Relationship to Insulin Resistance of the Adult Treatment Panel III Diagnostic Criteria for Identification of the Metabolic Syndrome

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The Adult Treatment Panel III (ATP III) has published criteria for diagnosing the metabolic syndrome, a cluster of closely related abnormalities related to insulin resistance that increase cardiovascular disease risk. The present analysis was performed to evaluate the ability of these criteria to identify insulin-resistant individuals. The population consisted of 443 healthy volunteers, with measurements of BMI, blood pressure, fasting plasma glucose, triglycerides, HDL cholesterol concentrations, and steady-state plasma glucose (SSPG) concentration. Insulin resistance was defined as being in the top tertile of SSPG concentrations. Of the population, 20% satisfied ATP III criteria for the metabolic syndrome. Although insulin resistance and the presence of the metabolic syndrome were significantly associated ($P < 0.001$), the sensitivity and positive predictive value equaled 46% (69 of 149) and 76% (69 of 91), respectively. Being overweight, with high triglycerides, low HDL cholesterol, or elevated blood pressure, most often resulted in a diagnosis of the metabolic syndrome. Thus, the ATP III criteria do not provide a sensitive approach to identifying insulin-resistant individuals. The individual components vary both in terms of their utility in making a diagnosis of the metabolic syndrome and their relationship to insulin resistance, with the obesity and lipid criteria being most useful. *Diabetes* 53:1195–1200, 2004

The recent report (1) of the National Cholesterol Education Program (Adult Treatment Panel III [ATP III]) has recognized the importance of a "constellation of lipid and nonlipid risk factors of metabolic origin" as cardiovascular disease (CVD) risk factors. The ATP III report designated this cluster of related CVD risk factors as "the metabolic syndrome" and stated that "this syndrome is closely linked to insulin resistance." There is now considerable evidence that insulin resistance and/or compensatory hyperinsulinemia are CVD risk factors (2–8), and ATP III recognition of the importance of insulin resistance, and of its manifestations, as increasing CVD risk has focused attention on the metabolic syndrome.

In addition to emphasizing the CVD risk of insulin resistance and its manifestations, the ATP III recommended criteria for identifying individuals with the metabolic syndrome. Application of these criteria to the database of the Third National Health and Nutrition Examination Survey (NHANES III) demonstrated that ~22% of the population at large met the ATP III criteria for the diagnosis of the metabolic syndrome (9). Although insulin resistance is presumed to be the basic defect leading to the metabolic syndrome (1), neither assessment of insulin resistance nor hyperinsulinemia were among the proposed ATP III criteria. This omission was not surprising because specific measurements of insulin resistance are not clinically practical. Plasma insulin concentrations are often used as surrogate measures of insulin resistance, but their ability to predict insulin resistance is relatively modest (10). Furthermore, because techniques for measuring plasma insulin concentration are not standardized, values will vary substantially from one clinical laboratory to another. Finally, no specific plasma insulin concentration has been validated as a predictor of CVD. Thus, the decision of the ATP III to use putative manifestations of insulin resistance and compensatory hyperinsulinemia to identify subjects with the metabolic syndrome is understandable.

Reports have subsequently been published showing that application of the criteria proposed by the ATP III for the diagnosis of the metabolic syndrome identifies individuals at increased CVD risk (11,12). However, because the abnormalities selected by the ATP III to diagnose the metabolic syndrome (obesity, hyperglycemia, hypertriglyceridemia, a low HDL cholesterol concentration, and hypertension) are known CVD risk factors (13–17), it might have been anticipated that CVD risk would be increased in those individuals who had at least three of these abnormalities. On the other hand, the relationship between insulin resistance and the five abnormalities selected by the ATP III to diagnose the metabolic syndrome has not been defined. Furthermore, CVD is not the only clinical syndrome with increased prevalence in insulin-resistant individuals; in addition to type 2 diabetes (18)

