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Relationships between components of metabolic syndrome and coronary intravascular ultrasound atherosclerosis measures in women without obstructive coronary artery disease: the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation Study

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Abstract

Objective—In women, metabolic syndrome (MetS) is associated with higher risk of ischemic heart disease-related adverse outcomes versus individual components. We examined the relationship of MetS to subclinical coronary atherosclerosis.

Methods—Women ($n = 100$) undergoing coronary angiography for suspected ischemia but without obstructive coronary artery disease (CAD) underwent intravascular ultrasound (IVUS) of a segment of the left coronary artery. A core lab, masked to other findings, assessed IVUS measures and normalized volume measures to pull-back length. MetS [defined using ATPIII criteria (fasting glucose ≥ 100 mg/dl per revised NCEP guideline)] and its components were entered into multiple regression models to assess associations with IVUS measures.

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Conflicts of interest

Dr Noel Bairey Merz would like to declare that she worked with QMED Inc., Laurence Harbour, NJ, a commercial funder, in the context of receiving digital Holter monitors free of charge for several other Women's Ischemic Syndrome Evaluation (WISE) substudies. This has no conflict of interest with the content of this paper as no Holters were used in the methods. For the remaining authors there are no conflicts of interest.

Results—Detailed IVUS measurements were available in 87 women. Mean age was 54 ± 10 years, 36% had MetS, and 78% had atheroma. Comparing women with MetS versus without MetS, significant differences were observed for seven IVUS atherosclerosis measures, but were not significant after adjusting for the MetS components. Systolic blood pressure and waist circumference components remained independently positively associated with the IVUS measures after adjusting for age, diabetes, CAD family history, dyslipidemia, smoking, and hormone replacement.

Conclusion—In women with signs and symptoms of ischemia and no obstructive CAD, MetS is associated with coronary atherosclerosis presence and severity. However, these associations appear largely driven by components of waist circumference and systolic blood pressure versus MetS cluster. This supports the concept that MetS is a convenient clustering of risk factors rather than an independent risk predictor, and emphasizes that the critical factors for coronary atherosclerosis are potentially modifiable.

Keywords

adverse outcomes; coronary angiography; coronary artery disease; coronary atherosclerosis; intravascular ultrasound; ischemic heart disease; metabolic syndrome; risk assessment; women

Introduction

Obesity is increasing in prevalence as about seven of 10 adult Americans are either obese (BMI $> 30 \text{ kg/m}^2$) or overweight (BMI 25–29.9 kg/m^2) [1]. Among adults, the prevalence of grade 3 obesity (BMI ≥ 40) is almost double in women (8.3%) versus men (4.4%). Among women aged at least 60 years, obesity prevalence rose from 31.5% in 2003–2004 to 38.1% in 2011–2012 [2]. Obese and overweight patients, particularly women with abdominal obesity, are at high risk for developing diabetes and ischemic heart disease (IHD) [3]. Metabolic syndrome (MetS) has emerged as a health concern due to links with IHD [4], as has been described previously in the Women's Ischemic Syndrome Evaluation (WISE) [5]. Nevertheless, debate continues as to whether MetS, *per se*, is a distinct pathophysiologic entity or simply reflects an association of its component cardiovascular risk factors [6–8].

The present analysis assessed the relative contribution of MetS versus its individual components on intravascular ultrasound (IVUS) measures of coronary atherosclerosis in a cohort of women with symptoms/signs of ischemia but without obstructive coronary artery disease (CAD). The WISE is a National Heart, Lung and Blood Institute-sponsored prospective cohort study to improve the understanding of IHD in women [9]. WISE and other studies have confirmed that many women referred for coronary angiography with signs and symptoms of suspected chronic stable IHD do not have obstructive CAD – about half of these women have so-called ‘normal coronary angiograms’ [9] and the remainder have only non-obstructive CAD [10]. We and others have also found that these women, even in the absence of obstructive CAD, have an increased risk of adverse events [11–15]. The exact mechanisms responsible, however, are not completely understood.

