insulin resistance are unfeasible for clinical use. While fasting insulin has shown to be a useful estimate of insulin resistance, it is invasive and the lack of standardized assays limits its use (11). Alternatively, triglycerides (>1.47 mmol/l) could function as a good marker (11).

Anthropometric measures have served as noninvasive markers because obesity, particularly abdominal obesity (12), is closely associated with insulin resistance. However, studies using direct methods revealed that only ~25–50% of all obese nondiabetic and normotensive subjects are clinically significantly insulin resistant (11,13) and that waist girth or waist-to-hip ratio (WHR) was not better than BMI in identifying insulin resistance (13). More recently, "abdominal height" or sagittal abdominal diameter (SAD) has shown to be strongly associated with glucose intolerance (14), cardiovascular risk (14–18), and mortality (19,20) (SAD was divided by thigh girth in the study by Kahn et al. [19]) independently of other anthropometric measures. SAD is also an excellent estimate of visceral fat (21–23), implying that SAD might be a particularly good marker of insulin resistance (12,24). Despite these compelling data, the role of SAD has been overlooked, whereas waist girth has received more attention (14,25,26). Given that insulin resistance is a major health culprit (4), there are sur-

Table 1—*Baseline characteristics*

	Mean ± SD (range)
Age (years)	53 ± 8.2 (35–65)
SAD (cm)	28.5 ± 2.05 (25.5–34.3)
BMI (kg/m^2)	30.6 ± 2.30 (27.7–39)
Waist girth (cm)	113.9 ± 7.70 (100–139)
WHR	1.01 ± 0.04 (0.95–1.12)
Triglycerides	2.04 ± 1.2 (1.7–8.3)
HDL cholesterol	0.98 ± 0.2 (0.7–1.4)
M (mg $\cdot$ kg^{-1} $\cdot$ min^{-1})*	4.07 ± 1.56 (1.06–7.0)
Proinsulin (pmol/l)	16.2 ± 10.6 (3.9–47)
Insulin (pmol/l)	11.4 ± 4.3 (5.7–21.9)
Glucose (mmol/l)	5.7 ± 0.64 (4.8–7.0)
C-peptide (pmol/l)	879.1 ± 306.3 (402–1832)
IGFBP-1 (μg/l)	14.3 ± 7.40 (4–34)

*Data from the euglycemic clamp (i.e., insulin sensitivity) were available in 59 men, whereas all other variables were available in 60 men.

prisingly little data comparing different anthropometric measures as correlates to insulin resistance determined by gold standard techniques.

Hence, the aim of this study was to identify the best noninvasive marker of insulin resistance that would be suitable for both clinical and research use. In a common high-risk group of obese men, we compared anthropometric measures (BMI, waist girth, WHR, and SAD) in relation to insulin sensitivity, as determined directly using a euglycemic clamp. We also measured the related, clinically relevant variables, including proinsulin, insulin, C-peptide and glucose concentrations, and serum insulin and IGF binding protein-1 (IGFBP-1), that also reflect cardiovascular risk (27,28).

RESEARCH DESIGN AND METHODS — A total of 60 adult Caucasian moderately obese men (Table 1) were recruited in Uppsala, Sweden, through local advertisements to initially take part in an intervention study (29). The inclusion criteria were waist girth >102 cm, WHR >0.94, BMI 27–39 kg/m^2, triglycerides >1.7 mmol/l, and/or HDL cholesterol <0.9 mmol/l. In addition, all men had an SAD >25 cm, a cutoff point corresponding to a waist girth >100 cm (14). No one had heart, liver, or renal disease or diabetes.

Anthropometry
All anthropometric measurements were performed by one investigator. Body weight was measured using an electronic scale to the nearest 0.1 kg, with the subjects wearing light clothing and no shoes. Height was measured to the nearest 0.5 cm without shoes, and BMI was calculated as weight (in kilograms) divided by the square of height (in meters). SAD (anteroposterior) or "abdominal height" was measured to the nearest 0.1 cm after a normal expiration while in the supine position with bent knees on a firm examination table and without clothes in the measurement area (Fig. 1). At the level of iliac crest (L$_{4–5}$), SAD was measured (using a sliding-beam caliper) as the distance between the examination table up to the horizontal level, allowing the caliper arm to touch the abdomen slightly but without compression. Waist girth was measured in underwear with a stretchless tape in standing position after normal expiration, midway between the caudal part of the lateral costal arch and the iliac crest (World Health Organization standard),

and hip girth was measured at the symphysis trochanter level.

