Intra-Abdominal Fat Is a Major Determinant of the National Cholesterol Education Program Adult Treatment Panel III Criteria for the Metabolic Syndrome

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The underlying pathophysiology of the metabolic syndrome is the subject of debate, with both insulin resistance and obesity considered as important factors. We evaluated the differential effects of insulin resistance and central body fat distribution in determining the metabolic syndrome as defined by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III. In addition, we determined which NCEP criteria were associated with insulin resistance and central adiposity. The subjects, 218 healthy men (n = 89) and women (n = 129) with a broad range of age (26–75 years) and BMI (18.4–46.8 kg/m^2), underwent quantification of the insulin sensitivity index (S_i) and intra-abdominal fat (IAF) and subcutaneous fat (SCF) areas. The metabolic syndrome was present in 34 (15.6%) of subjects who had a lower S_i [median: 3.13 vs. 6.09 × 10^{-5} min^{-1}/(pmol/l)] and higher IAF (166.3 vs. 79.1 cm^2) and SCF (285.1 vs. 179.8 cm^2) areas compared with subjects without the syndrome (P < 0.001). Multivariate models including S_i, IAF, and SCF demonstrated that each parameter was associated with the syndrome. However, IAF was independently associated with all five of the metabolic syndrome criteria. In multivariable models containing the criteria as covariates, waist circumference and triglyceride levels were independently associated with S_i and IAF and SCF areas (P < 0.001). Although insulin resistance and central body fat are both associated with the metabolic syndrome, IAF is independently associated with all of the criteria, suggesting that it may have a pathophysiological role. Of the NCEP criteria, waist circumference and triglycerides may best identify insulin resistance and visceral adiposity in individuals with a fasting plasma glucose <6.4 mmol/l. *Diabetes* 53:2087–2094, 2004

In 2001, the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III [ATP III]) suggested a clinical definition for the metabolic syndrome that included blood pressure, waist circumference, HDL cholesterol, and triglyceride and fasting plasma glucose levels (1). According to Third National Health and Nutrition Examination Survey (NHANES III) data, the age-adjusted rate for the NCEP-defined metabolic syndrome in the U.S. population is 23.7% (2). The high prevalence of the metabolic syndrome has significant public health implications due to the twofold increased risk of prevalent coronary heart disease (3), three- to fourfold increased risk of mortality due to coronary heart disease (4), and a sixfold risk of developing type 2 diabetes (5).

The underlying pathophysiology of the metabolic syndrome is a subject of debate. Initial studies in this area suggest that insulin resistance has a primary role (6–9). However, more recent investigations show that visceral adiposity is a significant independent predictor of the insulin sensitivity (10–14), impaired glucose tolerance (15), elevated blood pressure (16–18), and dyslipidemia (12,19–25) seen in the metabolic syndrome. Furthermore, intra-abdominal fat (IAF) is metabolically active as a source of free fatty acids (26,27) and adipokines, such as adiponectin (28,29), tumor necrosis factor-α (TNF-α) (27,30,31), and plasminogen activator inhibitor type 1 (PAI-1) (32,33). Thus, a role of IAF in the metabolic syndrome is biologically plausible.

To evaluate the differential effects of insulin resistance and central body fat distribution on the metabolic syndrome, we examined the relation of insulin sensitivity and IAF and subcutaneous fat (SCF) areas with the criteria for the NCEP ATP III metabolic syndrome in a nondiabetic population. Our specific aims were to *1*) examine whether insulin sensitivity and abdominal fat distribution, alone or together, were associated with the individual NCEP ATP III criteria, the number of criteria, and the metabolic syndrome; *2*) evaluate the effect of sex and age on these relations; and *3*) determine which NCEP ATP III criteria

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ATP III, Adult Treatment Panel III; BP, blood pressure; FPG, fasting plasma glucose; GEE, generalized estimating equation; IAF, intra-abdominal fat; NCEP, National Cholesterol Education Program; NHANES III, Third National Health and Nutrition Examination Survey; PAI-1, plasminogen activator inhibitor type 1; SCF, subcutaneous fat; TG, triglyceride; TNF-α, tumor necrosis factor-α; WC, waist circumference.

were the best correlates of insulin resistance and central body fat distribution.

