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Increased Subclinical Atherosclerosis in Young Adults With Metabolic Syndrome

The Bogalusa Heart Study

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OBJECTIVES The purpose of this study was to investigate the association of metabolic syndrome (MetS) with subclinical atherosclerosis, determined by ultrasound carotid intima-media thickness (CIMT) measurements, in young adults.

BACKGROUND Metabolic syndrome is associated with subclinical atherosclerosis and increased cardiovascular risk in older and middle-aged adults; however, these associations have not been studied among young adults.

METHODS Non-diabetic subjects from Bogalusa Heart Study, a longitudinal study of atherosclerosis in young adults, underwent B-mode ultrasonography of the carotid arteries. Metabolic syndrome was defined with the National Cholesterol Education Program Adult Treatment Panel III ($MetS_{NCEP}$) and World Health Organization ($MetS_{WHO}$) definitions. CIMT and MetS associations were evaluated with multivariable regression and area under receiver-operator characteristic curve (AUC) analyses.

RESULTS Of 507 subjects (29% black, 39% male, mean [SD] age 32 [3] years), 67 (13%) had $MetS_{NCEP}$ and 65 (13%) had $MetS_{WHO}$. Common (mean = 0.70 [0.11] mm vs. 0.66 [0.08] mm, $p = 0.002$) and internal CIMT (0.72 [0.21] mm vs. 0.68 [0.12] mm, $p = 0.020$) were higher among those with $MetS_{NCEP}$ than those without $MetS_{NCEP}$. Common (0.69 [0.11] mm vs. 0.66 [0.08] mm, $p = 0.020$) and internal CIMT (0.73 [0.23] mm vs. 0.68 [0.12] mm, $p = 0.012$) also were higher among those with $MetS_{WHO}$ than those without $MetS_{WHO}$. Composite CIMT increased with the number of MetS components present ($MetS_{NCEP}$ $r = 0.997$, $p < 0.001$; $MetS_{WHO}$ $r = 0.946$, $p = 0.053$). Metabolic $syndrome_{NCEP}$ (AUC = 0.557, 95% confidence interval [CI] 0.513 to 0.601) and $MetS_{WHO}$ (AUC = 0.539, 95% CI 0.495 to 0.584) both predicted composite CIMT ≥75th percentile.

CONCLUSIONS In young adults, MetS is associated with increased atherosclerotic burden, and therefore, increased cardiovascular risk. These results support the importance of screening and early intervention in this population. (J Am Coll Cardiol 2005;46:457–63) © 2005 by the American College of Cardiology Foundation

The Third National Health and Nutrition Examination Survey recently reported a 24% prevalence of metabolic syndrome (MetS) in the U.S., accounting for an estimated 47 million affected individuals in 2000 (1). Those affected have insulin resistance with metabolic abnormalities that place them at increased risk for cardiovascular disease and increased mortality (2–5). In asymptomatic middle-aged adults, MetS also is associated with accelerated atherosclerosis (6).

Although several studies have associated the presence of atherosclerosis risk factors with subclinical atherosclerosis in younger adults, no study has specifically evaluated MetS and atherosclerosis in young adults, a population that increasingly is becoming more overweight (7–12). Finding evidence of an increased burden of subclinical and potentially reversible vascular disease in young adults would emphasize the need for heightened awareness and early treatment of MetS. Additionally, comparing available definitions from the World Health Organization ($MetS_{WHO}$) and the National Cholesterol Education Program Adult Treatment Panel III ($MetS_{NCEP}$) (13,14) might help determine the relative utility of diagnostic criteria in this age group.

