A Cross-sectional Study of Intima-Media Thickness, Ethnicity, Metabolic Syndrome, and Cardiovascular Risk in 2268 Study Participants

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OBJECTIVE: To describe the association between intima-media thickness (IMT) and metabolic syndrome (MetS) and to examine if the addition of IMT to a traditional MetS definition adds value to the assessment of predicted cardiovascular disease (CVD) risk in a large multiethnic population.

PARTICIPANTS AND METHODS: In this cross-sectional study, carotid IMT was measured in 2268 men and women as part of a wellness physical examination between August 1, 2000, and October 1, 2001. The wellness examination included a fasting lipid panel, physical examination, and medical history. Mean IMT was described by sex, ethnicity, and the MetS. Predicted risk for CVD was determined with IMT as a component of the diagnostic criteria for MetS.

RESULTS: Intima-media thickness increased with each additional component of the MetS, increasing from 0.516 mm for 0 components to 0.688 mm for 4 or more components ($P < .001$). In each ethnic group (non-Hispanic whites, blacks, Hispanics, and Asians), those with the MetS had higher mean IMT (increased by 0.084 mm to 0.134 mm) than those without MetS. The addition of IMT as a "new" component in the diagnosis of MetS allowed us to identify 78 (3.4%) participants who were not previously diagnosed as having MetS but who had a high 10-year estimated risk of MetS as measured by the Framingham risk score (11.67%).

CONCLUSION: The addition of IMT to the traditional criteria for the diagnosis of the MetS may help identify individuals who otherwise would not have been identified to be at high risk of CVD.

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ATP III = Adult Treatment Panel III; BMI = body mass index; CI = confidence interval; CVD = cardiovascular disease; HDL-C = high-density lipoprotein cholesterol; HR = hazard ratio; IMT = intima-media thickness; LDL-C = low-density lipoprotein cholesterol; MetS = metabolic syndrome; OR = odds ratio; TC = total cholesterol; TG = triglyceride; VLDL-C = very low-density lipoprotein cholesterol

Risk factors for cardiovascular disease (CVD) tend to cluster together and include age,¹⁻⁴ sex,¹⁻⁴ increased waist circumference,¹⁻⁴ atherogenic dyslipidemia,^{1,5} smoking,¹⁻⁴ hypertension,¹⁻⁵ insulin resistance and diabetes,¹⁻⁵ increased carotid intima-media thickness (IMT),^{6,7} and high levels of inflammatory markers (high-sensitivity C-reactive protein, lipoprotein-associated phospholipase A₂, myeloperoxidase).⁸⁻¹² A number of these risk factors, such as increased waist circumference, hypertension, and insulin resistance, have been defined by the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP) as the metabolic syndrome (MetS).¹³ Other organizations have developed variations on the definition of the MetS.^{2-4,14} Blaha et al¹⁵ recently recommended a simplified, evidence-based approach for diagnosing and treating patients with the MetS. However, not all experts

agree that the MetS is a syndrome that is separate from its components.¹⁶ Whether the MetS is a "unique syndrome" or whether clinicians find it useful as a unifying concept when addressing multiple treatment issues, the MetS has become a useful paradigm in clinical medicine.¹⁷ One important aspect of the MetS, regardless of definition, lies with the 1.5- to 2.0-fold increased risk of CVD and stroke mortality in patients with the MetS relative to those without the syndrome.¹⁸⁻²³

Intima-media thickness has also been consistently linked to CVD. As one of the better CVD and stroke markers,^{6,7} intima-media thickness can be measured noninvasively throughout life, yielding a risk assessment for future events.^{6,7,24-28} Intima-media thickness is an index of atherosclerosis in the vascular bed^{24,29-33} and is highly predictive of the development of atherosclerosis.³⁰⁻³² Changes in IMT were adopted as a surrogate end point for the diagnosis of atherosclerosis in randomized clinical trials designed to decrease levels of low-density lipoprotein cholesterol (LDL-C).³⁴⁻³⁷

Given the relationship of both MetS and IMT with CVD, we sought to determine if the addition of IMT to a traditional definition of the MetS would offer any advantage in CVD risk estimation. In this cross-sectional study, we evaluated a number of male and female participants of diverse ethnic origins to describe the association between the IMT and the MetS and to examine if the addition of IMT measurement to a traditional MetS definition (NCEP ATP III criteria) would add value to the assessment of CVD risk.