RESEARCH DESIGN AND METHODS

We recruited 232 healthy subjects by advertisement in the Seattle/King County, Washington, area between 1997 and 1998 to participate in a study evaluating the impact of body weight and insulin resistance on the lipoprotein response to egg consumption (34). Subjects were screened for study eligibility by physical examination, laboratory evaluation, and a review of their medical history. Subjects were excluded from participation for the following reasons: fasting plasma glucose (FPG) >6.3 mmol/l or a history of diabetes, renal or liver disease, uncontrolled thyroid disease or hypertension, coronary artery disease, anemia, LDL cholesterol >4.91 mmol/l, or triglycerides (TGs) >5.65 mmol/l.

Subjects underwent baseline measurements of blood pressure, anthropometrics and body fat distribution, fasting plasma glucose, lipid/lipoproteins, and a frequently sampled intravenous glucose tolerance test for the quantification of the insulin sensitivity index (S_i). Of the 232 subjects recruited for the egg consumption study, 218 had baseline data collected on all of the NCEP ATP III criteria and were therefore eligible for this analysis. The Human Subjects Review Committee at the University of Washington reviewed and approved the study protocol. All subjects gave written informed consent prior to participating in the study.

BMI (kg/m^2) was calculated from height and weight measurements. Waist circumference (WC) was measured at the smallest circumference of the waist, the "natural" waistline, using a modified protocol from the NHANES III Anthropometric Measurements videotape (National Center for Health Statistics). To further assess central body fat distribution, a single-slice computed tomography scan was performed at the level of the umbilicus for measurement of IAF and SCF areas, as previously described (35,36).

After a 12-h, overnight fast, a tolbutamide-modified frequently-sampled intravenous glucose tolerance test was performed to quantify insulin sensitivity as the S_i, using Bergman's minimal model of glucose kinetics (37,38).

All chemical analyses were performed on blood samples obtained after a 12-h overnight fast and stored at −70°C until assayed. Plasma glucose levels were determined in duplicate using a glucose oxidase method (Beckman, Palo Alto, CA). Plasma immunoreactive insulin levels were measured in duplicate using a modification of the double antibody radioimmunoassay technique of Morgan and Lazarow (40). Plasma TG levels were measured by enzymatic analytical chemistry. HDL cholesterol was precipitated using dextran sulfate and measured enzymatically.

Definitions. The metabolic syndrome was defined according to the NCEP ATP III as the presence of three or more of the following clinical criteria: blood pressure (BP) ≥130/85 mmHg, WC >102 cm in men and >88 cm in women, HDL cholesterol <1.036 mmol/l (40 mg/dl) in men and <1.295 mmol/l (50 mg/dl) in women, TG ≥1.695 mmol/l (150 mg/dl), and FPG ≥6.1 mmol/l (110 mg/dl) (1).

Statistical analyses. Statistical analyses were performed using STATA 7.0 for Windows (STATA, College Station, TX). Descriptive statistics were performed for the study population. Continuous variables are presented as means ± SE or medians with ranges, if not normally distributed. Categorical variables are presented as absolute numbers and percentages. Continuous variables were compared by independent samples t test or Wilcoxon's rank-sum test if the variables were not normally distributed.

The relation between continuous variables was visually examined using scatterplots. Linear regression analyses were used to assess the relation between independent variables and continuous dependent variables. Logarithmic or square-root transformation of the dependent variable was performed when necessary to satisfy the statistical assumptions of linear regression.