Carotid intima-media thickness (CIMT), a validated method for detecting subclinical atherosclerosis and predicting cardiovascular risk, was used to investigate the relationships between MetS and subclinical atherosclerosis in

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Abbreviations and Acronyms

AUC = area under receiver-operator characteristic curve
BMI = body mass index
BP = blood pressure
CI = confidence interval
CIMT = carotid intima-media thickness
HDL-C = high-density lipoprotein cholesterol
ICA = internal carotid artery
LDL-C = low-density lipoprotein cholesterol
MetS = metabolic syndrome
NCEP = National Cholesterol Education Program
OR = odds ratio
SBP = systolic blood pressure
WHO = World Health Organization

asymptomatic young adults from the Bogalusa Heart Study, applying and comparing both $MetS_{NCEP}$ and $MetS_{WHO}$ definitions (13–15).

METHODS

Subjects and study design. The institutional review boards of the Tulane University Health Sciences Center and the University of Wisconsin approved this study. Participants provided written informed consent. The Bogalusa Heart Study is a longitudinal epidemiological study of the natural history of atherosclerosis in children and young adults in Bogalusa, Louisiana (7,11). Detailed study methods and descriptions have been described previously (7,11,16). Briefly, a subgroup of 519 subjects who were 20 to 38 years old (mean age 32 years; 29% black, 71% white; 39% men) underwent B-mode ultrasonography of the carotid arteries during the 1995 to 1996 survey (7,11). These subjects were similar to the total population (N = 1,420) in regard to race ($p = 0.92$), gender ($p = 0.72$), body mass index (BMI, $p = 0.92$), systolic blood pressure (SBP, $p = 0.20$), high-density lipoprotein cholesterol (HDL-C, $p = 0.80$), low-density lipoprotein cholesterol (LDL-C, $p = 0.52$), and triglycerides ($p = 0.26$), but, on average, were approximately four years older ($p < 0.001$) (7,11,16). In this study, subjects with diabetes mellitus (screening glucose ≥126 mg/dl or taking antiglycemic medications) or missing data necessary to determine diabetes status were excluded from further analysis (n = 12). All of the remaining 507 subjects were analyzed for the presence of $MetS_{NCEP}$ and then, in separate analysis, for $MetS_{WHO}$.

Study procedures. Study procedure protocols have been described previously (11). Subjects fasted for at least 12 h before assessments. Height and weight were measured in duplicate and averaged to calculate BMI. Waist circumference was measured midway between the rib cage and superior border of the iliac crest. Blood pressure (BP) was measured in triplicate in the right arm in a seated, relaxed position. Serum lipids were measured with a Technicon Auto Analyzer II (Technicon Instrument, Tarrytown, New York) with the standardized procedures of the Lipid Research Clinics Program (17). Plasma insulin levels were measured by radioimmunoassay (Phaadebas Insulin Kit, Pharmacia Diagnostics AB, Portage, Michigan). Plasma glucose was measured on a Beckman glucose analyzer by the glucose oxidase method.

Carotid ultrasonography. Images of common carotid, carotid bulb, and internal carotid artery (ICA) segments were recorded with a Toshiba Sonolayer SSH 160A (Toshiba Medical, Tustin, California) and a 7.5-MHz linear array transducer (11). Carotid artery segments were interrogated and measured with previously developed protocols for the Atherosclerosis Risk in Communities study (18). Certified readers conducted measurements with a semi-automated measurement program, as previously described (7). Mean values of three right and three left far-wall measurements were calculated separately for each of the three bilateral carotid segments. Right and left measurements for common carotid, carotid bulb, and ICA segments were averaged to create segmental and overall composite values.

Definition of MetS. Metabolic $syndrome_{NCEP}$ was identified when three of the following five criteria were present: 1) waist circumference >102 cm in men or >88 cm in women; 2) triglycerides ≥150 mg/dl; 3) HDL-C <40 mg/dl in men or <50 mg/dl in women; 4) BP ≥130/≥85 mm Hg or on antihypertensive medication; 5) fasting glucose ≥110 mg/dl (14). Metabolic $syndrome_{WHO}$ was identified if: 1) the insulin level was greater than the upper quartile of the study population or fasting plasma glucose ≥110 mg/dl; and 2) at least two of the following were present: a) BMI >30 kg/m^2; b) serum triglycerides ≥150 mg/dl or HDL-C <35 mg/dl for men or <40 mg/dl for women; and c) BP ≥140/90 mm Hg or on BP medication (5,13). The latter criteria were modified from the original 1999 $MetS_{WHO}$ definition and recently were shown to accurately predict incident diabetes mellitus (19,20).