PARTICIPANTS AND METHODS

Study participants aged 14 to 79 years were recruited during a wellness examination at a comprehensive wellness and screening clinic in Nevada. More than 4000 self-referred patients of unknown socioeconomic status attended

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the clinic between August 1, 2000, and October 1, 2001, and were provided with an informed consent document at their first visit. The wellness examination included a medical history, physical examination, and blood tests. For the purpose of this study, IMT of the carotid artery was measured. One of 2 physicians evaluated patients, and IMT measurements were taken by one of the physicians. No selection criteria were applied to the choice of physician. Approximately half of the clinic population had IMT measurements documented (n=2443) and were eligible for this study.

IMAGE ANALYSIS

Intima-media thickness was measured within 1 cm of the carotid bulb using a Sonoline Prima High-Resolution B-mode Digital Ultrasound System (Siemens, Issaquah, WA) with a 7.5-MHz transducer in standard settings in both the right and left carotid artery. On a longitudinal 2-dimensional ultrasonographic image of the carotid artery, the near and far walls of the carotid artery are displayed as 2 bright lines separated by a hypoechoic space. The distance between the leading edge of the first bright line (lumen-intima interface) and the leading edge of the second bright line (media-adventitia interface) indicates the intima-media thickness of the far wall of the vessel. The far wall of the vessel was used because results obtained with it are reported to be reproducible.^{4,25,26} Three measurements were taken within 1 cm of the carotid bulb; however, for 4 participants only 2 measurements were taken because of distortion in the artery. The mean $\pm$ SD within-participant variation was 0.033 ± 0.182 mm³⁸ and the within-participant coefficient of variation was 10.69%.

STUDY VARIABLES

Fasting blood samples were screened using a metabolic panel, a complete blood cell count, and a lipid panel, including total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C), calculated LDL-C (TC – [TGs/5 + HDL-C]), and calculated very low-density lipoprotein cholesterol (VLDL-C) (TGs/5). If the TG level was greater than 400 mg/dL (to convert to mmol/L, multiply by 0.0113), the LDL-C value was not calculated because the linear relationship described by the already provided equation is not valid. The remaining study variables were determined from the physical examination or the medical history.

STATISTICAL ANALYSES

We excluded participants from the analysis for the reasons that follow in the order given: unknown race (n=1; IMT, 0.57 mm), unknown age (n=7; mean IMT, 0.59 mm), no fasting blood work (n=73; mean IMT, 0.57 mm), a recorded HDL-C greater than TC (n=1; IMT, 0.53 mm), extreme obesity (body mass index [BMI] >60 kg/m² [calcu-

lated as the weight in kilograms divided by height in meters squared], n=6; mean IMT, 0.54 mm), known diabetes (n=46; mean IMT, 0.80 mm), known CVD (n=25; mean IMT, 0.94 mm), unrecorded information on CVD (n=7; mean IMT, 0.68 mm), and unknown IMT (n=9). Thus, 2268 participants comprised the study population, of whom 937 (41.3%) were male and 1331 (58.7%) were female.