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ADA, American Diabetes Association; ATP III, Adult Treatment Panel III; CVD, cardiovascular disease; NHANES III, Third National Health and Nutrition Examination Survey; SSPG, steady-state plasma glucose; SSPI, steady-state plasma insulin; WOSCOPS, West of Scotland Coronary Prevention Study.

and hypertension (19), it is now clear that polycystic ovary syndrome (20), nonalcoholic liver disease (21), sleep-disordered breathing (22), and several types of cancer (23) are also associated with insulin resistance. Given the apparent clinical importance of identifying insulin-resistant individuals, it seemed worthwhile to see how useful the ATP III criteria were in accomplishing this task. The analysis to be presented was initiated in an effort to address this issue, and its goal was the definition of the relationship between the diagnosis of the metabolic syndrome with ATP III criteria and specific measurements of insulin-mediated glucose disposal in 443 nondiabetic individuals.

RESEARCH DESIGN AND METHODS

A population of 443 subjects was selected from our database of individuals who have participated in various institutional review board–approved studies over the past 10 years. All were nondiabetic (24) and in good general health, with normal findings on medical history, physical examination, blood count, urinalysis, and chemical screening battery and not taking lipid-lowering drugs.

Insulin resistance was quantified by a modification (25) of the insulin suppression test as originally described (26) and validated (27). Briefly, subjects were infused for 180 min with octreotide ($0.27\ \mu g \cdot m^{-2} \cdot min$), insulin ($32\ mU \cdot m^{-2} \cdot min$), and glucose ($267\ mg \cdot m^{-2} \cdot min$). Blood was drawn at 10-min intervals from 150 to 180 min of the infusion to measure plasma glucose and insulin concentrations, and the mean of these four values were used as the steady-state plasma insulin (SSPI) and glucose (SSPG) concentrations. Because SSPI concentrations were similar in all subjects, the SSPG concentration provided a direct measure of the ability of insulin to mediate disposal of an infused glucose load; the higher the SSPG concentration, the more insulin resistant the individual.

An individual was defined as being insulin resistant if their SSPG concentration was in the upper tertile of the 443 apparently healthy individuals in the study population. This decision was based on results of two prospective studies showing that subjects in the upper SSPG tertile of an unselected subset of these individuals were at a significantly greater increased risk to develop type 2 diabetes, hypertension, CVD, and cancer (5,7). Measurements of body weight, plasma glucose, insulin, lipid and lipoprotein concentrations, and blood pressure were similar throughout the period of study and were described previously (5,7).

Each individual was assessed for the presence of the metabolic syndrome using data collected on height, weight, blood pressure, and fasting plasma concentrations of glucose, triglycerides, and HDL cholesterol. Four of the specific ATP criteria were used, i.e., blood pressure ≥130/85 mmHg, triglycerides ≥1.695 mmol/l (150 mg/dl), glucose ≥6.105 mmol/l (110 mg/dl), and HDL cholesterol <1.036 mmol/l (40 mg/dl) for men or <1.295 mmol/l (50 mg/dl) for women (1). Because measurements of waist circumference were not available for the entire population, we substituted a BMI ≥25.0 kg/m^2 among women and ≥29.0 kg/m^2 among men as an index of obesity, rather than abdominal circumference. We believe that the use of BMI as the index of obesity, rather than waist circumference, does not substantially alter our findings for the following reasons: *1*) recent analysis of 4,024 adults in the NHANES 1999–2000 indicated that the correlation coefficient between BMI and waist circumference ranged from 0.91 to 0.94 among men and from 0.88 to 0.94 among women, and it did not vary as a function of age, sex, race, or ethnicity (28); *2*) the results of the European Group for the Study of Insulin Resistance demonstrated, on the basis of 1,146 direct estimates of insulin-mediated glucose disposal, that the relationship between obesity and insulin resistance is similar, regardless of whether abdominal circumference or BMI is the index of obesity (29); and *3*) when applied to the NHANES dataset, the chosen BMI cut points resulted in a metabolic syndrome distribution similar to that obtained with the waist circumference criteria (30).