Statistical analysis. Statistical analyses were performed with the SAS system (SAS Institute, Cary, North Carolina). Two-tailed Student *t* tests were performed to compare continuously distributed variables (age, glucose, insulin, lipids, waist girth, BMI, weight, SBP, diastolic BP, and CIMT) between genders and races and to compare CIMT measurements between individuals with and without MetS. Exact binomial analysis was used to compare binomial variables (presence of MetS, hypertension, hyperlipidemia, smoking, family history) (21). To correct for potentially increased type I error rates with multiple testing, the Benjamini and Hochberg (22) false discovery rate adjustment was performed.

Unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) and p values for trends of increasing MetS prevalence among increasing CIMT quintiles were formulated from Cochran-Armitage trend test models, in which CIMT quintiles were the independent variables. Subsequent adjustments for age and gender and then age, gender, race, and smoking were made to formulate adjusted OR and p values. Linear regression was used to assess the relation-

ship between number of MetS components and increasing CIMT. Multiple regression analyses with the general linear model were used to ascertain the relative impact of each component of MetS on increased CIMT. Finally, two area under receiver-operator characteristic curves (AUC) were generated, with composite CIMT ≥75th percentile as the dependent variable, and the presence of $MetS_{NCEP}$ and $MetS_{WHO}$ as independent variables in respective models. Models were then compared after deriving 95% CIs (23).

RESULTS

Baseline characteristics. Characteristics of the 507 nondiabetic subjects who underwent carotid ultrasonography are summarized in Table 1. Men had significantly higher serum glucose, LDL-C, SBP, and diastolic BP, greater waist circumference, and lower HDL-C than women. Men had a lower rate of reporting a family history of coronary artery disease. All CIMT measurements were significantly higher in men than in women, except for the ICA, which only tended to be higher (Table 1). Black subjects had higher HDL-C, SBP, diastolic BP, and composite and common carotid artery CIMT measurements, and lower total cholesterol and LDL-C than white subjects. Black subjects also were more likely to be current cigarette smokers. No significant differences between genders or races were seen in regard to age or BMI. Only 26 subjects used antihypertensive medications; black men were most likely to use these medications ($p < 0.001$).

$MetS_{NCEP}$ was present in 67 (13%) subjects, and $MetS_{WHO}$ was present in 65 (13%) subjects. There were no significant differences in the prevalence of MetS by either definition among genders or races (Table 1). Ninety-five subjects were classified as having either $MetS_{NCEP}$ or $MetS_{WHO}$; however only 37 (39%) met criteria for both. Of the 95, 28 (29%) only met criteria for $MetS_{WHO}$ and 30 (32%) only met criteria for $MetS_{NCEP}$. Subjects with $MetS_{WHO}$ and $MetS_{NCEP}$ did not differ significantly in anthropometric, hemodynamic, or metabolic characteristics (Table 2), although those with $MetS_{NCEP}$ tended to have smaller waist circumference, lower BMI, and a higher proportion of smokers and treated hypertensives than those with $MetS_{WHO}$.

Carotid wall thickness and MetS. Composite and all segmental CIMT values were significantly higher among those with $MetS_{NCEP}$ than those without (Table 3). Common and ICA CIMT also were significantly higher among those with $MetS_{WHO}$, but composite and bulb CIMT values were not.