Participants were classified as having the MetS if they had at least 3 components of a slightly modified 2001 NCEP ATP III definition³⁴ of MetS: (1) a fasting glucose level of 110 mg/dL or greater (to convert to mmol/L, multiply by 0.0555), (2) a TG level of 150 mg/dL or greater, (3) an HDL-C level less than 40 mg/dL for men and less than 50 mg/dL for women (to convert to mmol/L, multiply by 0.0259), (4) a blood pressure of 130/85 mm Hg or greater or pharmacological treatment for hypertension, and (5) BMI greater than 28.4 kg/m² for men and greater than 27.0 kg/m² for women, as reported by Andreadis et al.³⁹ The 2001 MetS criteria were used rather than the revised 2005 MetS criteria because the 2001 version was better able to predict all-cause mortality than the 2005 version (relative risk, 1.79; 95% confidence interval [CI], 1.35-2.38 vs relative risk, 1.46; 95% CI, 1.14-1.88).⁴⁰

Study variables are described as mean $\pm$ SD and the number of participants (percentage) by ethnic group. Pairwise comparisons between non-Hispanic whites, the largest ethnic group, and each of the other ethnic groups were evaluated using a *t* test (means) or a χ^2 test (proportions). Trends in mean IMT (stratified by sex and ethnicity) were evaluated by the significance of the coefficient when regressing the number of MetS diagnostic criteria against IMT. Logistic regression was used to model the association between MetS (positive ≥ 3 MetS criteria; negative <3 MetS criteria) and IMT (continuous and categorized as less than the mean value [<0.576 mm], the mean value to 1 SD above the mean value [0.576 - 0.741 mm], and ≥ 1 SD above the mean value [>0.741 mm]) while controlling for age, sex, and ethnicity. These categories were chosen because the distribution of IMT was skewed to the right with a long tail beyond 1 SD; thus, we chose the mean and greater than or equal to 1 SD as cut points. We further stratified the model by ethnic and age groups. Trends were evaluated with the 2-sided Cochran-Armitage trend test. The variables included in the model were predictive of MetS (likelihood ratio test; $P < .001$), and the model fit the data well (Hosmer-Lemeshow goodness-of-fit test; $P = .65$). Statistical analyses were performed using SAS software (version 9.1.3; SAS Institute, Cary, NC).

RESULTS

The study population, which included people from 4 different ethnic groups, is described by demographic, metabolic,

TABLE 1. Characteristics of the Study Population by Ethnicity^{a,b}

	Non-Hispanic white (n=1542)	Black (n=175)	Hispanic (n=285)	Asian (n=266)	Total (N=2268)
Age (y)	43.0±11.4	39.0±11.3 ^c	40.0±11.3 ^c	41.0±10.5 ^d	42.0±11.4
Male, No. (%) of participants	697 (45)	58 (33) ^d	113 (40)	69 (26) ^c	937 (41)
Body mass index (kg/m ²)	27.4±5.8	28.4±6.1 ^d	28.0±5.8	23.8±4.1 ^c	27.2±5.8
History of hypertension, No. (%) of participants	96 (6)	21 (12) ^d	13 (5)	20 (8)	150 (7)
Current smokers, No. (%) of participants	454 (29)	25 (14) ^c	47 (16) ^c	47 (18) ^c	573 (25)
TC (mg/dL)	204.0±42.2	194.6±40.1 ^d	198.1±39.9 ^d	195.4±37.0 ^d	201.5±41.3
Triglycerides (mg/dL)	136.5±130.6	94.7±70.2 ^c	147.4±124.6	110.2±70.9 ^d	131.5±121.3
HDL-C (mg/dL)	53.2±15.2	57.1±15.4 ^d	49.8±12.8 ^c	57.4±14.9 ^c	53.6±15.0
LDL-C (mg/dL)	124.4±36.6	118.8±37.4	119.6±34.7 ^d	114.9±32.2 ^c	122.2±36.1
VLDL-C (mg/dL)	27.3±26.1	18.9±14.0 ^c	29.5±24.9	22.0±14.2 ^d	26.3±24.3
TC/HDL-C ratio	4.1±1.5	3.6±1.2 ^c	4.2±1.3	3.6±1.2 ^c	4.0±1.4
Non-HDL-C (mg/dL)	150.7±44.0	137.5±41.0 ^c	148.3±40.9	138.0±36.9 ^c	147.9±42.9
Blood pressure (mm Hg)					
Systolic	123.2±16.7	123.7±20.3	119.2±14.9 ^c	117.5±17.6 ^c	122.0±17.0
Diastolic	75.3±9.7	77.3±12.5 ^d	73.6±9.0 ^d	73.3±10.1 ^d	75.0±9.9
Glucose (mg/dL)	88.1±16.4	86.1±14.1	91.1±25.0 ^d	89.7±22.0	88.5±18.3
IMT (mm)	0.588±0.169	0.584±0.158	0.546±0.159 ^c	0.536±0.136 ^c	0.576±0.165

