

Analysis of Obesity and Hyperinsulinemia in the Development of Metabolic Syndrome: San Antonio Heart Study

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Abstract

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Objective: To use standardized cut-offs of body mass index (BMI), waist circumference, waist-to-hip ratio, and fasting insulin levels to predict the development of metabolic disorders and metabolic syndrome.

Research Methods and Procedures: We performed an 8-year follow-up study of 628 non-Hispanic whites and 1340 Mexican Americans, ages 25 to 64 years, from the second cohort of the San Antonio Heart Study. We defined metabolic disorders as dyslipidemia (triglycerides ≥ 2.26 mM or high-density lipoprotein < 0.91 mM in men and < 1.17 mM in women), hypertension (blood pressure $\geq 140/\geq 90$ mm Hg, or receiving antihypertensive medications), and type 2 diabetes (fasting glucose ≥ 7.0 mM, 2-hour test glucose ≥ 11.1 mM, or receiving anti-diabetic medications). People with at least two metabolic disorders were defined as having metabolic syndrome.

Results: High waist-to-hip ratio and fasting insulin levels were significant predictors of developing metabolic syndrome. High anthropometric indices remained significant predictors of metabolic syndrome after adjusting for fasting insulin. Waist circumference, BMI, and insulin had similar areas under the receiver operating characteristic curves

(0.74 to 0.76). Further multivariate analyses combining these indices showed minimal increase in prediction. Of subjects who had a combination of high BMI (≥ 30 kg/m²) and high waist circumference (above “Action Level 2”), 32% developed metabolic syndrome, compared with 10% of subjects with both low BMI and low waist circumference.

Discussion: These findings support the National Institutes of Health recommendations for reducing the risk of metabolic syndrome. Adjustment for baseline fasting insulin levels had only a small effect on the ability of anthropometric indices to predict the metabolic syndrome.

Key words: health promotion, fat distribution, hyperinsulinemia, metabolic syndrome, longitudinal study

Introduction

The prevalence of obesity has reached an epidemic proportion worldwide. This has multiple medical consequences, including cardiovascular disease, which is particularly related to central (intra-abdominal) fat distribution (1–3). The National Institutes of Health of the United States (4) and Scottish Intercollegiate Guidelines Network (5) have recently recommended weight management based on standardized cut-offs for body mass index (BMI) at 25 and 30 kg/m², and on waist circumference “Action Levels” (“Action Level 1” at 94 cm in men and 80 cm in women and “Action Level 2” at 102 cm in men and 88 cm in women). These standardized indices are now accepted internationally as health risk indicators in health promotion and have been derived largely from cross-sectional studies of anthropometry related morbidity and mortality (3,6). Waist circumference has a particular relevance for health promotion. Above “Action Level 1,” individuals are at increased health risk and should take personal steps to avoid weight gain. Above “Action Level 2,” they are at high health risk and should seek professional help (4,5).

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Information on the relationships between obesity and central-fat distribution and a cluster of metabolic disorders including dyslipidemia [hypertriglyceridemia and reduced high-density lipoprotein (HDL)-cholesterol], hypertension, and type 2 diabetes has largely been obtained from cross-sectional studies (7–10). These studies, in different populations whose absolute levels of risk vary, generally showed waist circumference to be associated more strongly than BMI with metabolic disorders. In addition to anthropometrics, hyperinsulinemia has also been shown as a risk factor for developing metabolic syndrome (11) and cardiovascular disease (12).

This study assessed the value of standardized anthropometric indices related to obesity and central body-fat distribution as well as hyperinsulinemia in predicting the metabolic syndrome in subjects from the 8-year longitudinal San Antonio Heart Study.

Research Methods and Procedures

This study is an 8-year follow-up of subjects from the second cohort of the San Antonio Heart Study, a population-based study of diabetes and cardiovascular disease in Mexican Americans and non-Hispanic whites. In this second cohort, indices of body-fat distribution (waist and hip circumferences) were measured in addition to other measurements made in the first cohort (11).