The prevalence of $MetS_{NCEP}$ increased significantly over quintiles of composite, common carotid artery, and bulb CIMT (Table 4). These relationships remained significant even after adjusting for age, gender, race, and current smoking. For $MetS_{WHO}$, increasing common carotid artery CIMT also was associated with increasing odds of having MetS (adjusted OR 2.5, 95% CI 1.1 to 5.6, $p = 0.025$). Similar trends were observed for the ICA (adjusted OR 1.8, 95% CI 0.8 to 4.2, $p = 0.151$), but not for the bulb, so the association between prevalence of $MetS_{WHO}$ and increasing composite CIMT was

Table 1. Baseline Characteristics

	White		Black		P_{adj} (Gender)	P_{adj} (Race)
	Men	Women	Men	Women		
Age (yrs)	32 (3)	32 (3)	32 (3)	32 (2)	0.247	0.464
Glucose (mg/dl)	81 (9)	77 (8)	80 (9)	77 (10)	0.006	0.475
Insulin (μU/ml)	12 (7)	11 (7)	12 (9)	15 (21)	0.190	0.087
Lipids (mg/dl)						
Total cholesterol	204 (43)	193 (39)	189 (52)	183 (34)	0.071	0.013
Triglycerides	137 (96)	124 (163)	119 (123)	83 (45)	0.093	0.068
High-density lipoprotein cholesterol	42 (10)	52 (13)	52 (23)	57 (16)	0.006	0.006
Low-density lipoprotein cholesterol	137 (33)	122 (32)	120 (48)	114 (29)	0.006	0.006
Systolic blood pressure (mm Hg)	115 (11)	108 (11)	119 (12)	115 (15)	0.006	0.006
Diastolic blood pressure (mm Hg)	77 (9)	73 (9)	78 (10)	76 (11)	0.006	0.087
Waist circumference (cm)	95 (13)	82 (14)	90 (18)	89 (17)	0.006	0.542
Body mass index (kg/m^2)	28 (5)	27 (7)	27 (7)	30 (8)	0.277	0.120
CIMT (mm)						
Composite	0.76 (0.12)	0.71 (0.09)	0.76 (0.10)	0.75 (0.09)	0.008	0.073
Common carotid artery	0.67 (0.09)	0.64 (0.08)	0.71 (0.09)	0.69 (0.09)	0.024	0.006
Bulb	0.91 (0.22)	0.81 (0.14)	0.89 (0.18)	0.89 (0.16)	0.017	0.136
Internal carotid artery	0.71 (0.14)	0.66 (0.14)	0.71 (0.12)	0.69 (0.11)	0.056	0.464
Hypertension, n (%)	7 (5)	6 (3)	6 (10)	7 (8)	0.330	0.073
Current smoker, n (%)	45 (32)	68 (30)	35 (56)	35 (40)	0.198	0.006
Family history of coronary artery disease, n (%)	84 (59)	166 (73)	31 (49)	59 (68)	0.008	0.136
Metabolic syndrome, n (%)						
NCEP	22 (16)	29 (13)	7 (11)	9 (11)	0.568	0.464
WHO	17 (12)	28 (13)	9 (14)	11 (14)	0.989	0.648

All values expressed as mean (SD), unless otherwise noted; all p values are adjusted for multiple testing.
CIMT = carotid intima-media thickness; NCEP = National Cholesterol Education Program; WHO = World Health Organization.

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Table 2. Characteristics of Subjects With Metabolic Syndrome by NCEP Compared with WHO Criteria

	NCEP	WHO	p_{adj}
Age (yrs)	32 (2)	32 (3)	0.807
Men (%)	43	40	0.851
White race (%)	76	69	0.807
Systolic blood pressure (mm Hg)	123 (14)	121 (13)	0.807
Diastolic blood pressure (mm Hg)	84 (9)	82 (10)	0.807
Glucose (mg/dl)	83 (10)	84 (11)	0.851
Waist circumference (cm)	103 (10)	107 (13)	0.452
Body mass index (kg/m^2)	34 (5)	37 (7)	0.165
Total cholesterol (mg/dl)	211 (53)	208 (56)	0.851
High-density lipoprotein cholesterol (mg/dl)	36 (10)	38 (11)	0.807
Low-density lipoprotein cholesterol (mg/dl)	126 (37)	127 (35)	0.875
Triglycerides (mg/dl)	265 (282)	221 (276)	0.807
Current smokers (%)	31	23	0.807
Antihypertensive medication (%)	19	15	0.851