^a All data are given as mean ± SD, unless otherwise indicated. HDL-C = high-density lipoprotein cholesterol; IMT = intima-media thickness; LDL-C = low-density lipoprotein cholesterol; TC = total cholesterol; VLDL-C = very low-density lipoprotein cholesterol.

^b SI conversion factors: To convert TC, LDL-C, VLDL-C, and HDL-C values to mmol/L, multiply by 0.0259; to convert triglyceride values to mmol/L, multiply by 0.0113.

^c $P < .001$ for pairwise comparisons between non-Hispanic whites and each of the other ethnic groups.

^d $P < .05$ for pairwise comparisons between non-Hispanic whites and each of the other ethnic groups.

and clinical characteristics, as well as carotid IMT, in Table 1. Pairwise comparisons between non-Hispanic whites and each of the other ethnic groups revealed that, on average, age was slightly younger, smoking was less common, and TC was lower in the other 3 ethnic groups ($P < .05$ for all comparisons). The mean ± SD BMI for non-Hispanic whites (27.4±5.8 kg/m²), blacks (28.4±6.1 kg/m²), and Hispanics (28.0±5.8 kg/m²) was higher (in the overweight category) than that for Asians (23.8±4.1 kg/m²), whose mean BMI was in the normal category. All ethnic groups had a mean systolic and diastolic blood pressure as well as a mean fasting blood glucose level in the normal range. Lipid profiles were variable across ethnic groups but generally tended to be poorer among non-Hispanic whites and Hispanics. Levels of HDL-C were significantly higher in blacks and Asians and lower in Hispanics than in non-Hispanic whites, whereas LDL-C levels were significantly lower in Hispanics and Asians. Triglycerides and VLDL-C levels were also lower in the black and Asian groups than in non-Hispanic whites. Average IMT was significantly lower in Hispanics (0.55 mm) and Asians (0.54 mm) relative to non-Hispanic whites (0.59 mm, $P < .05$ for both), whereas blacks had an IMT (0.58 mm) similar to non-Hispanic whites.

We found a strong association between IMT and the number of components for MetS (Figure 1). Intima-media thickness increased with a corresponding increase in the

number of MetS diagnostic criteria in all participants, increasing from 0.516 mm for 0 components to 0.576 mm for 1 component, 0.593 for 2 components, 0.660 mm for 3 components, and 0.688 mm for 4 or more components ($P < .001$).

We then stratified the analysis by sex and ethnicity (Figure 2). We found 2 consistent patterns: females had

FIGURE 1. Mean intima-media thickness (IMT) by the number of components for diagnosis of metabolic syndrome. The number of participants is shown above standard error bars.

FIGURE 2. Mean intima-media thickness (IMT) by the number of components for diagnosis of the metabolic syndrome, stratified by sex and ethnicity. The number of participants is shown above the columns. None of the black female participants had 4 or more risk factors.

lower mean IMT relative to males in each ethnic group, and mean IMT increased with the increasing number of components for MetS in all sex- and ethnicity-specific subgroups ($P < .001$ for all subgroups except black males [$P = .05$], Asian males [$P = .05$], and Hispanic females [$P = .03$]). The borderline statistical significance of the pattern seen in some subgroups could be related to the small number of men and women with 3 or more components for MetS in these groups.