Baseline Examination

Between 1985 and 1988, a total of 2941 men and non-pregnant women, ages 25 to 64 years, were recruited randomly from three neighborhoods (Barrio, Transitional, and Suburban) in San Antonio, Texas. A detailed description of this study has been published previously (13). The study was approved by the Institutional Review Board of the University of Texas Health Science Center at San Antonio, and all subjects gave informed consent. In the present study, a total of 1968 subjects who did not have metabolic syndrome at baseline were analyzed. There were 290 male and 338 female non-Hispanic whites and 535 male and 805 female Mexican Americans.

Blood samples were obtained after a 12- to 14-hour fast for the measurements of serum lipids, lipoproteins, and insulin, and plasma glucose concentrations. Insulin was measured by a commercial radioimmunoassay (Diagnostic Products, Los Angeles, CA), with coefficients of variation for intra-assay of 6.5% and interassay of 9% (14). The lower limit of sensitivity was 15 pM, and cross-reactivity of insulin with proinsulin in this assay was 30%. A 75-g glucose equivalent load was then administered, and blood was sampled 1 and 2 hours after the glucose load for plasma glucose measurements (11).

Diabetes was diagnosed as fasting plasma glucose ≥ 7 mM (126 mg/dL) or a 2-hour glucose level ≥ 11.1 mM (200

mg/dL). Subjects who did not meet these criteria but who were receiving oral antidiabetic agents or insulin were also considered to have diabetes (15).

Systolic (first Korotkov phase) and diastolic (fifth Korotkov phase) blood pressures were measured three times to the nearest even digit with a random-zero sphygmomanometer (Hawksley-Gelman, Lancing, Sussex, UK). The average of the second and third readings were defined as the subject's blood pressure (16). Hypertension was defined as systolic ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or the use of antihypertensive agents, which was confirmed by reviewing the medications that subjects were asked to bring to the examination (11).

Hypertriglyceridemia was defined as ≥ 2.26 mM (≥ 200 mg/dL). HDL concentration was considered low if it was ≤ 0.91 mM (≤ 35 mg/dL) in men and ≤ 1.17 mM (≤ 45 mg/dL) in women (17). Subjects with any one of these factors were considered to have dyslipidemia. Insulin concentration was dichotomized at a median value of 60 pM (10 IU/mL).

Metabolic syndrome was defined as subjects having two or more of the metabolic disorders (dyslipidemia, hypertension, or type 2 diabetes). Those having one or none were not considered to have metabolic syndrome (11). The definition was based on the description of metabolic syndrome developed by Professor Reaven (18).

Anthropometric measurements (height, weight, and waist and hip circumferences) were taken with subjects in bare feet and an examining gown. BMI was calculated as weight (kilograms) divided by square height (square meters). Waist circumference and waist-to-hip ratio were used as indices for central-fat distribution.

Ethnicity was defined as Mexican Americans and non-Hispanic whites. Mexican Americans were defined as people whose ancestry and cultural traditions derived from a Mexican national origin (19). Smoking was defined as current smokers or nonsmokers; alcohol consumption was defined as currently drinking alcohol or not; physically active as a positive answer to the question "Have you been exercising in the past year." Socioeconomic status was defined by the neighborhood of residency (13). Parity was defined as the number of children born alive.

Follow-up Examination

After 8 years, subjects were recalled to ascertain the incidence of dyslipidemia, type 2 diabetes, and hypertension. Subjects were initially interviewed at home or by telephone (completed by 95% of surviving subjects) and then received a medical examination that was attended by 70% of the surviving subjects. The response rates at 7 to 8 years were 72% male and 70% female non-Hispanic whites and 68% male and 72% female Mexican Americans. All anthropometric, biochemical, and physiological measurements were performed in an identical manner to those used at the baseline examination (11). Of the 1968 subjects

without the metabolic syndrome at baseline, 1315 came to the follow-up exam. Of these, 1103 (84%) had dyslipidemia at baseline, 183 (14%) had no metabolic disorder, 17 (1%) had hypertension, and 12 (1%) had diabetes. A total of 223 subjects developed metabolic syndrome between baseline and follow-up. Of these incident metabolic syndrome cases, 189 (85%) had dyslipidemia at baseline and developed either hypertension or diabetes between baseline and follow-up.