The ATP III suggested that diagnosis of the metabolic syndrome required that an individual meet at least three of the five criteria outlined. Thus, using all possible combinations of these five criteria, we determined *1*) how many subjects were identified as having the metabolic syndrome and *2*) whether an individual so identified was also insulin resistant (in the upper SSPG tertile). The sensitivity, specificity, and positive predictive value of using the metabolic syndrome to diagnose insulin resistance were computed. In addition, the distributions of the five components of the metabolic syndrome were examined alone as well as with respect to insulin resistance for men and women. The relationship between the number of components an individual had and insulin resistance was also explored. The ability of the 10 possible combinations of any three of the ATP III criteria to identify individuals as being in the upper SSPG tertile was studied. A χ^2 test was used to test for associations between categorical variables, and Pearson and Spearman correlation coefficients were calculated for continuous variables. All analyses were conducted using SAS version 8.2 (SAS Institute, Cary, NC).

TABLE 1
Prevalence of individual components of the metabolic syndrome among men and women

Condition	Men	Women	*P*
High BMI*	53 (25.5)	127 (54)	<0.0001
High glucose (6.105 mmol/l, 110 mg/dl)	18 (8.5)	9 (4)	0.04
High triglycerides (1.695 mmol/l, 150 mg/dl)	56 (27)	52 (22)	0.24
Low HDL cholesterol†	79 (38)	92 (39)	0.80
Hypertension (130/85 mmHg)	79 (39)	45 (19)	<0.0001

Data are *n* (%). *High BMI: female 25.0 kg/m^2, male 29.0 kg/m^2; †low HDL: male <1.036 mmol/l (<40 mg/dl), female <1.295 mmol/l (<50 mg/dl).

RESULTS

The population was predominantly white (87%), and 220 men and 223 women were included in the study. Their ages ranged from 19 to 79 years, with a mean age and standard deviation of 48.5 and 13 years, respectively.

Application of the modified ATP III criteria to the 443 volunteers included in this analysis led to the diagnosis of the metabolic syndrome in 20.5% (18.3% in men and 22.6% in women), a figure comparable to the findings in the 8,814 men and women included in the analysis of the NHANES III results (9). Thus, use of BMI, rather than waist circumference, did not change prevalence of the metabolic syndrome diagnosed by the ATP III criteria in our population as compared with the NHANES data.

Among men, 27.4% had one component, 22.6% two components, 10.6% three components, 5.8% four components, and 1.9% five components of the metabolic syndrome. These percentages were relatively comparable in women, with values of 25.1, 19.6, 16.2, 6.4, and 0%, respectively. The prevalence of the individual components of the metabolic syndrome by sex are given in Table 1. These results indicate that the most common abnormality in women was a high BMI, whereas men were more likely to have higher blood pressure than women. The dyslipidemic criteria for the metabolic syndrome were met frequently in both sexes, with no difference in the prevalence between them. Perhaps the most striking finding was how infrequently a high plasma glucose concentration was seen in either group, with only 27 of the 443 subjects (~6%) meeting this criterion.

Insulin resistance and the metabolic syndrome were significantly associated (χ^2, $P < 0.001$), and the odds of being insulin resistant increased 10-fold for those individuals meeting the criteria for having the metabolic syndrome (odds ratio 10.7; 95% CI 6.2–18.3). The results in Table 2 provide further information on the magnitude of the association between the metabolic syndrome (meeting at least three of the ATP III criteria) and insulin resistance (being in the upper SSPG tertile). These results indicate that 91 subjects were diagnosed as having the metabolic syndrome, and of this total 60 met three criteria, 27 met four criteria, and 4 met all five criteria. It can also be seen from Table 2 that 69 of the 149 individuals classified as

TABLE 2
Relationship between diagnosis of the metabolic syndrome with the ATP III criteria and the presence of insulin resistance

Metabolic syndrome	SSPG Tertile		Total
	Upper 1/3	Lower 2/3	
Yes	69	22	91
No	80	272	352
Total	149	294	443

Sensitivity: 69 of 149 = 46%; positive predictive value: 69 of 91 = 76%; specificity: 272 of 294 = 93%.

being insulin resistant met the ATP III criteria for the metabolic syndrome (sensitivity = 46%). However, both the specificity (93%) and the positive predictive value (76%) were considerably greater.

