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ORIGINAL RESEARCH

Association Between Measures of Body Composition and Coronary Calcium: Findings From the Multi-Ethnic Study of Atherosclerosis

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BACKGROUND: Obesity, as measured by body mass index, is widely recognized as a risk factor for the development of cardiovascular disease. However, the role of body composition components such as fat and lean mass is not well studied.

METHODS AND RESULTS: A total of 3129 patients who underwent computed tomography scans for quantification of coronary artery calcification and had bioelectrical impedance analysis of body composition (fat mass and fat-free mass) during exam 5 of MESA (Multi-Ethnic Study of Atherosclerosis) were included in this cross-sectional analysis. Multivariable adjusted linear regression analysis was performed to assess the relationship between both fat mass and fat-free mass to prevalent coronary artery calcification, a marker of subclinical coronary artery disease quantified by both the coronary artery calcification (CAC) Agatston score and the spatially weighted calcium score. CAC and spatially weighted calcium score were natural log–transformed for analysis as continuous variables. Fat-free mass, but not fat mass, was independently associated with CAC. There was a 7.6% prevalence risk difference for CAC>0 per 10 kg. Fat-free mass was also significantly associated with natural log of CAC (coefficient=0.272, P<0.001). Both fat-free mass and fat mass were positively associated with natural log of spatially weighted calcium score, with risk difference coefficients of 0.729 and 0.359, respectively (P<0.001).

CONCLUSIONS: In this cross-sectional study, higher lean mass by bioelectrical impedance analysis and, to a lesser extent, higher fat mass by bioelectrical impedance analysis were significantly associated with higher coronary calcium, a marker of subclinical cardiovascular disease. Further exploration of the relationship between components of body composition and the development of cardiovascular disease is warranted.

Key Words: body composition ■ coronary calcium ■ obesity

Overweight and obesity are prevalent in the United States and considered important risk factors for the development of cardiovascular disease (CVD).[1,2] Body mass index (BMI) is the most commonly used anthropometric measure to assess obesity and is recommended by major CVD guidelines for obesity screening.[3,4] Overweight and obesity are defined by BMI levels of 25 to 29.9 and ≥30 kg/m^2, respectively, and both increase the risk of developing hypertension, dyslipidemia, and diabetes[5] and incident CVD.[6,7] However, some studies have shown that increased BMI may not be associated with developing CVD, particularly in patients without risk factors such as hypertension, high cholesterol, or elevated blood glucose.[8,9] One hypothesis to explain this inconsistent relationship between BMI and CVD incidence is that BMI cannot discriminate between fat and muscle mass as well as the distribution or quality of body fat; all of which have important implications for cardiovascular health.[2,10,11] As noted in the most recent American Heart Association statement on obesity, waist

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CLINICAL PERSPECTIVE

What Is New?

- This cross-sectional analysis of MESA (Multi-Ethnic Study of Atherosclerosis) is the first to assess the relationship between body composition (fat and lean mass) as assessed by bioelectrical impedance analysis and the presence or level of coronary artery calcification, a marker of subclinical cardiovascular disease.
- Higher fat-free mass and, to a lesser extent, higher fat mass were significantly and independently related to the presence and higher levels of coronary calcium.

What Are the Clinical Implications?

- Measuring body composition by body composition scales using bioelectrical impedance analysis may be a better method of assessing obesity in the context of assessing cardiovascular disease risk compared with the commonly used body mass index.
- A body composition consisting of excess fat-free mass or lean mass may predispose to the development of cardiovascular artery disease; further research is needed in this area.

Nonstandard Abbreviations and Acronyms

BIA	bioelectrical impedance analysis
lnCAC	natural log of coronary artery calcification
MESA	Multi-Ethnic Study of Atherosclerosis
SWCS	spatially weighted calcium score
WC	waist circumference

circumference (WC) and waist-to-hip ratio are anthropometric measures that are more highly correlated with the presence of visceral adiposity and also have been shown to be better predictors of myocardial infarction compared with BMI.[1,12,13] Therefore, it is unclear whether BMI is an acceptable form of measurement for assessing CVD risk.[14,15]

The study described next assessed how fat mass and fat-free mass from bioelectrical impedance analysis (BIA), as well as waist and hip circumferences, are associated with prevalent coronary artery calcification (CAC) score. CAC is a well-established CVD risk marker and feasible measure of subclinical coronary artery disease.[16,17] We hypothesized that higher fat mass, as measured by BIA, and higher visceral adiposity, as reflected in WC,[3] would be associated with higher CAC, whereas higher fat-free mass by BIA would be associated with lower CAC.