Statistical Analyses

Dependent Variables. Analyses were performed separately for men and women, using SAS statistical package version 8.01 (SAS Institute Inc., Cary, NC). Univariate logistic regression analyses among subjects without metabolic syndrome at baseline were used to determine the relative risks for the development of each of the metabolic disorders (hypertriglyceridemia, low HDL-cholesterol, hypertension, and type 2 diabetes) and metabolic syndrome (diagnosed as a combination of at least two of the metabolic disorders) predicted by baseline anthropometric indices and insulin levels.

Independent Variables. Baseline anthropometric variables were stratified into three categories of BMI based on standardized cut-offs at 25 and 30 kg/m² or on waist circumference “Action Level 1” at 94 cm in men and 80 cm in women and “Action Level 2” at 102 cm in men and 88 cm in women. Two groups of subjects were created based on waist-to-hip ratio at the level of 0.95 for men and 0.80 for women and for baseline fasting insulin at the median value (60 pM).

Analysis of covariance was carried out to assess the differences in mean values of anthropometry and insulin in different groups of subjects who developed different numbers of new metabolic disorders. Multivariate logistic regression analyses were also performed using anthropometric variables and insulin as covariates. Receiver operating characteristic (ROC) analyses were performed to determine the areas under the curves as a measure for comparing the predictive ability of each independent variable and of various combinations of these variables.

Confounding Factors. The relationships of metabolic disorders and metabolic syndrome with anthropometric variables and hyperinsulinemia were adjusted for confounding factors including age, ethnicity, socioeconomic status, and lifestyle factors (cigarette smoking, alcohol consumption, and physical activity) and parity in women.

Results

Table 1 shows the baseline characteristics of 825 men and 1143 women. Both sexes had similar age, BMI, and insulin levels. Men had larger waist circumference and waist-to-hip

Table 1. Baseline characteristics of 825 (290 non-Hispanic whites and 535 Mexican Americans) men and 1143 (338 non-Hispanic whites and 805 Mexican Americans) women in the San Antonio Heart Study

	Men (n = 825)		Women (n = 1143)	
	Mean	SE	Mean	SE
Age (years)	42.5	0.4	43.0	0.3
Weight (kilograms)	82.3	0.5	69.5	0.5
Height (centimeters)	173.0	0.3	159.1	0.2
Body mass index (kg/m ²)	27.5	0.2	27.5	0.2
Waist circumference (centimeters)	94.5	0.4	84.6	0.4
Hip circumference (centimeters)	100.8	0.3	102.5	0.4
Waist-to-hip ratio	0.937	0.002	0.824	0.002
Fasting insulin (pM)	79.2	2.8	73.4	2.4
Fasting glucose (mM)	4.95	0.04	4.77	0.03
Triglycerides (mM)	1.67	0.04	1.33	0.02
HDL-cholesterol (mM)	1.12	0.01	1.34	0.01
Systolic blood pressure (mm Hg)	120.2	0.05	114.1	0.5
Diastolic blood pressure (mm Hg)	73.3	0.03	69.4	0.3

HDL, high-density lipoprotein.

ratio, slightly higher glucose levels, and substantially higher triglyceride levels and systolic and diastolic blood pressure. Men had lower levels of HDL-cholesterol. There were 25% men and 37% women who had BMI <25 kg/m², 49% men and 30% women who had BMI between 25 and 30 kg/m², and 25% men and 34% women who had BMI ≥30 kg/m². There were 46% men and 35% women who had waist circumference below “Action Level 1,” 30% men and 23% women who had waist circumference between “Action Levels 1 and 2,” and 24% men and 42% women who had waist circumference above “Action Level 2.”