All values expressed as mean (SD), unless otherwise noted; all p values are adjusted for multiple testing.
Abbreviations as in Table 1.

not statistically significant. Nevertheless, the ability of $MetS_{NCEP}$ and $MetS_{WHO}$ to predict composite CIMT ≥75th percentile did not differ significantly ($MetS_{NCEP}$ AUC = 0.557 [95% CI 0.513 to 0.601] vs. 0.539 [95% CI 0.495 to 0.584] for $MetS_{WHO}$).

As shown in Figure 1, there was a direct relationship between the number of $MetS_{NCEP}$ components and increasing composite CIMT ($r = 0.997$, $p < 0.001$). A similar trend was observed between number of $MetS_{WHO}$ components and composite CIMT ($r = 0.946$, $p = 0.053$). The results of the multiple regression analyses that evaluated the independent and related effects of components of $MetS_{NCEP}$ on composite CIMT are shown in Table 5 ($F = 5.385$, $p < 0.001$). Increased BP was most predictive of increased composite CIMT, followed by low HDL-C. Elevated triglycerides, serum glucose, and abdominal adiposity did not independently significantly predict increased composite CIMT. Similarly, with WHO criteria, presence of elevated triglycerides or low HDL-C most strongly predicted increased composite CIMT ($F = 4.550$, $p = 0.001$). Very similar results were obtained after excluding the 26 subjects receiving antihypertensive medication (data not shown).

DISCUSSION

In this population of asymptomatic young adults, MetS, defined by either NCEP ATP III or WHO guidelines, was associated with increased common and internal CIMT; $MetS_{NCEP}$ also was associated with increased bulb and composite CIMT. These findings indicate an increased burden of subclinical atherosclerosis and suggest an increased risk of future cardiovascular events in young adults with MetS. As CIMT increased, the prevalence of MetS also increased, culminating in nearly a 2.5-fold increased likelihood of MetS in the highest quintile of common CIMT and a 3.4-fold increased likelihood of $MetS_{NCEP}$ in the highest composite CIMT quintile. The strengths of these relationships were maintained even after adjusting for age, gender, race, and current smoking. Regression analysis corroborated the strength of these associations by showing that increasing numbers of MetS components were directly associated with higher composite CIMT. Of the $MetS_{NCEP}$ components, increased BP and low HDL-C independently predicted increased CIMT; of $MetS_{WHO}$ components, high triglycerides or low HDL-C were most predictive. Both NCEP and WHO definitions identified those with more advanced subclinical atherosclerosis equally well.

Studies in middle-aged and older adults have demonstrated that MetS predicts cardiovascular disease and mortality. The Botnia Study, for instance, demonstrated that middle-aged adults with MetS have an approximately three-fold increased risk of incident coronary heart disease and more than a two-fold increased risk of stroke (4). A compelling finding was that the risk of coronary heart disease morbidity associated with MetS exceeded that associated with its individual components, suggesting that

Table 3. Carotid Intima-Media Thickness Values Among Subjects With and Without Metabolic Syndrome

	NCEP Definition			WHO Definition		
	MetS Present	MetS Absent	p_{adj}	MetS Present	MetS Absent	p_{adj}
Composite	0.78 (0.13)	0.73 (0.10)	0.002	0.76 (0.14)	0.73 (0.10)	0.125
Common carotid artery	0.70 (0.11)	0.66 (0.08)	0.002	0.69 (0.11)	0.66 (0.08)	0.020
Bulb	0.92 (0.21)	0.85 (0.17)	0.005	0.88 (0.22)	0.86 (0.18)	0.399
Internal carotid artery	0.72 (0.21)	0.68 (0.12)	0.020	0.73 (0.23)	0.68 (0.12)	0.012

All values expressed as mean (SD) mm, unless otherwise noted; all p values are adjusted for multiple testing.
MetS = metabolic syndrome; other abbreviations as in Table 1.