To evaluate the role of S_i and IAF and SCF areas in determining the number of NCEP ATP III criteria, multivariate models using generalized estimating equations (GEEs) were performed (41,42). The outcome was the prevalence of each criterion in each individual (five outcomes per individual). The logit of this outcome was modeled on S_i, IAF area, and SCF area, which were first considered separately and then combined. This analysis is equivalent to modeling the number of criteria for each person: the greater the number of metabolic syndrome criteria each individual has, the stronger the probability of prevalence of the metabolic syndrome for that individual. The GEE model allows for correlation of outcomes within an individual, as subjects with one criteria should be more likely to have another criteria (i.e., someone with low HDL cholesterol is more likely to have a high TG level).

Simple and multiple logistic regression analyses were used to determine the relation of S_i and SCF and IAF areas (independent continuous variables) with the metabolic syndrome (dichotomous dependent variable). Results from the logistic regression and GEE analyses are presented as odds ratios (ORs) with 95% CIs. All ORs are presented as the odds of the metabolic syndrome for a single SD increase in the independent variable.

All models were reanalyzed with sex and age (categorized as age quartiles) as adjustments. Interaction terms between age or sex and S_i, IAF area, or SCF area were included in multiple regression models of individual criteria to assess the impact of sex and age on these associations.

All statistical analyses were two-sided. Statistical significance was considered at $P < 0.05$.

TABLE 1
Characteristics of the study population

	Total	Male	Female
n	218	89	129
Age (years)	52.5 ± 0.7	52.8 ± 1.1	52.4 ± 0.9
BMI (kg/m^2)	26.2 ± 0.3	26.7 ± 0.4	25.9 ± 0.4
Systolic BP (mmHg)	117.4 ± 0.9	119.5 ± 1.2	116.0 ± 1.2
Diastolic BP (mmHg)	72.3 ± 0.6	74.2 ± 0.8	71.0 ± 0.*
Waist circumference (cm)	87.1 ± 1.0	94.7 ± 1.2	81.9 ± 1.1†
HDL (mmol/l)	1.34 ± 0.03	1.13 ± 0.03	1.48 ± 0.03†
TG (mmol/l)	1.38 ± 0.06	1.47 ± 0.11	1.32 ± 0.07
FPG (mmol/l)	5.4 ± 0.03	5.6 ± 0.05	5.3 ± 0.04†

Data are means ± SE. *$P < 0.01$ and †$P < 0.001$ for male vs. female subjects, determined by independent samples t or Wilcoxon's rank-sum test.

RESULTS

Demographic measures and prevalence of the metabolic syndrome. Subject characteristics are listed in Table 1. A broad range in age (26–75 years) and BMI (18.4–46.8 kg/m^2) was represented in the study population, with the average subject being middle-aged and overweight. Consistent with known sex differences, male subjects had higher diastolic BP, larger WC measurements, and decreased HDL cholesterol compared with female subjects.

The metabolic syndrome was present in 15.6% of the study population (Fig. 1); 42% of the population met none of the criteria for the syndrome. The prevalence of the metabolic syndrome and the number of criteria were not significantly different between male and female subjects (Fig. 1). Low HDL cholesterol was the most frequent of the criteria met, being present in 35% of subjects (Fig. 2). Syndrome criteria other than HDL cholesterol were present in ~21–24% of study subjects, with the exception

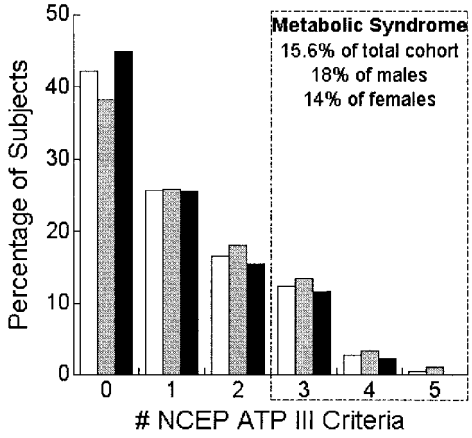

FIG. 1. The frequency of the number of NCEP ATP III metabolic syndrome criteria in the whole study population (n = 218; □), the male subjects (n = 89; ▨), and the female subjects (n = 129; ■)