METHODS

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure because of participant privacy issues. However, investigators interested in analyzing MESA (Multi-Ethnic Study of Atherosclerosis) data may contact the MESA Coordinating Center at the University of Washington or use the National Heart, Lung, and Blood Institute Biologic Specimen and Data Repositories Information Coordinating Center repository.

Study Design and Population

The MESA has been previously described.[18] In brief, between July 2000 and August 2002 (exam 1), 6814 men and women, without clinically apparent CVD, aged between 45 and 84 years, and identified as non-Hispanic White race and ethnicity, Black race, Hispanic ethnicity, or Chinese American race were recruited from the following 6 US communities: Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; Northern Manhattan and the Bronx, New York; and St. Paul, Minnesota. At exam 1, all participants provided informed consent, and all procedures were approved by the institutional review boards of each field center.

Data used in this analysis were collected at exam 5 (n=4655, 2010–2011).[19] Questionnaires were used to assess age, sex, race and ethnicity, education and income levels, occupational information, smoking status, medical history, physical activity, and medication use for diabetes, lipid lowering, and/or hypertension.

Body weight, height, WC, and hip circumference were measured to the nearest 0.5 kg, 0.1 cm, and 0.1 cm, respectively. Body mass index (BMI) was calculated as weight (kilograms) divided by height (meters) squared. WC was measured using a steel measuring tape (standard 4-oz tension) from midway between the last rib and the iliac crest at normal breathing. Hip circumference was measured from the largest diameter of the hip. Blood pressure was measured in the seated position 3 times at 1-minute intervals using an appropriately sized cuff and following a standardized protocol. The average of the last 2 measurements was used for analysis. A central laboratory (University of Vermont, Burlington, Vermont) measured levels of total and high-density lipoprotein cholesterol, triglycerides, plasma glucose, and glycosylated hemoglobin (hemoglobin A1c). Diabetes was defined as being on treatment with insulin or oral medication for diabetes or

fasting glucose ≥126 mg/dL; the variable was divided into the following 4 categories: no diabetes, impaired fasting glucose, untreated diabetes, and diabetes.[20]

Body Composition Assessment

The Valhalla BCS-2 Body Composition Scale was used to obtain body composition measurements using BIA. Participants were asked to remove shoes and socks for this procedure and instructed to stand on the middle of the platform of the balance scale. The participants were then asked to grip the metal handles on each side of the Body Composition Scale device and remain in this position until results were analyzed in a few seconds. Using a calibration system internal to the impedance scale, an output of total body fat (kilograms), fat-free mass (kilograms), and total body water (liters) were recorded and printed.

Coronary Calcium Scans

CAC scores were obtained from chest computed tomography (CT) scans on a subset of participants (MESA AIR study of pollution) during MESA exam 5. Images were interpreted at the MESA CT reading center (Los Angeles Biomedical Research Institute at Harbor—University of California Los Angeles, Torrance, CA). The CAC was calculated using the Agatston method and spatially weighted calcium score (SWCS).[21] For the Agatston score, images were calibrated using a calcium phantom to control for variability between scanners. Participants were scanned twice, and CAC was reported as the average Agatston CAC[22] score, with phantom-adjusted values used. The intra- and interobserver agreements were κ=0.93 and 0.90, respectively. A representative CT scan image from MESA used for calcium scoring is shown in the .

An alternative method of quantifying coronary calcium, the SWCS, has been used in previous MESA analyses to assign scores to those with CAC=0.[23] SWCS has been shown to align well with the Agatston CAC score for those with CAC>0 and also to correlate with cardiovascular outcomes.[24] SWCS is first computed using the set of voxels that were identified by the MESA CT reader as representing the coronary arteries. A weight was then assigned to each voxel using a weighting function with parameters derived from the scan's phantom. Voxels were assigned scores based on weight assigned to it and its neighboring voxels. The SWCS uses surrounding information to increase accuracy by assigning a higher score to voxels with neighboring voxels that had high attenuation levels and assigning a lower score to those with low attenuation-level neighbors.[21,23]

Statistical Analysis

This is a cross-sectional analysis of exam 5 data. Characteristics of the cohort contrasting participants with 0 CAC to those with CAC>0 are shown in Table 1. Linear regression analysis was performed to assess the relationship between both fat mass and fat-free mass (per 10 kg) to prevalent coronary calcium. The following 3 outcomes were assessed: CAC score>0 (yes/no), CAC scores>0 as a continuous variable analyzed using the natural log of CAC (lnCAC), and SWCS as a continuous variable analyzed using the natural log of SWCS. Linear regression was used to model the outcome variables.