Table 2 shows the adjusted means of anthropometric variables and fasting insulin in groups of people who developed different numbers of metabolic disorders. There were only a few subjects who developed three or four disorders (n = 17), so they were grouped together with

Table 2. Mean values of baseline anthropometry and fasting insulin in groups of subjects who developed different numbers of new metabolic disorders over 8 years in the San Antonio Heart Study: data were adjusted for age, sex, and ethnicity

	Number of new metabolic disorders developed						<i>p</i> †	<i>p</i> for trend
	0 (<i>n</i> = 456)		1 (<i>n</i> = 337)		≥2 (<i>n</i> = 117)*			
	Mean	SE	Mean	SE	Mean	SE		
Body mass index (kg/m ²)	25.7	0.2	26.6	0.3	27.3	0.4	<0.001	<0.001
Waist circumference (centimeter)	84.3	0.5	86.8	0.6	87.8	1.0	<0.001	<0.001
Waist-to-hip ratio	0.852	0.003	0.860	0.004	0.864	0.006	0.106	0.038
Fasting insulin (pM)	9.3	0.4	10.7	0.5	12.5	0.8	<0.001	<0.001

* There were only 17 subjects with ≥3 metabolic disorders.

† Analysis of covariance.

those who developed two disorders. Analysis of covariance showed that the adjusted means differed significantly (except waist-to-hip ratio) for those who developed more disorders, and tests for trends showed that these differences were linear.

After 8 years, 21% of men and 18% of women developed triglyceride levels ≥2.26 mM; HDL levels were reduced to ≤0.91 mM in 33% of men and to ≤1.17 mM in 32% of women. The incidence of hypertension was 7% in men and 12% in women, and the incidence of type 2 diabetes was 10% in men and 12% in women. Fifteen percent of men and 17% of women developed two or more of these disorders (i.e., metabolic syndrome). Table 3 shows that in terms of dyslipidemia, anthropometric indices only predicted significantly the development of low HDL-cholesterol and hypertriglyceridemia in women. Anthropometric indices were significant predictors of hypertension and type 2 diabetes in both sexes. Insulin levels were significant predictors of the development of all individual disorders.

Figure 1 shows that age-, sex-, and ethnicity-adjusted incidences of metabolic syndrome were 10% in subjects with a BMI below 30 kg/m² or waist circumference below "Action Level 2," 19% in subjects with either a BMI above 30 kg/m² or waist circumference above "Action Level 2," and 32% in subjects with both BMI and waist circumference above these levels. Figure 2 shows that women tended to have higher risk (not significant) of developing metabolic syndrome than men. The odds ratio for developing metabolic syndrome was 3.7 in men and 8.3 in women with BMI ≥30 kg/m² compared with those with BMI <25 kg/m². The odds ratio for developing metabolic syndrome was 2.8 in men and 5.9 in women with waist circumference above

"Action Level 2," compared with those with waist below "Action Level 1."

Analyses of four separate subgroups based on sex and ethnic groups were also carried out. The incidence of the metabolic syndrome was higher in male (20.4%) and female (26%) Mexican Americans than male (12.1%) and female (11.5%) non-Hispanic whites. The odds ratios of developing metabolic syndrome tended to be higher (not significant) in male [12.2 (95%CI, 4.1 to 36.4)] and female [5.2 (95%CI, 1.7 to 16.5)] non-Hispanic whites than in male [8.5 (95%CI, 4.2 to 16.9)] and female [3.1 (95%CI, 1.5 to 6.6)] Mexican Americans with BMI ≥30 kg/m² compared with those with BMI <25 kg/m². Ethnic differences in odds ratios for developing the metabolic syndrome were less apparent when comparison between groups based on waist circumference "Action Levels" was made: 2.8 (95%CI, 1.0 to 7.3) in male and 5.0 (95%CI, 2.0 to 12.6) in female non-Hispanic whites compared with 2.9 (95%CI, 1.5 to 5.5) in male and 6.9 (95%CI, 3.7 to 12.7) in female Mexican Americans with waist circumference above "Action Level 2" vs. those with waist circumference below "Action Level 1." Compared with subjects whose baseline fasting insulin levels were below the median (60 pM), the relative risks for male and female non-Hispanic whites were 2.8 (95%CI, 1.2 to 6.9) and 3.1 (95%CI, 1.7 to 5.6), respectively, and for male and female Mexican Americans were 2.5 (95%CI, 1.7 to 5.6) and 5.1 (95%CI, 3.2 to 8.2), respectively.