Because approximately two-thirds (60 of 91) of the individuals identified as having the metabolic syndrome were diagnosed on the basis of three criteria, the utility of these possible combinations was evaluated. Thus, we calculated the number of individuals identified as having the metabolic syndrome by the combination of meeting only three of the ATP III criteria, as well as the number of such individuals defined as being insulin resistant by their presence in the highest SSPG tertile. The results in Table 3 demonstrate that the ability of the five ATP III criteria to identify individuals with the metabolic syndrome varied considerably when the minimum number of criteria was met. For example, the glucose criterion does not appear to be useful. In contrast, being overweight (BMI $\geq$25.0 kg/m^2 among women and $\geq$29.0 kg/m^2 among men), in combination with high plasma triglycerides and/or low HDL cholesterol, was a powerful predictor of having the metabolic syndrome. Furthermore, the combination of being overweight and having either high blood pressure, high triglycerides, or low HDL cholesterol was also relatively useful in identifying those with the metabolic syndrome. These three combinations accounted for 49 of the 60 individuals (82%) that were identified as having met only three of the five suggested criteria. It can also be seen that the positive predictive value to identify insulin-resistant individuals using any one of these three combinations of ATP III variables to diagnose the metabolic syndrome was comparable, for most combinations, to the results shown in Table 2 when all five ATP III criteria were used.

Table 4 presents the likelihood of an individual being insulin resistant if they had any one of the individual components of the metabolic syndrome. It should be noted that more women exceeded the BMI cut point than men, but that the men considered to be obese by the BMI cut points used were significantly more likely to be insulin resistant ($P < 0.01$). No other significant sex differences were observed. The components most likely to be associated with insulin resistance were hypertriglyceridemia and hyperglycemia, but, as emphasized when discussing the results in Table 1, hyperglycemia was rarely present. In this context, it is of interest that not only was hypertriglyceridemia a frequent component in both men and women, but also its prevalence was essentially identical in the two groups. Finally, the data in Table 4 demonstrate that the greater the number of metabolic syndrome components present, the higher the prevalence of insulin resistance.

To gain insight as to why there were such profound differences seen in Table 4 between the abilities of various combinations of any three of the ATP III diagnostic criteria to identify insulin-resistant individuals, we analyzed the relationship between the individual ATP III criteria and the SSPG concentration. These results are shown in Table 5, and they demonstrate that the correlation coefficients (r values) between the individual criterion and the measure of insulin-mediated glucose disposal ranged from 0.35 and 0.59. Although all five of the components were significantly related to SSPG concentration, it was not surprising, in light of the information in Tables 3 and 4, that the closest association was with high BMI and hypertriglyceridemia, and the weakest was with high glucose concentration.

DISCUSSION

The notion of a metabolic syndrome stems from a suggestion, first explicated in 1988 (31), that there is a cluster of related abnormalities that occur more commonly in nondiabetic individuals, secondary to insulin resistance, that increases CVD risk. If insulin resistance is the fundamental abnormality, it is necessary to ask what magnitude of insulin resistance is required to result in untoward consequences. Two prospective studies (5,7) have addressed this issue by quantifying insulin resistance at baseline, and they showed that one-third of the experimental population with the greatest impairment in insulin action was at

TABLE 3
Identification of the metabolic syndrome and insulin resistance using all combinations of any three ATP III criteria