Euglycemic-hyperinsulinemic clamp
A 2-h euglycemic-hyperinsulinemic clamp was performed to determine whole-body insulin sensitivity as previously described (29). Insulin (Actrapid Human; Novo Nordisk, Copenhagen, Denmark) was infused (336 pmol/l $\cdot$ m^{-2} $\cdot$ min^{-1}), resulting in a mean steady state with insulin levels of 624 pmol/l. The target plasma glucose level was 5.1 mmol/l, which was maintained by determining glucose levels every 5 min. During the last hour of the clamp, the range of the glucose levels was between 4.8 and 5.2 mmol/l. Insulin sensitivity (M) was calculated as the glucose infusion rate adjusted for body weight during the last hour of the clamp (mg $\cdot$ kg body wt^{-1} $\cdot$ min^{-1}). Plasma glucose levels were assayed in a Beckman Glucose Analyzer II (Beckman Instruments, Fullerton, CA), using an enzymatic method.

Biochemical analyses
Venous blood was drawn into vacuum tubes, coagulated, and centrifuged at room temperature. All plasma and serum samples used for analyses were stored at −70°C (storage time <2 years).

Insulin peptides, including proinsulin, have been shown to be stable at −70°C for 27 years (8). Specific plasma insulin (intra-assay and interassay coefficient of variation [CV] 2.8%), was measured by using an enzyme-linked immunosorbent assay (ELISA) kit (Mercodia, Uppsala, Sweden). Plasma intact proinsulin (intra-assay CV 3.2% and interassay CV 5.2%) was measured by an ELISA kit (Mercodia). Cross-reactivity with insulin and C-peptide was <0.03
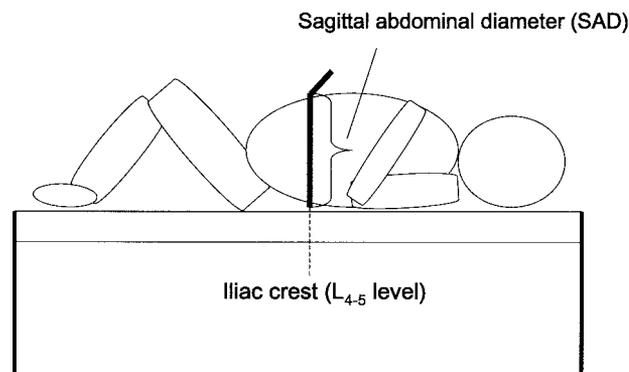

Figure 1—*Measurement of the SAD in a supine subject.*

Table 2—*Correlation coefficients between anthropometric and metabolic variables*

	SAD	BMI	Waist	WHR
SAD (cm)	—	0.81†	0.84†	0.38‡
M (mg $\cdot$ kg^{-1} $\cdot$ min^{-1})*	−0.61†	−0.48§	−0.43§	−0.40‖
Proinsulin (pmol/l)	0.47†	0.28‖	0.25	0.19
Insulin (pmol/l)	0.41‡	0.29‖	0.28‖	0.24‖
Glucose (mmol/l)	0.32‡	0.09	0.10	0.06
C-peptide (pmol/l)	0.44§	0.30‖	0.27‖	0.35‡
IGFBP-1 (μg/l)	−0.32‖	−0.19	−0.22	−0.09

*Data from the euglycemic clamp (i.e., insulin sensitivity) were available in 59 men, whereas all other variables were available in 60 men. †$P < 0.0001$; ‡$P < 0.01$; §$P < 0.001$; ‖$P < 0.05$.

and 0.006%, respectively. Plasma C-peptide (intra-assay CV 3.1% and interassay CV 4.4%) was measured using a specific ELISA kit (Mercodia). All insulin-like peptides were measured in a Bio-Rad Coda automated EIA analyzer (Bio-Rad Laboratories, Hercules, CA). Serum samples were acid-ethanol extracted to partially separate IGFBP-1 from IGF-1. IGFBP-1 was determined by radioimmunoassay as previously described (intra-assay CV 3% and interassay CV 10%) (30).

Statistics

All anthropometric measures were skewed (Shapiro-Wilk W test) and logarithmically transformed before a statistical analysis was performed, but all metabolic and anthropometric variables were normally distributed after transformation. Pearson's correlation coefficients were used to investigate the associations between anthropometric and metabolic variables. To evaluate possible independent relationships between anthropometric and metabolic variables, multiple linear regression analyses were used, with the four anthropometric measures and age as independent variables and insulin sensitivity as a dependent variable. R^2 was determined for each anthropometric variable to evaluate the proportion of the variability that can be explained by its univariate relationship to each metabolic variable. Differences between the anthropometric correlations to insulin sensitivity were tested for statistical significance using the method described by Morrison (31). $P < 0.05$ was regarded as significant. A JMP software package was used for statistics (SAS Institute, Cary, NC).