As opposed to the angiographic luminograms, IVUS provides a more comprehensive in-vivo assessment of atherosclerotic plaque. When utilized previously, in mostly men with ‘normal’

coronary angiograms, IVUS imaging has shown evidence of subclinical atherosclerosis. It is accepted that in the majority of patients with acute coronary syndrome, the culprit vessel often has relatively minor non-flow-limiting stenosis ($< 50\%$) [16,17]. This finding has been seen more often in women than in men [18]. We previously reported that IVUS imaging, in a subset of women with ischemic symptoms and 'normal' or nonobstructive CAD, identified a high prevalence of coronary atherosclerosis [19]. The purpose of this analysis was to extend these observations to determine the impact of MetS relative to its individual components on IVUS measures of coronary atherosclerosis.

Methods

Participants

The WISE protocol, published in detail elsewhere [9], was approved by the local institutional review board at each participating center, and all women provided written informed consent. In addition, centers participating in the IVUS substudy had that protocol approved by local review boards and each participant provided additional informed consent.

Briefly, women were eligible if they were above 18 years of age and were undergoing a clinically indicated coronary angiogram as part of their regular medical care for symptoms and/or signs of myocardial ischemia. Major exclusion criteria included comorbid conditions that would compromise 1-year follow-up, pregnancy, contra-indications to provocative diagnostic testing, cardiomyopathy, New York Heart Association class IV congestive heart failure, recent myocardial infarction, significant valvular or congenital heart disease, or a language barrier to questionnaire testing. Women with prior coronary angioplasty or coronary bypass surgery were excluded for this substudy.

After baseline clinical and laboratory data collection using standardized forms, the women underwent clinically indicated coronary angiography. Candidates for this substudy were eligible if angiography showed no evidence ($< 20\%$ diameter stenosis) or minimal evidence ($> 20\%$ but $< 50\%$ diameter stenosis) of CAD. Angiograms were assessed, masked to all other clinical data, by the WISE Coronary Angiographic Core Laboratory (Brown University) using quantitative and qualitative methods as described elsewhere [20].

Acquisition and analysis of IVUS images

IVUS was used to interrogate the proximal left anterior descending (LAD) (preferred site) or circumflex coronary artery if the LAD was technically inaccessible. Following intravenous heparin and intracoronary nitroglycerin, a 30 MHz, 2.6 Fr (0.87 mm) single element beveled IVUS transducer (Ultracross; Boston Scientific Scimed Inc., Maple Grove, Minnesota, USA) was advanced into the vessel over a guidewire, and the transducer was positioned distally. An automated pull-back device progressively withdrew the transducer at a speed of 0.5 mm/s. Images were obtained at 30 frames/s, stored on videotape, and then digitized for analysis in a core laboratory (Cleveland Clinic) by individuals masked to the clinical and angiographic data [19]. Briefly, using the National Institutes of Health Image (version 1.62; National Institutes of Health public domain software, Bethesda, Maryland, USA), the operator performed a calibration by measuring 1 mm grid marks encoded in the image. The

leading edge of the lumen and the external elastic membrane (EEM) were defined with the use of manual planimetry.

As described previously [19], for each woman, EEM volume, lumen volume, atheroma volume (difference between vessel and lumen volume), percent atheroma volume, percent vessel involvement (percentage of segments analyzed that contain atherosclerosis), and atherosclerosis (defined as plaque thickness ≥ 0.5 mm) were measured. Normal reference points with plaque thickness less than 0.5 mm that were adjacent to areas of atherosclerosis were used to determine vessel tapering and to calculate an expected vessel cross-sectional area (CSA) for each 1 mm diseased segment. Vessel and lumen volumes were calculated as the sum of their respective CSAs across all segments evaluated. Similarly, total atheroma volume was calculated as the sum of the differences between the EEM and lumen areas across all segments analyzed. Percent atheroma volume was calculated as atheroma volume/vessel volume times 100. All volumes were normalized for pull-back length. For each segment, the presence of atherosclerosis was defined as a maximum plaque thickness of at least 0.5 mm by IVUS. Percent vessel involvement was defined as the number of CSAs meeting criteria for atherosclerosis divided by the total number of CSAs analyzed.