Figure 3 shows the ROC analyses to study the ability of BMI and waist circumference in the prediction of metabolic syndrome. In general, these indices gave very similar values for the areas under the curves. Fasting insulin gave an almost identical plot (data not presented). The use of fasting

Table 3. Odds ratios for developing metabolic disorders from either individual anthropometric measurements or insulin with adjustments for baseline age, ethnicity, cigarette smoking, alcohol consumption, physical activity, socioeconomic status, and parity (women)

	Men (n = 559)		Women (n = 756)	
	OR	95% CI	OR	95% CI
High triglycerides§				
Body mass index <25 kg/m ²	1.0	—	1.0	—
Body mass index = 25 to 30 kg/m ²	1.6	1.0, 2.5	1.4	0.9, 2.1
Body mass index ≥30 kg/m ²	1.3	0.7, 2.4	1.7*	1.1, 2.7
Waist below Action Level 1	1.0	—	1.0	—
Waist Action Levels 1 to 2	1.0	0.7, 1.6	1.5	0.9, 2.4
Waist above Action Level 2	1.1	0.8, 1.9	1.8†	1.2, 2.8
Waist-to-hip ratio <0.95 (M), <0.80 (F)	1.0	—	1.0	—
Waist-to-hip ratio ≥0.95 (M), ≥0.80 (F)	1.0	0.6, 1.5	1.8†	1.2, 2.7
Insulin <60 pM	1.0	—	1.0	—
Insulin ≥60 pM	1.5*	1.0, 2.2	1.6*	1.1, 2.3
Low HDL-cholesterol¶				
Body mass index = 25 to 30 kg/m ²	1.1	0.7, 1.6	1.7*	1.1, 2.6
Body mass index ≥30 kg/m ²	1.2	0.7, 2.1	1.1	0.7, 1.8
Waist Action Levels 1 to 2	0.8	0.5, 1.3	1.2	0.7, 1.8
Waist above Action Level 2	1.3	0.8, 2.1	1.4	0.9, 2.1
Waist-to-hip ratio ≥0.95 (M), ≥0.80 (F)	1.2	0.8, 1.8	1.4*	1.0, 2.0
Insulin ≥ 60 pM	1.7†	1.2, 2.4	1.6*	1.1, 2.3
Hypertension**				
Body mass index = 25 to 30 kg/m ²	1.1	0.5, 2.6	3.3‡	1.8, 6.1
Body mass index ≥30 kg/m ²	3.1*	1.3, 7.2	5.7‡	3.2, 10.4
Waist Action Levels 1 to 2	1.6	0.8, 3.3	1.9*	1.0, 3.63
Waist above Action Level 2	2.3*	1.1, 4.9	4.0‡	2.3, 7.0
Waist-to-hip ratio ≥0.95 (M), ≥0.80 (F)	1.4	0.8, 2.7	2.4‡	1.5, 3.9
Insulin ≥ 60 pM	3.0†	1.5, 6.0	2.0†	1.3, 3.0
Type 2 diabetes††				
Body mass index = 25 to 30 kg/m ²	3.6*	1.2, 10.4	5.1‡	2.5, 10.5
Body mass index ≥30 kg/m ²	16.0‡	5.5, 46.3	8.2‡	4.0, 16.8
Waist Action Levels 1 to 2	2.6†	1.3, 5.2	3.5‡	1.6, 7.6
Waist above Action Level 2	7.3‡	3.7, 14.4	8.2‡	4.1, 16.3
Waist-to-hip ratio ≥0.95 (M), ≥0.80 (F)	2.7‡	1.6, 4.6	3.5‡	2.0, 6.0
Insulin ≥ 60 pM	6.1‡	3.1, 11.9	4.4‡	2.7, 7.1