RESULTS — A total of 60 men were included in the analysis with complete data for all variables except for insulin sensitivity data (clamp), which was determined in 59 subjects (Table 1).

All anthropometric measures were significantly inversely correlated to insulin sensitivity (Table 2). SAD was more strongly correlated to insulin sensitivity (M) and to all other metabolic variables than to other anthropometric measures (Table 2). The correlation between insulin sensitivity and SAD was significantly stronger than to waist girth and BMI ($P < 0.01$) but not WHR. The correlations between SAD and insulin sensitivity also remained significant when analyzing subjects with BMI <30 kg/m^2 ($r = -0.54$, $n = 26$) and BMI >30 kg/m^2 ($r = -0.59$, $n = 34$) separately (both P values <0.01). Dividing SAD or waist girth for height did not improve the associations with insulin sensitivity or other metabolic variables (data not shown). For proinsulin, SAD and BMI were the only significant anthropometric predictors, but SAD was a much stronger correlate than BMI. Furthermore, SAD was the only significant predictor of fasting glucose and IGFBP-1 concentrations. In multiple analyses (including SAD, BMI, waist girth, and WHR), SAD remained the sole significant predictor of insulin sensitivity, proinsulin, and all other metabolic variables (all P values <0.01). Adjusting for age did not alter these associations. Using the regression line (slope), it was predicted that for every 1-cm increase in SAD, there is a decrease in the M value by 0.75 mg $\cdot$ kg^{-1} $\cdot$ min^{-1} (SE 0.14, $P < 0.001$). This decrease in insulin sensitivity corresponded to a mean decrease in insulin action by 18%. SAD consistently explained a greater proportion of the variation in all metabolic variables than did other anthropometric measures, and for fasting glucose and IGFBP-1, only SAD showed a significant R^2 (Fig. 2).

CONCLUSIONS — As insulin resistance predicts type 2 diabetes (2) and cardiovascular disease (3,4), we sought to
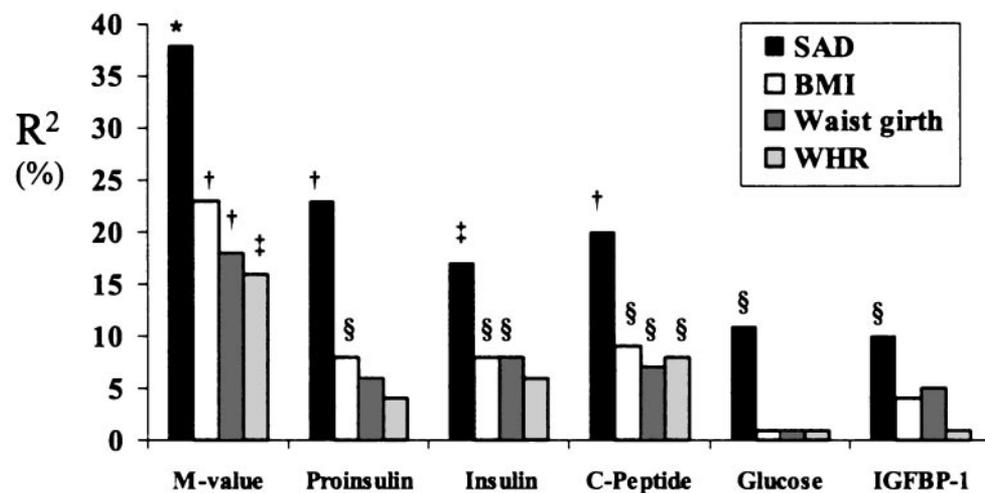

Figure 2—*Bars are* R^2 *coefficients (%) for different anthropometric measures with regard to metabolic variables.* *P < 0.0001; †P < 0.001; ‡P < 0.01; §P < 0.05.

identify the best anthropometric predictor of insulin resistance in obese men.

SAD was surprisingly strong in predicting insulin resistance and hyperproinsulinemia compared with other classic anthropometric measures. In fact, SAD exhibited the highest degree of association with all the signs of disturbed glucose metabolism, including increased concentrations of proinsulin, glucose, insulin, C-peptide, and lower levels of IGFBP-1.

The close correlation between SAD and hyperproinsulinemia is also novel and of clinical importance, as elevated proinsulin concentrations independently predict cardiovascular mortality (8,9) and type 2 diabetes (5–7). The correlations between SAD and proinsulin and C-peptide concentrations may also indicate that SAD is a good marker of elevated insulin secretion in nondiabetic obese men.