From the standardized WISE demographic data forms, women were stratified according to the presence or absence of MetS at baseline, as defined by the National Cholesterol Education Program's (NCEP) Adult Treatment Panel III criterion. Hence, participants were classified as having MetS if they fulfilled three or more of the following: (a) waist circumference of at least 88 cm (>35 inches); (b) triglycerides of at least 150 mg/dl; (c) HDL cholesterol less than 50 mg/dl; (d) blood pressure (BP) at least 130/85 mmHg; or (e) fasting glucose at least 100 mg/dl, per revised NCEP definition in concordance with American Diabetes Association criteria for impaired fasting glucose [21]. Patients with or without MetS were compared with regard to clinical characteristics and the extent of coronary atherosclerosis by IVUS measures.

Statistical methods

Statistical analysis was performed with the SAS statistical software package (version 9.3; SAS Institute Inc., Cary, North Carolina, USA). Continuous and categorical variables were expressed as mean $\pm$ SD and percentages, respectively. For univariate analysis comparing risk factors and IVUS measures in women with MetS versus without MetS, we used t-tests for continuous variables and χ^2 -analysis for categorical variables. For highly skewed variables, we show medians and interquartile ranges and used Kruskal–Wallis tests to compare differences.

For each IVUS measure, we performed stepwise forward linear regression analyses to evaluate MetS and its components as independent predictors. The MetS variables that were retained in the final model were then adjusted for other risk factors selected because they were significant univariate predictors of at least one of the IVUS measures. These included age, history of diabetes, family history of heart disease, history of dyslipidemia, ever smoking, and ever use of hormone replacement therapy. A *P*-value of less than 0.05 was considered statistically significant. Because of the small sample size, only significant independent predictors could be retained in the model.

Results

There were 154 women who consented for the IVUS substudy. Fifty-four (35%) had CAD (>50% stenosis) by on-site angiogram readings, resulting in exclusion. The remaining 100 women without obstructive CAD were enrolled, and qualitative IVUS analysis for presence of atherosclerosis (yes/no) was available in 92, whereas quantitative analysis for IVUS measures of atherosclerosis was possible in 87 women. The primary reason for not being able to obtain a satisfactory recording was that the LAD and circumflex branches originated at acute angles prohibiting safe guidewire placement, or the vessels were too small to safely manipulate the IVUS transducer.

The pertinent clinical characteristics of the 87 women are summarized in Table 1 according to MetS status. Their mean age was 54 ± 10 years. Of these, 31 (36%) had MetS and 56 did not. Over a sample pull-back length (mean 36 ± 16 mm), 19 women (21%) had no evidence of atherosclerosis (e.g. plaque thickness < 0.5 mm by IVUS). To adjust for pullbacks of differing lengths, 'normalized atheroma volume' was used in the current analyses. For the remaining 68 women (78%), the percent atheroma volume was $27 \pm 8\%$ and the mean maximum plaque thickness was 0.53 ± 0.22 mm. Figure 1 demonstrates the typical IVUS morphology in proximal LAD of a woman with no significant angiographic stenosis.