* $p < 0.05$; † $p < 0.01$; ‡ $p < 0.001$.

§ ≥2.26 mM, standard referent groups are indicated for the first metabolic disorder.

¶ Men: ≤0.91 mM, women: ≤1.17 mM.

** Systolic ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg or receiving anti-hypertensive medications.

†† Fasting glucose ≥ 7.0 mM and/or 2-hour glucose ≥ 11.1 mM and/or receiving anti-diabetic medications.

M, males; F, females.

The only significant gender-measure interactions were for high triglycerides: waist above “Action Level 2” ($p < 0.05$) and waist-to-hip ratio ≥0.95 (M), ≥0.80 (F) ($p < 0.01$) and for hypertension: body mass index = 25 to 30 kg/m² ($p < 0.001$), body mass index ≥30 kg/m² ($p < 0.05$) and waist Action Levels 1 to 2 ($p < 0.01$).

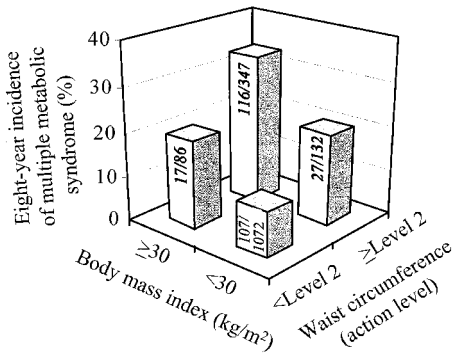


Figure 1: Eight-year incidence of metabolic syndrome in subject categories of different combinations of body mass index above or below 30 kg/m² and waist circumference above or below “Action Level 2.” Data were adjusted for age, sex, and ethnicity.

insulin as a covariate of BMI or waist circumference to predict the development of metabolic syndrome made a very small improvement. Similarly, there was little change in the area under the curve when BMI and waist circumference were used together as covariates (data not shown). Multivariate analyses using various combinations of anthropometric variables and insulin levels as covariates were also used to predict the development of metabolic syndrome, but there were only modest changes (data not shown) and little improvement in areas under the curves in ROC analyses (<0.02).

Using ROC analyses in the prediction of the development of individual metabolic disorders showed that the areas under the curves for BMI, waist circumference, and insulin were similar at around 0.60 for dyslipidemia, 0.70 for hypertension, and between 0.75 and 0.80 for diabetes (data not shown).

Discussion

The findings in this study extend our understanding of the development of metabolic syndrome and prospectively support the need for weight management of people at high health risks related to obesity and fat distribution identified by standardized classifications recommended by international public health authorities, including the World Health Organization (20), the National Institutes of Health in the United States (4), and the Scottish Intercollegiate Guidelines Network (5). The standardized cut-offs for indices of obesity (BMI at 25 and 30 kg/m²) and body-fat distribution (waist circumference “Action Levels”) evaluated in relation to the development of metabolic syndrome in this study are now accepted widely as guidelines for public health promotion and weight management as well as for obesity research (3,6,21,22).