In this study population, 394 participants (17.4%; 214 male, 180 female) had 3 or more components for MetS (Table 2). Participants with the MetS had higher mean IMT than those without the MetS, with values ranging from 0.084 mm to 0.134 mm higher across all ethnic groups (data not shown). For the entire study population, the likelihood of prevalent MetS significantly increased for each 0.1-mm incremental increase in IMT (odds ratio [OR], 1.35; 95% CI,

1.25-1.45; $P < .001$). A similar pattern was seen with other categories of IMT relative to the referent group of less than 0.576 mm: 0.576-0.741 mm (OR, 1.85; 95% CI, 1.38-2.47) and greater than 0.741 mm (OR, 3.86; 95% CI, 2.81-5.32). When we stratified the groups by ethnicity, the association between IMT and MetS was consistent across all groups; the likelihood of prevalent MetS increased with increasing IMT. In particular, the association between IMT and MetS was strong in Hispanics and Asians (>0.741 mm relative to <0.576 mm [OR, 5.06; 95% CI, 1.92-13.37 and OR, 12.52; 95% CI, 3.24-48.42, respectively]). However, this is tempered by the fact that these were small subgroups, which could lead to some imprecision in our estimates, as noted by the wide 95% confidence intervals. In addition, there were no blacks in our study population who had prevalent MetS and IMT values between 0.576 and 0.741 mm, which limited our ability to assess the trend in this group.

TABLE 2. Association Between the Prevalence of Carotid Bulb IMT and the Prevalence of MetS by Ethnicity and Age^a

IMT (mm)	No. of participants		OR (95% CI)	P value
	MetS (+)	MetS (–)		
Total ^b				
<0.576	165	1303	1.00 (Referent)	
0.576-0.741	102	372	1.85 (1.38-2.47)	
>0.741	127	199	3.86 (2.81-5.32)	
Continuous	394	1874	1.35 (1.25-1.45)	<.001
Ethnicity				
Non-Hispanic white ^c				
<0.576	108	836	1.00 (Referent)	
0.576-0.741	78	268	1.88 (1.34-2.64)	
>0.741	97	155	3.51 (2.43-5.06)	
Continuous	283	1259	1.34 (1.23-1.46)	<.001
Black ^c				
<0.576	12	101	1.00 (Referent)	
0.576-0.741	0	34		
>0.741	9	19	2.15 (0.63-7.33)	
Continuous	21	154	1.16 (0.85-1.57)	.02
Hispanic ^c				
<0.576	38	169	1.00 (Referent)	
0.576-0.741	16	36	1.96 (0.93-4.13)	
>0.741	14	12	5.06 (1.92-13.37)	
Continuous	68	217	1.41 (1.14-1.74)	<.001
Asian ^c				
<0.576	7	197	1.00 (Referent)	
0.576-0.741	8	34	5.80 (1.86-18.12)	
>0.741	7	13	12.52 (3.24-48.42)	
Continuous	22	244	1.51 (1.12-2.04)	<.001
Age (y) ^d				
<40				
<0.576	69	731	1.00 (Referent)	
0.576-0.741	25	90	2.57 (1.52-4.37)	
>0.741	10	21	4.36 (1.90-9.99)	
Continuous	104	842	1.45 (1.23-1.71)	<.001
40-49				
<0.576	65	383	1.00 (Referent)	
0.576-0.741	34	129	1.48 (0.93-2.37)	
>0.741	42	50	4.44 (2.68-7.36)	
Continuous	141	562	1.36 (1.20-1.54)	<.001
≥50				
<0.576	31	189	1.00 (Referent)	
0.576-0.741	43	153	1.71 (1.03-2.85)	
>0.741	75	128	3.54 (2.18-5.74)	
Continuous	149	470	1.33 (1.20-1.47)	<.001

^a CI = confidence interval; IMT = intima-media thickness; MetS = metabolic syndrome; OR = odds ratio.

^b Adjusted for age, sex, and ethnicity.

^c Adjusted for age and sex.

^d Adjusted for sex and ethnicity.