In univariate analysis, IVUS measures of atherosclerosis were consistently larger in women with MetS versus without MetS, and differences were statistically significant for 60% (six of 10) of these measures (Table 2). As MetS is a composite variable, we also examined relationships between the specific MetS components and IVUS variables. Systolic BP and waist circumference and, to a lesser extent, HDL were significantly associated with several IVUS measures (data not shown). Specifically, systolic BP was significantly and positively associated with number of lesions [β (SE) = 7.1 (2.6), $P = 0.009$], mean maximum plaque [β (SE) = 0.12 (0.05), $P = 0.011$], atheroma volume [β (SE) = 27.2 (11.5), $P = 0.020$], percentage atheroma volume [β (SE) = 0.05 (0.02), $P = 0.016$], and mean internal CSA [β (SE) = 0.83 (0.31), $P = 0.008$]. Waist circumference was positively associated with atheroma volume [β (SE) = 22.7 (10.7), $P = 0.034$], mean EEM CSA [β (SE) = 1.86 (0.75), $P = 0.015$], and mean internal CSA [β (SE) = 0.74 (0.28), $P = 0.011$]. In the final multiple regression models, the association between MetS as a cluster and IVUS components became nonsignificant. However, after model adjustment, two components of MetS, systolic BP and waist circumference, were significantly and strongly associated with several IVUS measures of atherosclerosis and plaque burden (Table 3).

In addition, given the significant cross talk between diabetes and MetS, a sensitivity analysis excluding the women with diabetes (29% of the total cohort) was also conducted. Consistent with the prior analyses that included diabetes, women with MetS continued to have worse risk factors compared with those without MetS even though most of these differences (except BMI) did not reach statistical significance. Not surprisingly, the exceptions were those risk factors used to classify MetS. When excluding the women with diabetes, the women with MetS still had consistently higher IVUS measures, although the P -values were attenuated because of smaller numbers and high standard deviation resulting in diminished statistical power (Table 4).

Discussion

To the best of our knowledge, the current study is the first to analyze the relationship between MetS, its components and IVUS-derived measure of atherosclerotic burden in women with suspected ischemia, but without obstructive CAD. The major findings of our study follow: (a) the relationship between the MetS cluster and IVUS measures of coronary atherosclerosis is not significant in a multiple regression model, suggesting that the relationship is largely driven by individual MetS components rather than the cluster. These findings support our hypothesis that the MetS is a convenient clustering of risk factors, rather than a novel or an independent risk predictor. (b) Systemic hypertension was an independent predictor of IVUS-measured disease burden (as defined by number of lesions, percentage of lesions, atheroma volume, and percentage atheroma volume). (c) Larger waist circumference (i.e. abdominal obesity) was associated with EEM, internal elastic membrane, and luminal expansion, suggesting positive or adaptive remodeling. (d) In contrast, several risk factors, including diabetes/hyperglycemia and dyslipidemia (high-LDL cholesterol and low-HDL cholesterol), appeared less important than expected.

In recent years, investigators have used IVUS to study the correlation between the MetS and the morphological characteristics of atherosclerotic plaques with variable results [22–25]. These studies largely focused on patients who had, or were undergoing, coronary intervention for severe obstructive CAD. The results from our study have important implications for understanding the relationship between MetS and major adverse cardiac events in this specific at-risk patient population. The concept of MetS evolved from the observation of a clustering of risk factors for CAD and diabetes in patients with abdominal obesity [26]. However, it has not been conclusively shown that the impact of the syndrome cluster exceeds that of the sum of its parts. Several studies have shown that adverse outcomes appear to be driven by the presence of the individual risk factors [7,8,27]. Our current results, in a sample of WISE women using invasive imaging to characterize the association between MetS and atherosclerotic coronary disease burden, are in line with those findings. Although in a univariate model several IVUS parameters were found to be significantly associated with presence of MetS, this association was lost in the subsequent multivariate model. Hypertension and waist circumference were observed to be the main variables associated with IVUS measures of CAD burden.

The interaction of CAD and hypertension is well established in both women and men, among those with and without known vascular disease [28]. Others have shown in prospective studies that the effectiveness of BP-lowering treatments does not depend on starting BP level, but depends on the individual risk factors [29]. It is therefore not surprising that, in this patient population, higher systolic BP was associated with greater disease burden as defined by IVUS. Similarly, demonstration of greater mean internal elastic lamina in patients with higher systolic BP is likely a response to pathologic remodeling.