In line with our results, previous data on men and women have shown that SAD is more closely related to hyperlipidemia (16) and cardiovascular risk (16–18,32), including the Framingham risk index (33), than BMI, waist girth, and WHR. Recent results also showed that SAD was the best correlate to hypertension (16,32) and plasminogen activating inhibitor-1 (16). Furthermore, in the large Swedish Obese Subjects (SOS) study, the change in SAD was most closely related to change in the metabolic syndrome (34). However, in a Chinese population in whom insulin sensitivity was measured indirectly using the homeostasis model assessment index, SAD was a better marker than WHR but comparable to waist girth and BMI (35). Also, in a study of nonobese subjects, SAD and waist girth showed the same correlation coefficient (-0.57) in men, but not in women, and both were the best markers of insulin resistance (minimal model) in men (36). These latter inconsistencies might be due to ethnicity, sex, phenotype, or methodological differences. Notably, in this and a previous larger study, we measured SAD with the legs bent. This procedure improves reliability compared with the measurement of SAD with straight legs (37). This slightly altered technique may contribute to the strong correlations between SAD and the metabolic variables found in both these studies.

For all metabolic variables, SAD showed an R^2 value that was about twofold higher than BMI, waist girth, and WHR. In addition, SAD was the sole anthropometric variable that explained the variations in fasting glucose and IGFBP-1 concentrations. The latter accords well with our results, as low IGFBP-1 reflects peripheral insulin resistance (38) and perhaps also hepatic insulin resistance (39). However, of more clinical relevance, low IGFBP-1 is a risk marker of cardiovascular disease (27,28).

Interestingly, SAD was the only anthropometric measure that remained a significant marker of insulin resistance in multiple analyses. The fact that SAD was associated with all metabolic disorders, even independently of age, BMI, waist girth, and WHR, indicates that SAD carries unique information beyond that given by other anthropometric measures. Similar to our results, in a large clamp study, waist girth or WHR did not add any information on insulin sensitivity beyond BMI (13). Unfortunately, SAD was not measured in that study.

The most likely explanation for the high predictive capacity of SAD is the higher measurement reliability of SAD compared with other anthropometric measures (37,40). SAD may also be the only measure with high reliability in both lean and obese subjects (37). In our study, SAD significantly predicted insulin resistance when analyzing overweight and obese men separately. Previous data in normal-weight Caucasian men indicated that SAD was the best anthropometric predictor of an adverse metabolic risk profile independent of BMI (15). In that study, SAD/height was a slightly better predictor than SAD alone, but adjusting SAD or waist girth for height did not improve the correlations in our study. However, it remains to be determined whether the current results can be confirmed in lean subjects, women, and other ethnic populations. Another limitation of this study could be the limited sample size.

These results were not only explained by a lower measurement error of SAD, but the strong relationship with insulin resistance may also be partly explained by SAD closely reflecting visceral adiposity (21–23,41). A detrimental effect of visceral fat on insulin sensitivity has been suggested. In obese boys, visceral adipose tissue area and SAD were the best diagnostic criteria of metabolic abnormalities, and SAD was the best anthropometric estimate of visceral adipose tissue area (42). However, as both visceral and subcutaneous fat are linked to insulin resistance (43–45), it is relevant that SAD is also a valid measure of total abdominal fat (23). Because abdominal obesity seems to be an early sign of insulin resistance (46) that is more genetically determined than generalized obesity (47), high SAD values might, to a larger extent than increments in other measures, reflect such a genetic component (48) as well as reflect a sedentary lifestyle (48).

Despite the rather homogenous group with central obesity, the current associations between SAD and metabolic disorders were quite strong. Interestingly, even among men classified as abdominally obese (waist girth >102 cm), insulin sensitivity varied sixfold in this study. A large waist girth is a useful tool to detect metabolic disorders (14,25,26), including insulin resistance (49). In one study, SAD and waist girth were equally good markers of various metabolic disorders (14). However, no previous studies have compared waist girth with SAD with respect to hyperproinsulinemia or insulin resistance determined directly.

Because 47 million people in the U.S. are obese and over one-third of the adult population is abdominally obese (50), our results are motivational for the use of SAD as a single, easy (takes ~20 s to measure), and cheap marker to identify the most insulin-resistant overweight subjects who would especially benefit from intensive lifestyle therapy (51). SAD may also be a useful screening tool in clinical trials evaluating insulin sensitizers (i.e., thiazolidinediones). Thus, a subject with a large SAD may prove to be an optimal target for intervention. An SAD >25 cm is most likely associated with metabolic disorders (14). Notably, in our study, all subjects had a relatively large SAD above that cutoff limit.

In summary, among the anthropometric measures studied, SAD was the best marker of insulin resistance and elevated proinsulin concentrations (i.e., cardiovascular risk) in overweight and obese men. If ongoing prospective studies will show that SAD predicts mortality, as already indicated in men (19,20), and our results can be confirmed in women, SAD might be worth including in future obesity guidelines.

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