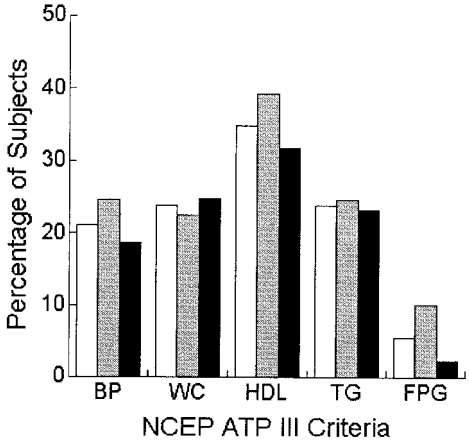

FIG. 2. Frequency of the individual NCEP ATP III criteria in the whole study population (n = 218; □), the male subjects (n = 89; ▨), and the female subjects (n = 129; ■)

of elevated FPG, which was present in only 5.5% of subjects and likely reflected the study exclusion criteria of an FPG >6.3 mmol/l. The frequency of the individual criteria was not significantly different between male and female subjects except for FPG, which was significantly more common in male subjects (P = 0.01) (Fig. 2).

Insulin sensitivity and relation to the metabolic syndrome. Insulin sensitivity was lower in subjects with the metabolic syndrome compared with subjects who did not have the syndrome [3.13 (0.65–10.45) vs. 6.1 (0.75–29.98) × 10^{-5} min^{-1}/(pmol/l); $P < 0.001$ min^{-1}/(pmol/l)]. The odds of the number of criteria increasing by one for each SD increase in S_i was 0.51 (CI 0.41–0.63; $P < 0.001$) (Fig. 3) in the GEE model. Furthermore, S_i was negatively associated with each of the criteria ($P < 0.001$) (Table 2) in simple regression models. Consistent with these findings, the odds of having the metabolic syndrome significantly decreased with each SD increase in S_i (OR 0.09 [CI 0.03–0.22]; $P < 0.001$). These associations remained significant after adjusting for sex and age.

Central body fat distribution and relation to the metabolic syndrome. The IAF area was higher in subjects with the metabolic syndrome compared with those without the syndrome (166.3 [43.6–363.9] vs. 79.1 [6.6–371.5] cm^2; $P < 0.001$), as was the median SCF area (285.1 [109.0–810.5] vs. 179.8 [4.2–489.3] cm^2; $P < 0.001$). As illustrated in Fig. 3, the odds of having an additional criterion increased with each SD increase in IAF (OR 2.1 [CI 1.75–2.53]; $P < 0.001$) and SCF areas (OR 1.97 [CI 1.66–2.34]; $P < 0.001$) in the GEE model. Furthermore, the IAF area was positively correlated with each of the criteria ($P < 0.001$) (Table 2) and was significantly associated with the metabolic syndrome (OR 3.83 [CI 2.4–6.11]; $P < 0.001$) in simple regression models. The SCF area was also positively correlated with each of the criteria ($P < 0.01$) (Table 2) in simple linear regression analyses and was significantly associated with the metabolic syndrome (OR 2.93 [CI 1.93–4.45]; $P < 0.001$). The association among the IAF area, SCF area, and individual criteria or metabolic syndrome remained significant after adjusting for sex and age.

Relation of insulin sensitivity, central body fat distribution, and criteria for the metabolic syndrome. In a GEE model of S_i and IAF and SCF areas on the prevalence of individual metabolic syndrome criteria, S_i (OR 0.73 [CI 0.58–0.91]), IAF area (OR 1.53 [CI 1.26–1.85]), and SCF area (OR 1.45 [CI 1.25–1.69]) were each independently associated with prevalence of metabolic syndrome criteria.