Our dataset is different from that of others in that we were able to stratify the groups by age and a substantial proportion (72.71%) of our study population was in the younger age groups (<40 and 40-49 years). Regardless of the age group, the likelihood of prevalent MetS increased with increasing IMT. For the highest category (>0.741 mm) relative to the lowest category (<0.576 mm), ORs are as follows: OR, 4.36 (95% CI, 1.90-9.99) for those younger than 40 years; OR, 4.44 (95% CI, 2.68-7.36) for those aged

TABLE 3. Predicted Framingham Risk for Participants With MetS as Defined by NCEP ATP III Criteria Alone vs NCEP ATP III Criteria Plus IMT >0.741 mm^a

MetS	No. of participants	IMT (mm), mean ± SD	Average Framingham risk (%), mean ± SD ^b
No	1796	0.542±0.132	3.77±3.81
Yes, traditional definition (NCEP ATP III criteria)	394	0.669±0.198	8.63±6.71
Yes, alternative definition (traditional definition plus IMT >0.741 mm as a risk factor for MetS)	78	0.893±0.148	11.69±8.12

^a ATP III = Adult Treatment Panel III; IMT = intima-media thickness; MetS = metabolic syndrome; NCEP = National Cholesterol Education Program.

^b Framingham risk was calculated with the National Heart, Lung, and Blood Institute's Framingham cardiovascular disease risk prediction score sheets, available at <http://www.nhlbi.nih.gov/about/framingham/riskabs.htm>.

40 to 49 years; and OR, 3.54 (95% CI, 2.18-5.74) for those aged 50 years and older.

Because IMT and the MetS are both known to be related to CVD,^{18,20,30-32,41} we wanted to determine if the inclusion of the IMT measurement in the definition of MetS would add value. The addition of IMT to the traditional definition of MetS may improve our ability to identify persons at higher risk of CVD. We created a new definition of MetS by adding to the traditional definition of MetS (see Participants and Methods) a variable for IMT (>0.741 mm), such that persons who exhibit 3 or more of the MetS definition criteria (including IMT) are said to be positive for MetS. Participants were placed in 1 of 3 groups: those negative for MetS by both MetS definitions, those positive for MetS using the traditional MetS definition, and those positive for MetS using the new definition. An additional 78 individuals (3.4%) were classified as positive for MetS using the new definition (Table 3).

Using the National Heart, Lung, and Blood Institute's Framingham prediction score sheets for 10-year risk, we determined the predicted risk of CVD for each of the 3 groups. As expected, those in the traditional MetS definition group had a higher predicted risk of CVD than those that did not have MetS (8.63% vs 3.77%). However, the 78 persons (3.4%) who had MetS by the new definition that included IMT (47 males [35 non-Hispanic whites, 6 blacks, 5 Hispanics, and 1 Asian] and 31 females [22 non-Hispanic whites, 7 blacks, 2 Hispanics]) had an even higher predicted risk (11.69%). Among the white and black males, 34.3% and 33.3%, respectively, had elevated BMI and blood pressure, and 31.4% and 50.0% had elevated blood pressure and TG levels in addition to high IMT (>0.741 mm). In contrast, the most prominent components in the Hispanic males and the 1 Asian male were elevated TGs and low HDL-C (40% for the

Hispanic males). In females, the most common components were elevated BMI and blood pressure (found in 31.8% of non-Hispanic white, 85.7% of black, and 50.0% of Hispanic females). In addition, non-Hispanic white females had either elevated TG levels and blood pressure (18.2%) or elevated TG levels and BMI (18.2%). Using the traditional definition of MetS for diagnosis, these 78 persons would not have been diagnosed as having MetS and would have been assumed to be at a low risk of CVD.