Abdominal obesity is a key component of the MetS and a marker of dysfunctional adipose tissue that has been shown to independently predict CAD mortality in women [30]. Adipose tissue is known to be a major endocrine organ that secretes a variety of bioactive substances, termed adipocytokines [30]. Adipocytokine secretion profiles are altered as obesity

develops, which may increase the risk of obesity-related cardiovascular disorders. Leptin, an adipocytokine up-regulation in obese individuals, has also been shown to play an important role in the pathophysiology of obesity-related atherogenesis through multiple mechanisms, such as its proinflammatory, prothrombotic, prooxidant, and proliferative effects. Similarly another adipocytokine, adiponectin down-regulation, leads to vascular remodeling and plaque destabilization among other atherogenic effects. Patients with excess of visceral adiposity have elevated plasma C-reactive protein concentrations accompanied by elevated interleukin-6 and tumor necrosis factor- α levels [31,32]. It has been shown that visceral adiposity is associated with positive remodeling, low-attenuation noncalcified plaques, and spotty calcification. All of these are characteristic of early proliferative lesions, allowing considerable plaque accumulation despite normal luminal size. These early plaques may be particularly vulnerable to rupture, leading to acute coronary syndrome in the setting of modest luminal stenosis [33,34]. Approximately 20% or more of women presenting with acute coronary syndrome have normal or non-obstructive CAD by angiography, yet these women have an increased risk of death or myocardial infarction at 30-day follow-up [18].

In addition, a pooled analysis of 97 cohort studies (with 1.8 million patients) showed that being overweight and obese is incrementally associated with higher risk of CAD and strokes. The hazard ratio for each 5 kg/m² higher BMI was 1.27 (95% confidence interval 1.23–1.31) for coronary heart disease and 1.18 (1.14–1.22) for stroke after adjustment for confounders. The analysis showed that this risk is driven by the metabolic mediators BP, cholesterol, and glucose. Interestingly, of these, BP was the most important mediator, accounting for 31% (28–35) of the excess risk for coronary heart disease and 65% (56–75) for stroke [35].

The absence of a strong association between HDL levels and IVUS measures of disease burden requires additional comment. Although HDL levels were predictive in univariate analysis, in a multiple regression model this association did not persist. Although some prior studies have shown HDL cholesterol concentration to be a strong predictor of coronary heart disease risk in women [36–38], current evidence shows otherwise. As indicated by recently published cholesterol guidelines, adding one or more nonstatin drugs to high-intensity statin therapy will not provide incremental cardiovascular disease risk reduction benefit with an acceptable margin of safety, suggesting that most likely HDL cholesterol is not a significant risk factor that merits intervention to reduce cardiovascular events [39]. Similarly, AIM-HIGH showed a lack of benefit of adding niacin in individuals with low-HDL cholesterol and high triglycerides, and ACCORD demonstrated the futility of adding fenofibrate in persons with diabetes [40–43]. Therefore, an association between HDL/triglyceride values and IVUS-defined CAD burden in the current analysis suggests an interaction of multiple complex mechanisms that drive atheroma accumulation.

As expected, there were significantly more diabetics in the MetS group versus the non-MetS group. Diabetes is known to confer higher risk of CAD in women than men (4–6- vs. 3–4-fold), a poorer prognosis after myocardial infarction, and a higher risk of death from cardiovascular disease [44]. However, we did not observe a significant correlation with fasting glucose, either when used as a categorical or continuous variable. Whereas older studies have suggested a diabetes-associated cardiovascular disease risk similar to that

observed among nondiabetic patients with a prior myocardial infarction (e.g. CAD risk equivalent), more recent trials suggest a substantially lower risk, likely due to improved effectiveness of contemporary antidiabetic and lipid therapies [45,46].