Multiple linear regression models including S_i and IAF and SCF areas as the independent variables were constructed for each of the metabolic syndrome criteria as dependent continuous variables (Table 3). IAF area was associated with all of the metabolic syndrome criteria independently of S_i and SCF area, whereas the SCF area

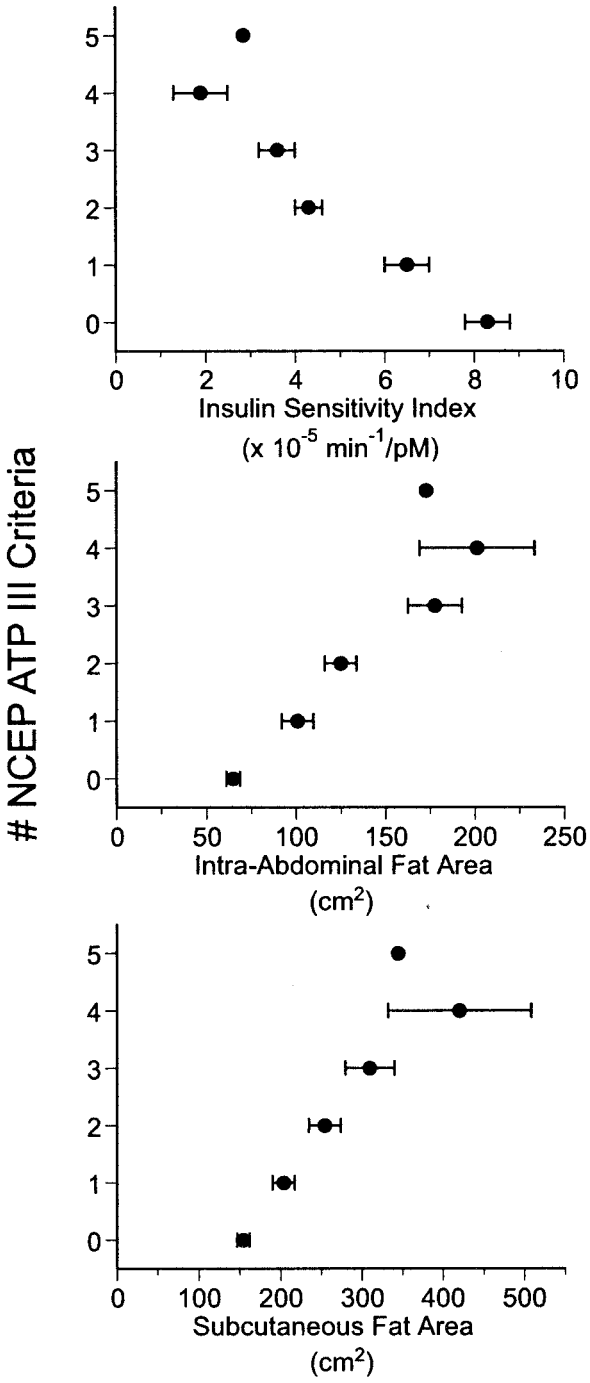

FIG. 3. S_i and IAF and SCF areas (mean ± SE) versus the number of NCEP ATP III criteria

TABLE 2
Simple linear regression analyses of the association of S_i, IAF area, or SCF area and the individual NCEP ATP III criteria as continuous dependent variables

	Systolic BP (mmHg)		Diastolic BP (mmHg)		Waist circumference (cm)		HDL (mmol/l)		log(TG [mmol/l])		FPG (mmol/l)	
	Slope	*P*	Slope	*P*	Slope	*P*	Slope	*P*	Slope	*P*	Slope	*P*
S_i [$\times 10^{-5}$ min^{-1}/(pmol/l)]	−1.0 ± 0.2	<0.001	−0.55 ± 0.13	<0.001	−1.6 ± 0.18	<0.001	0.028 ± 0.006	<0.001	−0.022 ± 0.004	<0.001	−0.04 ± 0.007	<0.001
IAF (cm^2)	0.08 ± 0.01	<0.001	0.045 ± 0.007	<0.001	0.15 ± 0.008	<0.001	−0.086 ± 0.013	<0.001	0.0014 ± 0.0002	<0.001	0.039 ± 0.008	<0.001
SCF (cm^2)	0.025 ± 0.007	0.001	0.018 ± 0.004	<0.001	0.064 ± 0.006	<0.001	−0.019 ± 0.008	0.01	0.0006 ± 0.0001	<0.001	0.015 ± 0.004	0.001