After 8 years, men and women with either BMI above 30 kg/m² or waist circumference above “Action Level 2” (≥102 cm in men and ≥88 cm in women) were between

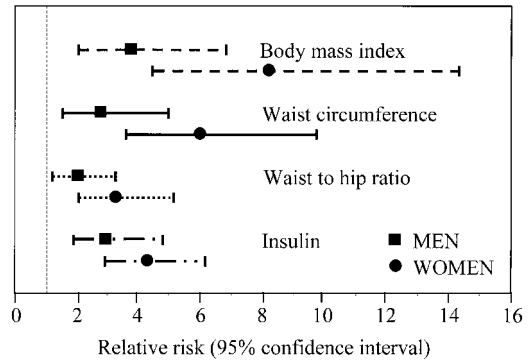


Figure 2: Relative risks and 95% confidence intervals of 8-year development of metabolic syndrome predicted from body mass index ≥30 kg/m² (reference group <25 kg/m²), waist circumference above “Action level 2” (reference group below “Action Level 1”), waist-to-hip ratio ≥0.95 in men and ≥0.80 in women (reference groups <0.95 and <0.80, respectively), and insulin ≥60 pM (reference group <60 pM). Data were adjusted for age, ethnicity, and lifestyle factors.

three and eight times more likely to develop metabolic syndrome than those with BMI below 25 kg/m² or waist circumference below “Action Level 1” (<94 cm in men and <80 cm in women). Up to one-third of the subjects with BMI above 30 kg/m² and waist above “Action Level 2” developed metabolic syndrome, compared with only one-tenth of those who had both indices below these levels. A recent survey has shown that according to self-reported weight, 18% of U.S. adults consider themselves obese (23) Flegal et al. (2) have shown that the prevalence of obesity (BMI ≥30 kg/m²) in U.S. adults had reached 23% (~40 million) in the National Health and Nutrition Examination Survey (NHANES) III survey conducted in 1994. Assuming our results can be extrapolated to the entire American population, at least 13 million more American adults will develop metabolic syndrome within 8 years. Furthermore, there would be more people at risk if those with a lower BMI with a waist circumference above “Action Level 2” were included. However, some ethnic groups might be at higher risk than others because of a higher prevalence of obesity and central-fat distribution (1). These subjects are likely to develop many more health problems secondary to obesity and central-fat distribution, particularly cardiovascular disease and poor quality of life (23,24), which are enormous burdens on health, social, and economic costs (25,26).

The definition of metabolic syndrome varies. In this study, we selected the four most widely used features (hypertriglyceridemia, low-HDL, hypertension, and diabetes) originally described by Reaven as linking to insulin resistance (18). Other newer features including elevated plasminogen activator inhibitor-1, uric acid, and small, dense low-density lipoprotein have also been suggested as part of

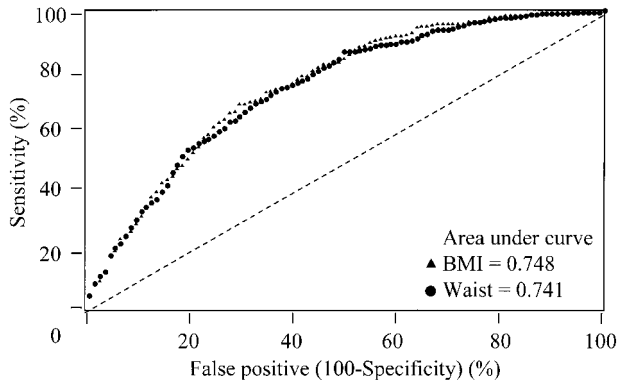


Figure 3: Receiver operating characteristic analyses of body mass index and waist circumference as univariates in the prediction of 8-year development of metabolic syndrome. Data were adjusted for age, ethnicity, and lifestyle factors. The higher the area under the curve, i.e., the greater the curvature away from the 50%-line (zero prediction), the greater is the predictive power.

the metabolic syndrome, but we did not consider these components in our present study (27) because these variables are not commonly measured in clinical practice. Although individual metabolic disorders were defined on the basis of recent international recommendations (15–17), the classification of metabolic syndrome in terms of the numbers of the disorders differs between studies. In the present study, we used the previously defined version in which subjects with one or less of the metabolic syndrome components were not considered to have metabolic syndrome (11). Thus, baseline data included subjects with no disorders as well as those with any one of the disorders; at follow-up, subjects who were considered to have metabolic syndrome included those who already had one disorder at baseline and then acquired one or more disorders 8 years later. A separate analysis of this study was also performed using different criteria that included only those without any disorder at baseline; this assessed their development of metabolic syndrome, but the number of incident cases was reduced, which decreased the power of the analyses.