Criteria used*	Number of individuals		Positive predictive value (%)
	Metabolic syndrome	Upper SSPG tertile	
BMI, triglyceride, HDL chloresterol	20	13	65
BMI, HDL cholesterol, blood pressure	15	10	67
BMI, triglycerides, blood pressure	14	11	78.5
Triglycerides, HDL cholesterol, blood pressure	7	3	43
BMI, HDL cholesterol, glucose	1	1	100
BMI, glucose, blood pressure	1	1	100
BMI, triglycerides, glucose	1	1	100
Triglycerides, blood pressure, glucose	1	0	0
HDL cholesterol, blood pressure, glucose	0	0	0
Triglycerides, HDL cholesterol, glucose	0	0	0

*BMI: female 25.0 kg/m^2, male 29.0 kg/m^2; blood pressure 130/85 mmHg; glucose 6.105 mmol/l (110 mg/dl); triglyceride 1.695 mmol/l (150 mg/dl); HDL: female <1.295 mmol/l (<50 mg/dl), male <1.036 mmol/l (<40 mg/dl).

TABLE 4
Prevalence of insulin resistance by individual components of the metabolic syndrome and the number of components among men and women

Condition	Total		Men		Women		
	n	Yes (%)	*n*	Yes (%)	*n*	Yes (%)	*P*
High BMI†	180	56	53	74	127	49	<0.01
High glucose (6.105 mmol/l, 110 mg/dl)	27	70	18	67	9	78	0.55
High triglycerides (1.695 mmol/l, 150 mg/dl)	108	69	56	70	52	69	0.96
Low HDL cholesterol‡	171	48	79	42	92	53	0.13
Hypertension (130 of 85 mmHg)	124	60	79	58	45	64	0.50
Number of components							
Only one	116	28	57	35	59	20	0.07
Any two	93	43	47	45	46	41	0.74
Any three	60	67	22	59	38	71	0.34
Any four	27	93	12	100	15	87	0.49
All five	4	100	4	100	0	N/A	N/A

*χ^2 test of association between sex and presence of insulin resistance for the different conditions; †high BMI: female 25.0 kg/m^2, male 29.0 kg/m^2; ‡low HDL: male <1.036 mmol/l (<40 mg/dl), female <1.295 mmol/l (<50 mg/dl).

significantly increased risk to develop clinically relevant disease. In the first study (5), 0 of 49 participants in the lowest tertile of insulin resistance, 1 of 49 participants in the middle tertile of insulin resistance, and 7 of 49 participants in the top tertile of insulin resistance developed CVD. In the second study (7), the 70 individuals in the upper tertile of insulin resistance had suffered 32 events within 6.3 years, including CVD, type 2 diabetes, hypertension, stroke, and cancer. In neither study did individuals in the most insulin-sensitive tertile develop any of the conditions outlined above. The results of these prospective studies provide support for our decision to classify individuals as being insulin resistant if they belonged to the one-third of the study population with the greatest impairment of insulin action.

Before considering the utility of the ATP III criteria in identifying insulin-resistant individuals, the relative contributions the individual components make in establishing the diagnosis of the metabolic syndrome merit some attention. The results in Table 3 indicate that of the 91 individuals determined to have the metabolic syndrome, 60 were diagnosed on the basis of meeting 3 criteria, and 49 of these were recognized by 3 of the 10 possible combinations. It is clear from these data that impaired fasting glucose was rarely one of the three ATP III criteria that led to the diagnosis of the metabolic syndrome, a finding that is not surprising because the prevalence of this abnormality was ~6% in this population of healthy volunteers. Parenthetically, the data in Table 5 also show that fasting glucose along with systolic blood pressure were the criteria with the weakest relationship to SSPG concentration (Table 5). Selection of a fasting plasma glucose concentration between 110 and 126 mg/dl as one of the five ATP III criteria was apparently based on the American Diabetes Association (ADA) definition of impaired fasting glucose (24). Because the ADA has recently reduced the lower level of impaired fasting glucose to 100 mg/dl (32), we thought it might be helpful to see how this action might affect our findings. Using this glucose cut point, the number of individuals with the metabolic syndrome increased from 91 to 110 (prevalence from 20.5 to 24.8%), with 12 of the 19 additional subjects diagnosed with the metabolic syndrome classified as insulin resistant. The results in Table 2 would also change somewhat with the lower glucose criteria, and in this instance the sensitivity of the ATP III criteria to identify insulin resistance would increase from 46 to 54%, the specificity would decrease from 93 to 90%, and the positive predictive value would be essentially unchanged (76 to 74%).