DISCUSSION

Approximately 47 million US residents, one million of them adolescents, have the MetS,⁴² and these numbers may rise as obesity in the population increases. The MetS represents a clustering of easily recognized clinical conditions^{2-5,13,14} that have been related to an increased risk of heart disease and stroke.^{18,27,28} Our study evaluated a large number of relatively healthy male and female participants, 72.71% of whom were younger than 50 years, who participated in a wellness examination in an outpatient clinical setting. The prevalence of MetS in our study population was 17.4%, which was lower than that reported for some other study populations (range, 23.0%-32.2%^{26,41,43-45}). However, this is not surprising given the younger age distribution in our study population.

A strong association was observed between the carotid IMT and the number of components for the risk of developing the MetS. Participants with a known history of atherosclerotic heart disease or stroke and those with known diabetes mellitus were excluded from the analysis to determine the association of MetS and IMT in a population without pre-existing end-organ damage. Using the entire study population of 2268 persons, we found that IMT increased with each additional risk factor. Male participants were found to have higher IMT values than female participants, as seen in previous reports.^{29,32} We also found that the association of IMT and MetS was similar when the population was divided by age (<40, 40-49, ≥50 years) or by ethnic group (non-Hispanic whites, blacks, Hispanics, and Asians).

Our results are consistent with those of other studies showing that even young adults in their twenties with MetS exhibit greater carotid IMT than those without MetS,^{30,43,46,47} which presumably places them at a higher than normal risk of developing CVD compared with those without MetS. Our results are also consistent with those of Scuteri et al³² who found that those with MetS had a 16% increase in the IMT and a 32% increase in "stiffness" of the common carotid artery vs those without MetS. Similarly, Fadini et al²³ found that a higher number of MetS diagnostic criteria were associated with a higher mean carotid IMT. Gustiene et al⁴⁵ evaluated the association between cardiovascular risk fac-

tors, the MetS, endothelial function, and carotid IMT. Carotid IMT was increased in the MetS participants and correlated with increased blood pressure, waist circumference, BMI, TG level, and glucose level. Intima-media thickness values were also higher in those participants with impaired endothelial function as measured by forearm brachial blood flow studies. Interestingly, no association was found between IMT and levels of TC, LDL-C, or C-reactive protein. The findings by Gustiene et al⁴⁵ suggest that the MetS and its components might affect endothelial function and carotid IMT in the development of atherosclerosis.

Because of the cross-sectional nature of our study, we could not directly evaluate CVD risk in those with and without MetS. However, in the National Health and Nutrition Examination Survey, those with MetS had an increased risk of CVD (hazard ratio [HR], 2.02; 95% CI, 1.42-2.89) and overall mortality (HR, 1.40; 95% CI, 1.19-1.66) relative to those without MetS after adjustment for age, sex, smoking status, physical activity, and serum cholesterol levels.¹⁹ Cuspidi et al²⁶ found that IMT and cardiovascular risk were greater in hypertensive participants with MetS relative to those without MetS, regardless of age group (17-40, 41-64, and >64 years). In addition, the HR progressively increased with the presence of each additional MetS risk factor. These results suggest a strong association between MetS and CVD risk and support the use of IMT as a surrogate for assessing CVD risk.

Other studies have reported IMT as a surrogate end point for CVD with variable success. In the Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol (ARBITER) study, patients with CVD who had IMT levels in the normal range at baseline had significant reductions in IMT values with high-dose atorvastatin.⁴⁸ In contrast, neither the Ezetimibe and Simvastatin in Hypercholesterolemia Enhances Atherosclerosis Regression (ENHANCE) study³⁷ nor the Carotid Atorvastatin Study in Hyperlipidemic Post-Menopausal Women (CASHMERE)⁴⁹ noted a reduction in IMT after treatment with lipid-lowering therapy, although the expected increase in carotid IMT of 50 µm during a 24-month period was not observed in the ENHANCE study.³⁷ One possible explanation for the differences in results may be that the participants in the ENHANCE study could have been on prestudy lipid-lowering therapy, whereas such therapy was an exclusion criteria in the ARBITER study. A further reduction in IMT may not be possible if IMT values are already in the normal range after treatment with lipid-lowering therapy.³⁷