A possible limitation of the present study is that the features of metabolic syndrome considered were given equal weight with generally accepted criteria. Because this study focused on the development of second features, irrespective of which had occurred first, it did not consider the predictors of specific sequences of development. The feature that occurred most often was dyslipidemia, with hypertension or diabetes occurring later. The predictors may be different for secondary development of further features in the situation where subjects develop isolated diabetes first.

A previous study of a subgroup of the cohort in the present study (28) and a 9-year follow-up study by Stevens et al. (29) of almost 13,000 African Americans and whites ages 45 to 64 years showed that the predictions of type 2

diabetes (one of the metabolic syndrome components) by BMI and by waist circumference were similar, with waist circumference being slightly stronger than BMI (28,29). Liese et al.'s (30) study of 6000 middle-aged African Americans and European Americans showed that high values of insulin, BMI, and waist-to-hip ratios were predictive of increased incidence of metabolic syndrome over 5 years.

In the present study, the proportions of subjects in the three groups based on standardized BMI cut-offs were different from the three groups based on waist circumference "Action Levels." Thus, direct comparison of these two independent variables required equal divisions. When BMI and waist circumference were both categorized by tertiles for analyses, BMI continued to show higher relative risks than waist circumference. Compared with the lowest tertile, the odds ratio of developing metabolic syndrome was increased by 3.3 (95% CI, 1.9 to 5.9) in men and 10.2 (95% CI, 5.5 to 19.0) in women with BMI in the highest tertile and 2.7 (95% CI, 1.5 to 4.7) in men and 4.6 (95% CI, 3.7 to 10.8) in women with waist circumference in the highest tertile. However, ROC analyses in the prediction of metabolic syndrome (Figure 3) showed that the areas under the curves of BMI and waist circumference were almost identical (0.74% to 0.75%). These results indicate BMI and waist circumference had similar power in the prediction of the development of metabolic syndrome.

Significant relationship between baseline fasting insulin and metabolic disorders observed in this study confirmed previous findings of Haffner et al. (11) in cohort 1 of the same San Antonio Heart Study and by Liese et al. (30) in the Atherosclerosis Risk In Community study. Multivariate analyses using baseline fasting insulin as a covariate for anthropometric prediction of metabolic disorders showed little improvement in the areas under the ROC curves. Therefore, a single indicator of either large waist circumference or high BMI is as highly predictive of the development of metabolic disorders as multiple measurements of anthropometry in combination with fasting insulin—the latter requires fasting blood specimen and biochemical analyses. The use of BMI and waist circumference has now been widely accepted as simple measures of obesity and increased central-fat distribution (3–5,19). In general, waist measurement is a practical method for self-assessment of health risks because of its ease of measurement and its simple concept of fat distribution. Changes in waist circumference are very sensitive to weight changes, and health benefits from waist reduction have been shown in relation to improved metabolic and cardiovascular risk factors (31).

These findings support international recommendations for weight management, emphasizing the importance of high BMI and large waist circumference based on standardized classifications, as an indication to seek professional

help to reduce the high health risks including metabolic syndrome. Adjustment for baseline fasting insulin levels had only a modest effect on anthropometry to predict metabolic syndrome. A single measurement of either waist circumference or BMI is as predictive of metabolic syndrome development as many measurements combined together. Standardized cut-offs for BMI and waist circumference "Action Levels" provide useful guidelines for public health promotion, to encourage self-monitoring of health risks. Above "Action Level 1," individuals are at increased health risk and should take personal steps to avoid weight gain. Above "Action Level 2," they are at a high health risk and should seek professional help.

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