For CAC=0, compared with CAC>0, linear regression was used because the prevalence risk difference (eg, the difference in the risk for a 1-unit change in the risk factor) is the quantity of most importance medically. The coefficients of this model estimate the prevalence risk difference. In addition to unadjusted analyses, 2 adjusted linear regression analyses were performed: a minimally adjusted model (age, race and ethnicity, sex) and a fully adjusted model. For each fully adjusted model, the final set of included covariates were chosen by backward elimination. Fat mass and fat-free mass were included in the model even if they were nonsignificant. Selection using backward elimination was carried out by sequentially dropping variables that were nonsignificant at each step using P<0.05 as significant. Variables tested for inclusion in the final model included age, sex, race and ethnicity, smoking history, cholesterol levels, high-density lipoprotein cholesterol levels, lipid-lowering medications, diabetes status, systolic

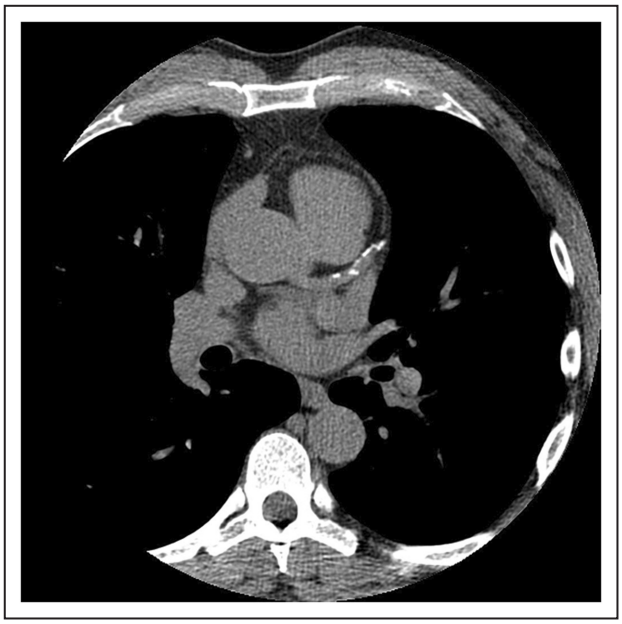

Figure. Representative computed tomography slice from MESA (Multi-Ethnic Study of Atherosclerosis) used for the calculation of the coronary artery calcification score with the Agatston method.
Calcium is noted in the left coronary artery.

Table 1. Baseline Characteristics of the Study Cohort at Exam 5

	Total cohort, N=3129	CAC=0, n=974	CAC>0, n=2155
CAC, Agatston score, mean (SD)	275.6 (570.2)	0	275.6 (570.2)
lnCAC, mean (SD)	4.8 (1.8)	…	4.8 (1.8)
SWCS, mean (SD)	295.7 (166.5)	56.7 (166.5)	403.5 (662.4)
lnSWCS, mean (SD)	3.9 (2.6)	1.6 (2.8)	4.9 (1.7)
Fat-free mass by BIA, kg, mean (SD)	51.3 (11.9)	49.5 (10.9)	52.2 (12.2)
Fat mass by BIA, kg, mean (SD)	24.9 (10.8)	24.9 (11.5)	24.9 (10.5)
Age, y, mean (SD)	69.4 (9.2)	64.8 (7.9)	71.5 (9.0)
Race and ethnicity, n (%)			
White participants	1236 (40)	321 (33)	915 (42)
Chinese American participants	369 (12)	122 (13)	247 (11)
Black participants	837 (27)	296 (30)	541 (25)
Hispanic participants	687 (22)	235 (24)	452 (21)
Sex, n (%)			
Female	1660 (53)	663 (68)	997 (46)
Male	1469 (47)	311 (32)	1158 (54)
Cigarette smoking, n (%)			
Never	1409 (45)	521 (54)	888 (41)
Former	1460 (47)	370 (38)	1090 (51)
Current	243 (8)	79 (8)	164 (8)
Total cholesterol, mg/dL, mean (SD)	183.0 (36.9)	190.7 (35.1)	179.5 (37.2)
HDL cholesterol, mg, mean (SD)	55.6 (16.7)	57.9 (16.7)	54.6 (16.6)
Lipid-lowering medication, n (%)			
No	1915 (61)	749 (77)	1166 (54)
Yes	1214 (39)	225 (23)	989 (46)
Diabetes categories, n (%)			
No	1837 (59)	661 (68)	1176 (55)
Impaired glucose	667 (21)	176 (18)	491 (23)
Untreated diabetic	53 (2)	12 (1)	41 (2)
Treated diabetic	558 (18)	118 (12)	440 (20)
Systolic blood pressure, mm Hg, mean (SD)	124.1 (20.66)	120.7 (20.1)	125.7 (20.7)
Diastolic blood pressure, mm Hg, mean (SD)	68.5 (10.0)	68.6 (9.9)	68.4 (10.0)
Antihypertension medication, n (%)			
No	1404 (45)	588 (60)	816 (38)
Yes	1725 (55)	386 (40)	1339 (62)
Waist circumference, cm, mean (SD)	99.4 (14.3)	97.0 (14.6)	100.5 (14.0)