In contrast to the glucose and systolic blood pressure criteria, the BMI and lipid criteria seem to be particularly helpful in identifying the metabolic syndrome, as well serving as a useful indicator of insulin resistance. Thus, a BMI ≥25.0 kg/m^2 for women or ≥29.0 kg/m^2 for men, associated with an abnormal value for any two of the following variables: hypertension, triglyceride concentration, or HDL cholesterol concentration, accounted for 82% (49 of 60) of the diagnoses of metabolic syndrome based on any combination of three ATP III criteria. It can also be seen from Table 4 that these three abnormalities occurred commonly in insulin-resistant individuals, and the results in Table 5 demonstrate that both BMI (r = 0.56) and triglyceride concentration (r = 0.59) were highly correlated with SSPG concentration.

If we now turn our attention to the ability of the ATP III criteria to identify insulin-resistant individuals, the data in Table 2 indicate that only 69 of the 91 individuals identified as having the metabolic syndrome were also insulin resistant to a degree that significantly increased their risk of an adverse clinical outcome. Furthermore, of the 149 individuals in the upper SSPG tertile, the population shown to be the most at risk to develop untoward consequences of

TABLE 5
Correlations between continuous components of the metabolic syndrome and SSPG among 443 men and women

Variable*	Correlation with SSPG	
	Pearson (*P* value)	Spearman (*P* value)
Triglycerides	0.50 (<0.0001)	0.59 (<0.0001)
HDL cholesterol	−0.40 (<0.0001)	−0.41 (<0.0001)
Fasting glucose	0.38 (<0.0001)	0.35 (<0.0001)
Systolic blood pressure	0.38 (<0.0001)	0.36 (<0.0001)
Diastolic blood pressure	0.44 (<0.0001)	0.43 (<0.0001)
BMI	0.59 (<0.0001)	0.56 (<0.0001)

being insulin resistant (5,7), only 46% (69 of 149) met the ATP III criteria for the metabolic syndrome. Thus, if there is clinical utility in identifying insulin-resistant individuals, the ATP III criteria are not very sensitive. On the other hand, it could be argued that it is not important to identify insulin-resistant individuals in the absence of the clinical manifestations associated with this defect in insulin action. Rather than focusing on how best to identify insulin-resistant individuals, emphasis should be placed on the need to be aware of the clinical syndromes associated with insulin resistance, and how to initiate the most clinically effective interventions when these diagnoses are made. Obviously, a discussion of the relative merits of these two alternative views is outside the purview of this report.

The fact that the five ATP III criteria do not effectively identify insulin-resistant individuals should not detract from the clinical benefit they provide by focusing attention on CVD risk factors that have not been emphasized in the past. Indeed, there is evidence that CVD risk is increased in association with obesity, impaired glucose tolerance, hypertension, hypertriglyceridemia, and a low HDL cholesterol concentration (13–17). Thus, it seemed highly likely that the combination of any three of these abnormalities would be of use in identifying patients at increased CVD risk, and evidence recently published from the West of Scotland Coronary Prevention Study (WOSCOPS) has confirmed this assumption (33). Furthermore, a diagnosis of the metabolic syndrome continued to predict CVD when the usual conventional risk factors were put in a multivariate model. In light of the data presented in Tables 3–5, it was also of interest to find that >95% of those diagnosed with the metabolic syndrome in WOSCOPS had hypertension and >85% had elevated triglycerides and low HDL cholesterol concentrations. Finally, and not surprisingly, the greater the number of components of the metabolic syndrome present, the greater the CVD risk.