Our study has some limitations. First, the findings are based on a small cohort of women. Therefore, we cannot exclude the possibility that our study may lack power to demonstrate the interaction of dyslipidemia and fasting glucose with IVUS atherosclerosis measures. Second, IVUS examination was limited to only a small proximal portion of the left coronary distribution, and this sampling limitation is likely to underestimate the true prevalence of atherosclerosis in this cohort. Third, we did not include information about hemoglobin A1C, as most were well controlled diabetic patients, contributing to the lack of association of diabetes status with atherosclerosis burden. Furthermore, all participants were likely to be somewhat glucose intolerant.

In summary, although the presence of atherosclerosis was observed in these women with MetS, this appears to be driven predominantly by individual components rather than the presence of the syndrome, *per se*. MetS as a cluster merely highlights presence of multiple atherogenic risk factors in an individual woman. This association appears to be largely driven by abdominal obesity and systolic BP.

Others have documented that intensive risk modification was as effective in causing plaque regression in women as in men: in women, substantial regression (defined as 5% reduction in atheroma volume vs. baseline) was observed with lowering of LDL cholesterol to less than 80 mg/dl, systolic BP less than 120 mmHg, and C-reactive protein less than 2 mg/l [47]. These data suggest important targets for potential therapeutic intervention to more effectively reduce risk in women. Our findings also emphasize the importance of focusing on BP control and weight management, as opposed to HDL/triglyceride management.

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Fig. 1.

Left coronary angiogram (top) and left anterior descending coronary artery (LAD) intravascular ultrasound images (bottom) from a 65-year-old woman with metabolic syndrome. Note plaque in the proximal LAD with maintenance of the lumen area. EEM, external elastic membrane.

Table 1Pertinent risk factors by metabolic syndrome status (means $\pm$ SD, unless specified otherwise)

	No MetS (<i>n</i> = 56)	MetS (<i>n</i> = 31)	<i>P</i> -value
Non-MetS risk factor			
Age (years, mean $\pm$ SD)	53 $\pm$ 9	55 $\pm$ 11	0.41
BMI (mean $\pm$ SD)	28.7 $\pm$ 7.0	38.6 $\pm$ 8.1	<0.0001
History diabetes (%)	5	29	0.007
Family history of CAD (%)	43	48	0.62
History dyslipidemia (%)	34	55	0.058
Ever smoker (%)	43	48	0.62
Ever HRT use (%)	46	55	0.45
MetS components (mean $\pm$ SD)			
Triglycerides (mg/dl) (IQR)	46 (32–73)	131 (72–160)	–
HDL cholesterol (mg/dl)	53 $\pm$ 14	42 $\pm$ 8	–
Systolic blood pressure (mmHg)	122 $\pm$ 16	138 $\pm$ 21	–
Diastolic blood pressure (mmHg)	72 $\pm$ 9	79 $\pm$ 12	–
Glucose (mg/dl)	95 $\pm$ 28	110 $\pm$ 34	–
Waist circumference (inches)	34 $\pm$ 5	43 $\pm$ 5	–
Other lab values (mean $\pm$ SD)			
Hemoglobin	12.7 $\pm$ 1.5	12.9 $\pm$ 1.5	0.66
LDL cholesterol	110 $\pm$ 32	106 $\pm$ 24	0.48
Non-HDL cholesterol	123 $\pm$ 35	133 $\pm$ 29	0.16

CAD, coronary artery disease; HRT, hormone replacement therapy; IQR, interquartile range; MetS, metabolic syndrome.

Table 2

Association between IVUS measures and metabolic syndrome (univariate analysis)

IVUS measure	No MetS (<i>n</i> = 56)	MetS (<i>n</i> = 31)	Age-adjusted <i>P</i> -value
Number of lesions	10.1 ± 11.0	15.0 ± 14.7	0.12
Lesions (%)	26.6 ± 27.9	36.3 ± 32.1	0.21
Mean maximum plaque thickness (mm)	0.42 ± 0.19	0.55 ± 0.26	0.014
Luminal volume	336 ± 110	376 ± 131	0.13
EEM volume	432 ± 128	512 ± 167	0.018
Atheroma volume	100 ± 46	138 ± 63	0.004
Atheroma volume (%)	23.5 ± 9.8	26.8 ± 8.2	0.19
Mean luminal CSA	9.2 ± 2.9	10.6 ± 3.0	0.035
Mean EEM CSA	12.0 ± 3.2	14.5 ± 3.8	0.002
Mean internal CSA	2.8 ± 1.2	3.9 ± 1.7	0.0006

CSA, cross-sectional area; EEM, external elastic membrane; IVUS, intravascular ultrasound; MetS, metabolic syndrome.