BIA indicates bioelectrical impedance analysis; CAC, coronary artery calcification; HDL, high-density lipoprotein; lnCAC, natural log of coronary artery calcification; lnSWCS, natural log of spatially weighted calcium score; and SWCS, spatially weighted calcium score.

blood pressure, diastolic blood pressure, antihypertension medications, WC, hip circumference, height, BMI, and amount of moderate to vigorous physical activity. Robust standard errors were used in computing the *t* tests for the coefficients.

Interactions by sex and race and ethnicity were tested separately. Because of the large number of interactions being tested, Bonferroni correction for multiple testing was used, and no interaction term was found to be significant. To test for nonlinear relationships of fat-free mass and fat to CAC>0, CAC, and SWCS, regression splines (MVRS function in STATA) were calculated, and no significant deviations from linearity were seen. All analyses were carried out using STATA 17.[25]

RESULTS

Of the 4655 participants available from MESA exam 5, a total of 3129 participants completed CT scans for coronary calcium and were included in this analysis. The baseline characteristics of the cohort, and for the

cohort stratified by the presence (CAC>0) or absence (CAC=0) of CAC by Agatston score, are summarized in Table 1. Of the cohort, 53% were women with a mean age of 69±9 years. A total of 974 participants had a CAC by Agatston score of 0, and among those, the mean SWCS was 56.68±166.47.

The correlation coefficient between fat-free and fat mass was 0.186. In unadjusted regression for the presence of CAC as well as unadjusted analyses for CAC as a continuous variable (lnCAC), fat-free mass was significantly and positively associated with the presence of CAC>0 and positively associated with lnCAC (P<0.0001 for both). On the other hand, fat mass had no significant association with CAC presence or CAC Agatston score (Tables 2 and 3). In unadjusted regression analyses, both fat-free and fat mass were significantly and positively associated with higher SWCS, with a prevalence risk difference of 0.565 and 0.346, respectively (P<0.0001; Table 4).

Minimally adjusted regression models revealed that higher fat-free mass and higher fat mass were both associated with the presence of CAC (P<0.05) and higher lnCAC (P<0.05 fat mass, P=0.06 fat-free mass) and natural log of SWCS (P<0.0001) (column 2 of Tables 2 through 4). Older age and male sex were also associated with the presence of CAC as well as higher CAC and SWCS in these minimally adjusted models (all P<0.0001).

The fully adjusted linear regression models are shown in the final column of Tables 2 through 4. Higher fat-free mass remained associated with higher likelihood of CAC presence, higher CAC Agatston score, and higher SWCS in the fully adjusted models (all P<0.01). Conversely, fat mass was not significantly associated with CAC presence or score (lnCAC). However, in the fully adjusted regression model assessing the natural log of SWCS as an outcome, higher fat mass was significantly associated with higher SWCS, with a risk difference of 0.359 (P<0.001). The anthropometric indexes of obesity, BMI, WC, and hip circumference were not associated with CAC in the fully adjusted models except for weak associations between higher WC and higher SWCS, with a prevalence risk difference of 0.196 (P<0.01), and higher hip circumference and lower SWCS, with a prevalence risk difference of −0.146 (P<0.05; Table 4).