Although the WOSCOPS findings support the notion that components of the metabolic syndrome identify individuals who may have missed ascertainment because of reliance on conventional CVD risk factors, the clinical utility of making the diagnosis is not as self-evident. The blood pressure and lipid components of the metabolic syndrome are certainly well established as increasing CVD risk. Blood pressure lowering should be initiated to reduce CVD risk, irrespective of whether the individual has two additional components of the metabolic syndrome as defined by the ATP III criteria. Furthermore, as recently emphasized by the results of the Copenhagen Male Study (34), the CVD risk associated with hypertension is accentuated in the presence of high triglycerides and low HDL cholesterol plasma concentrations. It seems in this instance that treatment must be directed to both abnormalities. In a related fashion, there is evidence that appropriate interventions can decrease the progression of abnormal glucose tolerance to manifest type 2 diabetes (35). Finally, the more obese an individual, the more likely they are to be insulin resistant and thereby at increased CVD risk (36). Thus, recognition of abnormal values for any one of the five individual components of the metabolic syndrome as defined in the ATP III guidelines, and responding with relevant therapeutic interventions, appears to be clinically useful, regardless of whether three of the five abnormalities are present. Indeed, placing the emphasis on whether an individual has satisfied the ATP III diagnostic criteria, rather than focusing on identifying and treating the individual components, has the potential to do more harm than good.

Because the ATP III criteria appear to be only modestly successful at identifying insulin-resistant individuals, they do not provide a very useful pathophysiological link between insulin resistance and the metabolic syndrome. However, this finding should be no more surprising than the success of the metabolic syndrome in identifying individuals at increased CVD risk. Perhaps the best example of this apparent paradox involves the relationship between insulin resistance, hypertension, and CVD. No more than 50% of patients with essential hypertension are insulin resistant (37), and the results in Table 5 indicate that <20% of the variance in SSPG can be attributed to differences in blood pressure. Furthermore, Table 5 also indicates that differences in plasma triglyceride concentration can account for no more than 40% of the variance in SSPG concentration. Thus, a substantial number of individuals can be hypertensive and/or hypertriglyceridemic without being insulin resistant. On the other hand, there is no reason to assume that CVD risk in individuals that share these abnormalities varies as a function of how they evolved, and the WOSCOPS study data demonstrate how central these components of the metabolic syndrome are in determining CVD outcome.

In conclusion, ~21% of the 443 healthy volunteers evaluated met the ATP III criteria for identification of the metabolic syndrome (1), an estimate comparable to the results of a similar analysis using data from NHANES III (9). Additionally, in the present study we demonstrated that approximately two-thirds of the individuals diagnosed as having the metabolic syndrome by these criteria were also insulin resistant. In this context, it should be emphasized that our findings are based primarily on individuals of European ancestry, and results might vary as a function of ethnic group. Indeed, the ATP III panel considered this issue, concluding that "limited data suggest that racial and ethnic groups vary somewhat in baseline risk for CHD [coronary heart disease]," but they indicated that they did not feel that available evidence permitted them to modify their general recommendations.

The discordance between the diagnosis of the metabolic syndrome and the presence of insulin resistance raises questions as to both the conceptual and clinical utility of making the diagnosis of the metabolic syndrome on the basis of any specific number of criteria. However, these data do suggest that certain combinations of criteria and meeting a larger number of criteria (four or five versus three) may be more indicative of insulin resistance. Nevertheless, the greatest benefit from the introduction of ATP III criteria may be emphasizing the fact that there are important CVD risk factors beyond hypercholesterolemia. By broadening awareness of the abnormalities associated with insulin resistance that increase CVD risk, the ATP III report has made an important contribution.

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