Table 4. Prevalence of Metabolic Syndrome* and Carotid Intima-Media Thickness

CIMT Quintiles	n (% MetS)	Odds Ratio (95% CI)		
		Unadjusted	Adjusted for Age and Gender	Adjusted for Age, Gender, Race, and Smoking Status
Composite (mm)				
≤0.66	79 (10.1)	1.00	1.00	1.00
0.67–0.70	60 (15.0)	1.30 (1.06–1.60)	1.29 (1.04–1.60)	1.35 (1.08–1.69)
0.71–0.74	68 (14.7)	1.69 (1.12–2.57)	1.67 (1.08–2.57)	1.83 (1.16–2.88)
0.75–0.79	54 (11.1)	2.21 (1.19–4.12)	2.16 (1.12–4.13)	2.48 (1.26–4.89)
≥0.80	70 (28.6)	2.88 (1.26–6.61)	2.79 (1.17–6.63)	3.37 (1.36–8.31)
p_{trend}		0.012	0.020	0.008
Common carotid artery (mm)				
≤0.59	102 (10.8)	1.00	1.00	1.00
0.60–0.63	91 (11.0)	1.24 (1.03–1.50)	1.21 (0.99–1.47)	1.25 (1.02–1.53)
0.64–0.67	110 (8.2)	1.55 (1.06–2.27)	1.47 (0.99–2.17)	1.57 (1.05–2.34)
0.68–0.73	92 (17.4)	1.94 (1.09–3.44)	1.78 (0.99–3.20)	1.96 (1.08–3.58)
≥0.74	93 (20.4)	2.42 (1.13–5.19)	2.16 (0.99–4.72)	2.46 (1.11–5.49)
p_{trend}		0.022	0.052	0.026
Bulb (mm)				
≤0.72	94 (11.7)	1.00	1.00	1.00
0.73–0.80	85 (9.4)	1.24 (1.02–1.50)	1.21 (0.99–1.48)	1.23 (1.01–1.51)
0.81–0.87	78 (16.7)	1.53 (1.04–2.25)	1.48 (0.99–2.21)	1.53 (1.02–2.29)
0.88–0.97	96 (9.4)	1.90 (1.07–3.38)	1.80 (0.98–3.28)	1.89 (1.03–3.48)
≥0.98	87 (25.3)	2.36 (1.10–5.08)	2.19 (0.98–4.89)	2.34 (1.04–5.27)
p_{trend}		0.027	0.054	0.039
Internal carotid artery (mm)				
≤0.58	79 (12.7)	1.00	1.00	1.00
0.59–0.64	95 (12.6)	1.15 (0.94–1.40)	1.12 (0.92–1.37)	1.14 (0.93–1.39)
0.65–0.69	78 (11.5)	1.32 (0.89–1.97)	1.27 (0.85–1.90)	1.30 (0.87–1.94)
0.70–0.76	82 (17.1)	1.53 (0.84–2.76)	1.43 (0.78–2.62)	1.49 (0.81–2.71)
≥0.77	78 (19.2)	1.76 (0.80–3.88)	1.92 (0.72–3.62)	1.70 (0.76–3.79)
p_{trend}		0.157	0.235	0.193

*National Cholesterol Education Program definition.
CI = confidence interval; other abbreviations as in Tables 1 and 3.

individuals with the constellation of metabolic abnormalities that characterize MetS should be targeted for aggressive primary prevention. Additionally, increased BP and dyslipidemia were the strongest predictors of vascular events (4). The present study demonstrated that the risk associations identified with MetS in middle-aged adults also are operant in young, asymptomatic adults.