DISCUSSION

The current study assessed the association between BIA-derived body composition variables (fat-free

Table 2. Association Between Fat Mass and Fat-Free Mass and Presence of CAC (>0) by Agatston Score

	Models for CAC>0		
	Unadjusted model coefficient (risk difference)	Minimally adjusted model (95% CI)	Fully adjusted model
Fat-free mass, per 10 kg	0.041 (0.028 to 0.055)§	0.033 (0.004 to 0.062)*	0.076 (0.032 to 0.120)‡
Fat mass, per 10 kg	−0.007 (−0.023 to 0.008)	0.028 (0.008 to 0.048)†	−0.007 (−0.030 to 0.016)
Age, per 10 y		0.182 (0.164 to 0.200)§	0.168 (0.148 to 0.188)§
Male sex		0.139 (0.072 to 0.207)§	0.083 (0.014 to 0.153)*
Race and ethnicity			
Chinese American participants		−0.016 (−0.069 to 0.037)	−0.006 (−0.058 to 0.047)
Black participants		−0.094§ (−0.133 to −0.056)	−0.098§ (−0.137 to −0.059)
Hispanic participants		−0.058 (−0.099 to −0.018)†	−0.063 (−0.104 to −0.022)†
Height, per 10 cm			−0.037 (−0.073 to −0.001)*
Cigarette smoking status			
Former			0.049 (0.017 to 0.081)†
Current			0.102 (0.041 to 0.162)‡
Total cholesterol, per 10 mg/dL			0.006 (0.002 to 0.011)†
HDL cholesterol, per 10 mg/dL			−0.012 (−0.023 to −0.002)*
Any lipid-lowering medication			0.132 (0.100 to 0.165)§
Systolic blood pressure, per 10 mm Hg			0.008 (0.001 to 0.015)*
Any hypertension medication			0.103 (0.070 to 0.136)§
Number of observations	3129	3129	3089

CAC indicates coronary artery calcification; and HDL, high-density lipoprotein.
*P<0.05.
†P<0.01.
‡P<0.001.
§P<0.0001.

Table 3. Association Between Fat Mass and Fat-Free Mass and CAC Agatston Score (lnCAC)

	Models for lnCAC		
	Unadjusted model coefficient (risk difference)	Minimally adjusted model (95% CI)	Fully adjusted model
Fat-free mass, per 10 kg	0.139 (0.080 to 0.199)§	0.064 (−0.067 to 0.195)	0.272 (0.075 to 0.469)†
Fat mass, per 10 kg	−0.055 (−0.126 to 0.015)	0.112 (0.020 to 0.203)*	−0.043 (−0.147 to 0.061)
Age, per 10 y		0.559 (0.467 to 0.651)§	0.529 (0.432 to 0.626)§
Sex		0.628 (0.320 to 0.937)§	0.367 (0.052 to 0.683)*
Race and ethnicity			
Chinese American participants		−0.078 (−0.322 to 0.166)	−0.111 (−0.361 to 0.139)
Black participants		−0.409§ (−0.584 to −0.234)	−0.483§ (−0.660 to −0.306)
Hispanic participants		−0.241 (−0.437 to −0.045)*	−0.352 (−0.553 to −0.152)‡
Cigarette smoking status			
Former			0.241 (0.095 to 0.387)†
Current			0.459 (0.176 to 0.742)†
Diabetes			
Impaired fasting glucose			−0.009 (−0.183 to 0.165)
Untreated diabetes			−0.179 (−0.723 to 0.366)
Treated diabetes			0.432 (0.238 to 0.625)§
Height, per 10 cm			−0.191 (−0.353 to −0.029)*
Any hypertension medication			0.204 (0.050 to 0.357)†
Systolic blood pressure, per 10 mm Hg			0.065 (0.031 to 0.099)‡
Any lipid-lowering medication			0.369 (0.217 to 0.521)§
Total cholesterol, per 10 mg/dL			−0.023 (−0.043 to −0.002)*
No. of observations	2155	2155	2128

CAC indicates coronary artery calcification; and lnCAC, natural log of coronary artery calcification.
*$P<0.05$.
†$P<0.01$.
‡$P<0.001$.
§$P<0.0001$.

mass, fat mass) and subclinical CVD as manifested by coronary calcium in men and women participating in MESA exam 5. This study describes the relationship between body composition by BIA in relationship to CAC as quantified by the Agatston score in conjunction with a newer index, the SWCS, which assigns nonzero scores to patients with Agatston CAC=0.

This cross-sectional study in a multiethnic cohort presents several interesting findings. Contrary to our expectations, higher fat-free mass was associated with higher likelihood of having CAC, higher CAC score, and a higher level of coronary calcium as measured by SWCS. It was also surprising that higher fat mass by BIA had no significant association with Agatston score on risk-adjusted models for the outcome of CAC; however, fat mass was positively associated with higher SWCS. Finally, the anthropometric variables, BMI and WC, were not associated with CAC; there was a small, yet significant, relationship between higher WC and higher SWCS.