Data are means ± SE, unless otherwise noted.

TABLE 3
Multiple linear regression analyses of the association of S_i, IAF and SCF areas and the individual NCEP ATP III criteria as continuous dependent variables

	Systolic BP (mmHg)		Diastolic BP (mmHg)		Waist circumference (cm)		HDL (mmol/l)		log(TG [mmol/l])		FPG (mmol/l)	
	Slope	*P*	Slope	*P*	Slope	*P*	Slope	*P*	Slope	*P*	Slope	*P*
S_i [$\times 10^{-5}$ min^{-1}(pmol/l)]	−0.39 ± 0.23	0.1	−0.15 ± 0.15	0.3	−0.06 ± 0.15	0.7	0.54 ± 0.26	0.04	−0.011 ± 0.004	0.02	−0.47 ± 0.15	0.002
IAF (cm^2)	0.06 ± 0.01	<0.001	0.03 ± 0.009	<0.001	0.122 ± 0.009	<0.001	−0.07 ± 0.02	<0.001	0.0009 ± 0.0003	0.001	0.021 ± 0.009	0.02
SCF (cm^2)	0.002 ± 0.008	0.8	0.007 ± 0.005	0.2	0.032 ± 0.005	<0.001	0.009 ± 0.008	0.3	0.0003 ± 0.0001	0.07	0.002 ± 0.005	0.7

Data are means ± SE, unless otherwise noted.

TABLE 4
Multivariate logistic regression determining the independent predictors of the metabolic syndrome

Independent variables	OR (95% CI)	*P*
Model 1		
S_i [$\times 10^{-5}$ min^{-1}/(pmol/l)]	0.30 (0.09–0.96)	0.04
IAF (cm^2)	2.40 (1.41–4.10)	0.001
SCF (cm^2)	2.12 (1.30–3.46)	0.003
Model 2		
S_i [$\times 10^{-5}$ min^{-1}/(pmol/l)]	0.30 (0.09–0.96)	0.04
IAF (cm^2)	2.43 (1.33–4.47)	0.004
SCF (cm^2)	2.09 (1.18–3.70)	0.012
Age (years)	1.008 (0.96–1.06)	0.7
Sex	1.13 (0.34–3.69)	0.8

All ORs are presented as the odds of the metabolic syndrome for a 1 SD increase in the independent variable.

was independently correlated with WC, and S_i was independently correlated with HDL cholesterol, TG levels, and FPG.

Multiple logistic regression was performed with S_i and IAF and SCF areas as the covariates predicting the metabolic syndrome to determine which parameter had an independent association with the metabolic syndrome. S_i and IAF and SCF areas were each independently associated with developing the metabolic syndrome (Table 4). After adjusting for age and sex, S_i and IAF and SCF areas remained independently associated with the metabolic syndrome.

Impact of sex and age on the relation of insulin sensitivity, central body fat distribution, and the metabolic syndrome. The relation of S_i and IAF and SCF areas with the number of criteria and diagnosis of the metabolic syndrome was not affected by sex or age. However, age did impact the relation between S_i and diastolic BP (interaction term $P = 0.007$) and IAF area and diastolic BP (interaction term $P = 0.02$). Diastolic BP was higher in subjects with lower S_i ($P \leq 0.01$) except for in the oldest group, for whom there was not a significant relation between S_i and diastolic BP ($P = 0.7$). Similarly, the younger age groups had a significant positive association between IAF area and diastolic BP ($P < 0.01$), whereas the older individuals did not show a significant relation between IAF area and diastolic BP ($P = 0.06$). Age also impacted the relation between S_i and FPG (interaction term $P = 0.01$); FPG was higher in subjects with lower S_i ($P < 0.001$) except for in the youngest subjects, for whom there was not a significant relation between S_i and FPG ($P = 0.4$).