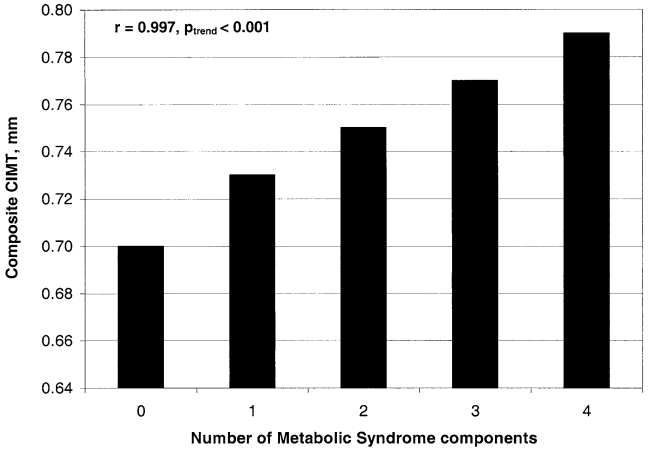

Figure 1. Effect of the number of components of metabolic syndrome* on composite carotid intima-media thickness (CIMT). *National Cholesterol Education Program definition.

To date, no studies have been published that specifically addressed the relationship between MetS and subclinical atherosclerosis in young adults, although associations between CIMT and atherosclerosis risk factors, some of which are MetS components, have been described (7–9,11,12,16,24,25). Recent reports indicated that the presence of such components in childhood are associated with increased adult CIMT (11,12). In the Bogalusa Heart Study, childhood BMI was one of the strongest predictors of increased adult CIMT (11), whereas in the Young Finns study, BMI and SBP predicted increased adult CIMT (12). In the Atherosclerosis Risk in Young Adults study of white 27- to 30-year-olds, BMI predicted common carotid artery CIMT; however, after adjustment for age, gender, and BMI, components of the MetS such as BP, triglycerides, and waist/hip ratio, did not predict CIMT (9). This study was limited because CIMT was measured only in the common carotid artery, a segment that usually lags the bulb and ICA in the development of atherosclerosis (9,26).

In the Atherosclerosis Risk Factors in Male Youngsters study of 17- to 18-year-old white men, MetS components of elevated diastolic BP and low HDL-C predicted increased CIMT (10). Body mass index was not higher in individuals with increased CIMT; however, this study was

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Table 5. Components of Metabolic Syndrome* as Predictors of Carotid Intima-Media Thickness

	Regression Coefficient	Standard Error	Standardized Coefficient	p Value
Increased blood pressure†	0.053	0.013	0.199	<0.001
Low HDL-C‡	0.030	0.010	0.145	0.006
Glucose ≥110 mg/dl	−0.142	0.103	−0.070	0.168
Triglycerides ≥150 mg/dl	0.011	0.014	0.043	0.411
Abdominal adiposity§	−0.006	0.012	−0.025	0.622

*National Cholesterol Education Program definition; †systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg or use of antihypertensive medication; ‡high-density lipoprotein cholesterol (HDL-C) <40 mg/dl (men) or <50 mg/dl (women); §waist circumference >102 cm (men) or >88 cm (women).

small and included few overweight individuals (mean body mass index 22.5 kg/m^2) (10). In the Muscatine Study, multivariate analysis showed that CIMT was associated with SBP, increasing age, and LDL-C in women and with smoking in men (27). Significant univariate correlations included BMI in men only, waist/hip ratio and triglycerides in women, but not HDL-C, glucose, or fasting insulin (27). These subjects, almost exclusively, were white; more than one-half were men >38 years old, and nearly one-half smoked cigarettes, limiting the generalizability of these data. On the basis of these previous studies, the relationships between MetS, MetS components, and CIMT could not be ascertained. Finally, MetS by modified NCEP criteria (using BMI instead of waist circumference) predicted the presence of coronary artery calcium among a population that included individuals as young as 20 years (adjusted OR 1.40, 95% CI 1.05 to 1.87, p = 0.02).(28). The mean age (52.7 [9.9] years) of the cohort, however, was notably older than in our study. Our study is the first to analyze the relationship between MetS as a diagnostic entity and subclinical atherosclerosis in young, asymptomatic adults.