Table 3

Relationships of MetS cluster and MetS components with IVUS anatomy (multivariate analysis)

IVUS measure	MetS cluster β (SE), <i>P</i>	Significant MetS component(s) ^a	β (SE), adjusted <i>P</i> -value
Number of lesions	3.28 (2.76), 0.24	Systolic BP	2.64 (0.65), 0.0001
Lesions (%)	0.04 (0.06), 0.50	Systolic BP	0.049 (0.015), 0.002
Mean maximum plaque thickness	0.10 (0.05), 0.037	Systolic BP	0.04 (0.01), 0.0002
Atheroma volume	27.3 (11.5), 0.020	Systolic BP	9.6 (2.9), 0.001
Atheroma volume (%)	0.02 (0.02), 0.30	Systolic BP	0.014 (0.005), 0.005
Mean internal EM CSA	0.88 (0.31), 0.005	Systolic BP	0.25 (0.07), 0.001
		Waist circumference	0.06 (0.02), 0.007
Mean luminal CSA	1.48 (0.70), 0.037	Waist circumference	0.13 (0.05), 0.013
Mean EEM CSA	2.36 (0.82), 0.006	Waist circumference	0.20 (0.06), 0.0009
Lumen volume	43.1 (27.8), 0.12	Waist circumference	4.10 (2.01), 0.04
EEM volume	75.7 (34.0), 0.024	Waist circumference	7.05 (2.43), 0.005

BP, blood pressure; CSA, cross-sectional area; EEM, external elastic membrane; EM, elastic membrane; IVUS, intravascular ultrasound; MetS, metabolic syndrome.

^a Systolic blood pressure analyzed in units of 10; waist circumference in inches.

Table 4

Relationships of MetS cluster and MetS components with IVUS anatomy excluding the women with diabetes

IVUS measure	MetS cluster β (SE), <i>P</i> (unchanged)	Significant MetS component(s) ^a	β (SE), adjusted <i>P</i> -value
Number of lesions	1.98 (2.96), 0.51	Systolic BP	2.68 (0.73), 0.0005
Lesions (%)	0.001 (0.07), 0.99	Systolic BP	0.044 (0.017), 0.013
Mean maximum plaque thickness	0.06 (0.05), 0.22	Systolic BP	0.04 (0.01), 0.002
Atheroma volume	12.0 (10.7), 0.27	Systolic BP	7.58 (2.77), 0.008
Atheroma volume (%)	-0.003 (0.02), 0.87	Systolic BP	0.012(0.005), 0.021
Mean internal EM CSA	0.50 (0.28), 0.08	Systolic BP	0.24 (0.07), 0.002
		Waist circumference	0.025 (0.028), 0.21
Mean luminal CSA	1.36 (0.74), 0.07	Waist circumference	0.10 (0.06), 0.07
Mean EEM CSA	1.86 (0.85), 0.032	Waist circumference	0.14 (0.06), 0.028
Lumen volume	32.4 (28.4), 0.26	Waist circumference	2.48 (2.12), 0.24
EEM volume	50.9 (34.1), 0.14	Waist circumference	4.05 (2.54), 0.12

BP, blood pressure; CSA, cross-sectional area; EEM, external elastic membrane; EM, elastic membrane; IVUS, intravascular ultrasound; MetS, metabolic syndrome.

^a Systolic blood pressure analyzed in units of 10; waist circumference in inches.