Our study found no significant difference in the IMT in non-Hispanic white participants (0.683 mm) compared with black (0.658 mm), Hispanic (0.616 mm), and Asian (0.659 mm) participants who met the definition of the MetS. The Bogalusa Heart Study reported that blacks were

more likely to have higher carotid IMT values than were whites (0.71 mm in black males vs 0.67 mm in white males).³⁰ However, values were not reported separately for those with and without MetS. One of the most important contributions of our study is the similarity of the association between the MetS and IMT within the different ethnic groups. The MetS was associated with an increase in the IMT in all ethnic groups. To our knowledge, this is the first study to assess MetS, IMT, and predicted CVD risk in a multiethnic group from the same base population.

Intima-media thickness and the MetS are known to be measures that help to identify people at higher than normal risk of cardiovascular events. Does the inclusion of IMT measurement add any value to the current definition of the MetS specified by the ATP III criteria? We added IMT as an additional variable to the ATP III MetS diagnostic criteria with a cutoff value of greater than 0.741 mm. Using this alternative definition of the MetS, we identified 78 participants (3.4%) who had fewer than 3 traditional components of MetS and IMT values 1 SD or more higher than the mean. These participants had the highest 10-year estimated risk of having a cardiovascular event (11.69%) according to the Framingham risk score, which was higher than the ATP III-defined MetS participants (8.63%) and those without MetS by both definitions (3.77%). The addition of IMT to the diagnostic criteria for MetS and the requirement that more than 3 components exist for diagnosis of MetS improved the prediction of cardiovascular risk for these patients. It is important to note that they would otherwise have been classified as negative for MetS and would therefore have been misclassified as being at low risk of CVD.

One of the limitations of this study is that it was a cross-sectional study that evaluated IMT only once, with no long-term follow-up examination of the participants to determine those who ultimately experienced a cardiovascular event (ie, myocardial infarction, stroke, hospitalization for angina or congestive heart failure, or cardiovascular death). The use of the BMI rather than waist circumference is another potential limitation to the applicability of the new definition to the MetS, although Andreadis et al³⁹ did show a significant association between BMI and waist circumference. We also had relatively small numbers of men and women who showed 3 or more of the diagnostic criteria for MetS in some of our subgroup analyses, which prevented a complete evaluation. Measures of insulin resistance, urine microalbumin, and inflammatory markers, which may have added information, were not measured in our study. Additionally, coronary artery calcium scores or levels of inflammatory markers (C-reactive protein levels) were not determined in our population because these were not widely used as significant markers of CV risk at the time of this study. A potential limitation of adding IMT measurements to the

MetS criteria is low access to the appropriate ultrasonographic equipment. However, carotid IMT is available in most radiology and cardiology offices and through third-party vendors at a cost of approximately \$100.00. Finally, because of its cross-sectional design, our study did not address improvement in patient outcomes. Our goal was to use the IMT to identify additional persons at high CVD risk who were not identified by the traditional ATP III criteria for MetS. The inclusion of IMT in the definition of MetS and the subsequent assessment of patient outcomes must be addressed in a different study. The US Preventive Services Task Force has not endorsed the use of carotid IMT screening as a criterion to be used in the diagnosis of MetS. Our study provides evidence-based data in support of the inclusion of IMT as a parameter to be evaluated in the diagnosis of MetS.

CONCLUSION

In our study population, male participants had higher IMT values than female participants on average. In participants with the MetS, no significant IMT differences were observed among the 4 ethnic groups. Intima-media thickness increased with each additional diagnostic component of the MetS observed in both sexes and in each ethnic group. The addition of the IMT as a variable to the traditional ATP III criteria for the diagnosis of the MetS identified a small but significant subgroup of participants who did not meet the traditional diagnostic criteria for the MetS, yet had a higher overall Framingham risk (11.69%) than participants without the MetS (3.84%), indicating that the inclusion of the IMT in the traditional definition of MetS increases the predictability of potential risks of cardiovascular events.

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