Carotid intima-media thickness values were similar among those with $MetS_{NCEP}$ or $MetS_{WHO}$. The lack of a significant difference in composite CIMT between those with and without $MetS_{WHO}$ appears to have been due to the lack of a significant difference between bulb CIMT values, because common and internal carotid CIMT measurements did differ significantly. It is unclear why bulb CIMT was higher among those with $MetS_{NCEP}$ but not those in the $MetS_{WHO}$ group. One reason might be that bulb CIMT images anatomically are more difficult to obtain and measurements are more variable than in the common carotid artery; however, these issues should not have differentially affected the MetS definitions. Another consideration is that more than one-half of those meeting criteria for either $MetS_{NCEP}$ or $MetS_{WHO}$ (61%) were different subjects and those with $MetS_{NCEP}$ tended to include more smokers and subjects on therapy for hypertension, qualities that have been shown to differentially increase bulb CIMT thickness (29). Despite these differences, trends for increasing composite CIMT were associated with increasing numbers of either $MetS_{NCEP}$ or $MetS_{WHO}$ components. Additionally, both NCEP and WHO criteria identified subjects with composite CIMT ≥75th percentile equally well, thus confirming their clinical value in primary cardiovascular disease prevention and intervention.

Direct comparisons with previous studies are difficult because of differing definitions of MetS. The WHO was the first to specify diagnostic criteria in 1999; however, the practical difficulties in meeting some of the criteria, such as using the insulin clamp method to measure insulin resistance or assessing impaired glucose tolerance with oral glucose tolerance testing, have limited the use of the strict definition (13). Additionally, inclusion of microalbuminuria among the diagnostic criteria has been controversial (19,20). Subsequent groups have employed modified $MetS_{WHO}$ definitions (3–6). The NCEP definition, which was presented more recently, is based on more easily measurable components; however, it has been criticized for being less sensitive for detecting insulin resistance, which is associated with cardiovascular risk factors in the absence of MetS (30,31). Nevertheless, despite differences in criteria used between studies, associations of MetS and increased CIMT in middle-aged adults have been fairly consistent. For example, the Atherosclerosis and Insulin Resistance study showed that middle-aged white men with $MetS_{WHO}$ had increased CIMT, and the Brunek Study of middle-aged and elderly adults demonstrated that carotid atherosclerosis was significantly higher in individuals with $MetS_{WHO}$ (using a modified WHO definition) and $MetS_{NCEP}$ (3,6). Our study provides the first analysis of the impact of MetS on the anatomic burden of subclinical atherosclerosis in young, asymptomatic adults. Furthermore, it provides a comparison of the established definitions of MetS and suggests that both sets of criteria are useful for detecting subclinical atherosclerosis in this age group. This is an important area of interest, especially given the increasing prevalence of childhood obesity, insulin resistance, and predicted cardiovascular risk (32).

Conclusions. Identification of MetS in young, otherwise healthy adults is an important marker of increased subclinical atherosclerosis and, therefore, increased cardiovascular risk. The burden of subclinical atherosclerosis in young adults increases with an increasing burden of components of MetS, and increased BP and low HDL-C are especially powerful predictors of increased CIMT. Both NCEP and WHO definitions identify those with more advanced subclinical atherosclerosis equally well. Because MetS charac-

teristics and the magnitude of subclinical atherosclerosis are modifiable, they might be appropriate targets for intervention in young adults.

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