NCEP ATP III criteria as correlates of insulin resistance and central body fat distribution. In simple linear regression analyses, each of the criteria was significantly associated with S_i ($P < 0.001$), IAF area ($P < 0.001$), and SCF area ($P \leq 0.01$). Multiple linear regression models that included all of the criteria as continuous independent predictors of S_i or IAF or SCF area were performed. Only WC and TGs were independently associated with S_i and IAF and SCF areas (Table 5). Finally, by simple linear regression, WC was more strongly correlated with IAF area ($r = 0.799$) than with SCF area ($r = 0.595$). When considering the correlation of WC with the sum of IAF and SCF areas, the correlation was not different to that of IAF alone ($r = 0.753$).

DISCUSSION

In this study of a large number of apparently healthy men and women of varying age, we sought to evaluate the differential effects of insulin sensitivity and central body fat distribution on the features of the metabolic syndrome as defined by NCEP ATP III (1). We showed that both insulin resistance and central adiposity are significant correlates of the metabolic syndrome. IAF area was independently associated with all of the metabolic syndrome criteria, whereas insulin sensitivity was independently associated with the criteria for HDL cholesterol, TGs, and FPG. In contrast, SCF area was independently correlated with only WC after adjusting for IAF area and insulin sensitivity. Our study results, therefore, suggest that accumulation of intra-abdominal adipose tissue is an important determinant of the metabolic syndrome. Furthermore, the significant relation of visceral adiposity with all the features of the metabolic syndrome was in part independent of the effect of insulin resistance and abdominal subcutaneous fat, suggesting an important role for visceral adiposity.

Our finding that visceral adiposity is significantly associated with the features of the metabolic syndrome is consistent with other studies that have examined the relation of this parameter to cardiovascular disease risk factors. Visceral adiposity, but not abdominal subcutaneous fat, is independently associated with insulin resistance (20), lower HDL cholesterol (20,21), higher apolipoprotein B (21,24) and triglyceride levels (20,21), smaller LDL particles (21,24), aortic stiffness (43), coronary artery calcification (44), and higher BP (16–18,25). Furthermore, a reduction in visceral fat by weight loss or surgical removal is associated with increases in insulin sensitivity

TABLE 5
Multiple regression models including all of the NCEP ATP III criteria as independent continuous variables to assess their association to S_i and IAF and SCF areas as dependent variables

	log{S_i[min^{-1}/(pmol/l)]}		sqrt(IAF [cm^2])		sqrt(SCF [cm^2])	
Independent variables	Slope	*P*	Slope	*P*	Slope	*P*
Systolic BP (mmHg)	−0.003 ± 0.001	0.02	0.035 ± 0.014	0.02	−0.026 ± 0.024	0.3
Diastolic BP (mmHg)	−0.001 ± 0.002	0.6	−0.024 ± 0.023	0.3	0.014 ± 0.039	0.7
Waist circumference (cm)	−0.009 ± 0.001	<0.001	0.179 ± 0.014	<0.001	0.215 ± 0.023	<0.001
HDL (mmol/l)	0.001 ± 0.001	0.3	0.005 ± 0.011	0.6	0.063 ± 0.019	0.001
TG (mmol/l)	−0.0007 ± 0.0002	<0.001	0.007 ± 0.002	<0.001	0.009 ± 0.003	0.003
FPG (mmol/l)	−0.006 ± 0.002	0.004	0.002 ± 0.018	0.9	−0.017 ± 0.03	0.6

Data are means ± SE.

(45,46) and HDL cholesterol (47) and decreases in TGs (47) and BP (17,47). Longitudinal studies have demonstrated a higher risk of developing impaired glucose tolerance (15), type 2 diabetes (15,48), and coronary heart disease (49–51) in subjects with visceral adiposity. Thus, visceral adiposity may have a significant pathophysiological role in the development of the metabolic syndrome and its sequelae, possibly as it is a source of a number of substances, including free fatty acids (26,27) and the adipokines adiponectin (28,29), TNF-α (27,30,31), and PAI-1 (32,33).

In our study, sex did not impact the relation of insulin resistance, central adiposity, and the metabolic syndrome, which supports the sex-specific NCEP ATP III criteria for WC and HDL cholesterol. In contrast, age did impact several relations. Older subjects did not exhibit the positive correlation between IAF area and diastolic BP, or a negative correlation between insulin sensitivity and diastolic BP seen in the younger subjects. This finding was likely due to the decrease in vascular compliance that is associated with a reduction in diastolic BP in older individuals (52). Age also affected the relation between insulin sensitivity and FPG. Specifically, the youngest subjects did not have a negative correlation between insulin sensitivity and FPG, suggesting that they had adequate compensatory pancreatic β-cell function for the prevailing degree of insulin sensitivity.

The NCEP ATP III suggests practical, clinical tools for physicians to use for diagnosing the metabolic syndrome (1). We have shown that both the WC and the TG criteria have consistently strong and independent relations with both insulin resistance and visceral adiposity in men and women with FPG <6.4 mmol/l. Further, from our data it would appear that WC is more strongly related to IAF than it is to SCF. Finally, McLaughlin et al. (53) recently reported that the TG-to-HDL ratio was a better predictor of insulin sensitivity than either measure alone or BMI. Unfortunately, those researchers did not measure WC, which we found in our cohort to be a better predictor of insulin sensitivity than the TG-to-HDL ratio (data not shown). Taken together, then, our findings are in agreement with the work published by Despres and colleagues demonstrating that the "hypertriglyceridemic waist" is a significant predictor of hyperinsulinemia (54), dyslipidemia (50,54), and coronary artery disease (50). Thus, the NCEP ATP III criteria for WC and TG levels appear to be strong clinical tools for assessing an individual's risk of having the underlying abnormalities in insulin resistance and visceral adiposity that are associated with the development of the metabolic syndrome.

By virtue of the fact that we performed a cross-sectional study, we could not determine causality among insulin resistance, central adiposity, and the metabolic syndrome. However, important associations between the clinical NCEP ATP III definition of the metabolic syndrome and abnormalities in insulin resistance and visceral adiposity could be examined using the sophisticated measurements of insulin sensitivity and abdominal body fat distribution in this large cohort. Our study population may have been healthier than the general population due to the exclusion of subjects with elevated fasting glucose, LDL cholesterol, and TG levels. However, the prevalence of the metabolic syndrome in our study was similar to the prevalence reported in the NHANES III analysis by Ford et al. (2). Although selecting healthy subjects may have attenuated the relation of insulin sensitivity, abdominal fat distribution, and the metabolic syndrome, we still managed to demonstrate significant associations of insulin resistance, central adiposity, and the clinical features of the metabolic syndrome.

In conclusion, our study demonstrated a significant relation of insulin resistance and central adiposity with the NCEP-defined metabolic syndrome. We found that visceral adiposity is significantly associated with of all of the metabolic syndrome criteria independent of insulin sensitivity and abdominal SCF area, suggesting that visceral adiposity may have a role in the development of the metabolic syndrome. In addition, our results suggest that clinical assessments of increased WC and TG levels are strongly associated with decreased insulin sensitivity and increased visceral adiposity in individuals with FPG <6.4 mmol/l. Thus, these clinical criteria may be a practical method for assessing an individual's risk for the metabolic syndrome and the adverse diseases associated with it over the long term.

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