Obesity, as indexed by the commonly used BMI, has been previously found to be associated with higher CAC by the Agatston score.[26] However, questions have been raised about the validity of BMI as a measure of adiposity. Large cross-sectional studies of National Health and Nutrition Examination Surveys (NHANES), in which both BMI and BIA were obtained, have shown that although BMI is highly correlated with percentage of body fat, it is also highly correlated with lean muscle mass and cannot discriminate between the 2[10] because the numerator of BMI is equal to fat mass+fat-free mass. A meta-analysis of 25 studies and 31 968 participants showed that a BMI ≥30 kg/m^2 had a high specificity (0.90) but low sensitivity (0.50) for identifying individuals who had above-normal levels of body fat.[27] Our previous analysis of body composition, assessed by dual-energy x-ray absorptiometry in a general population who participated in NHANES, showed that the combination of high muscle mass and low fat mass was associated with the lowest incident CVD, whereas low muscle mass and high fat mass was associated with the highest rates of incident CVD in both men and women.[28] Thus, we hypothesized that high fat mass would be significantly associated with the presence of

Table 4. Association Between Fat and Fat-Free Mass and SWCS

	Models for ln(SWCS)		
	Unadjusted model coefficient (risk difference)	Minimally adjusted model (95% CI)	Fully adjusted model
Fat-free mass, per 10 kg	0.565 (0.497 to 0.634)§	0.348 (0.198 to 0.497)§	0.729 (0.467 to 0.990)§
Fat mass, per 10 kg	0.346 (0.273 to 0.419)§	0.699 (0.596 to 0.801)§	0.359 (0.167 to 0.551)‡
Age, per 10 y		0.890 (0.786 to 0.993)§	0.814 (0.699 to 0.929)§
Sex		1.294 (0.938 to 1.651)§	0.749 (0.380 to 1.118)§
Race and ethnicity			
Chinese American participants		0.595 (0.325 to 0.864)§	0.508 (0.239 to 0.776)‡
Black participants		−0.488 (−0.700 to −0.277)§	−0.536 (−0.745 to −0.327)§
Hispanic participants		−0.111 (−0.326 to 0.103)	−0.286 (−0.502 to −0.071)†
Cigarette smoking status			
Former			0.279 (0.110 to 0.447)†
Current			0.607 (0.275 to 0.939)†
Diabetes			
Impaired fasting glucose			0.089 (−0.090 to 0.268)
Untreated diabetes			0.069 (−0.369 to 0.507)
Treated diabetes			0.460 (0.249 to 0.670)§
Height, per 10 cm			−0.403 (−0.611 to −0.196)‡
Waist circumference, per 10 cm			0.196 (0.053 to 0.339)†
Hip circumference, per 10 cm			−0.146 (−0.276 to −0.016)*
Any hypertension medication			0.309 (0.129 to 0.488)‡
Systolic blood pressure, per 10 mm Hg			0.062 (0.023 to 0.102)†
Any lipid-lowering medication			0.482 (0.318 to 0.647)§
No. of observations	3059	3059	3024

lnSWCS indicates natural log of spatially weighted calcium score; and SWCS, spatially weighted calcium score.
*$P<0.05$.
†$P<0.01$.
‡$P<0.001$.
§$P<0.0001$.

subclinical CVD and that high fat-free mass would be associated with lower levels of subclinical CVD.

Contrary to our expectations, we found that higher fat mass was positively associated with coronary calcium only for SWCS; furthermore, higher fat-free mass, rather than being associated with decreased subclinical CVD, was significantly and positively associated with the presence of CAC and higher CAC and SWCS. Previous investigations of body composition beyond the BMI and its relation to subclinical coronary artery disease have had varying findings. A study of 945 apparently healthy Korean adults who underwent BIA found both lean and fat mass to be higher in those with CAC present. However, after multivariable regression analysis that adjusted for demographics, cholesterol, glucose, and blood pressure, neither lean nor fat mass by BIA was associated with CAC. Moreover, the highest quartile of WC was the only anthropometric variable associated with higher CAC in this study.[29] In contrast, our study found WC to be associated with coronary calcium only as indexed by SWCS but not by Agatston score, possibly because SWCS, with a broader range than CAC, is a more robust variable because SWCS assigns scores to individuals with CAC=0 by Agatston. Similarly, a study of 582 postmenopausal women who underwent BIA and CAC scans found that neither fat mass index nor appendicular muscle index by BIA were significantly associated with CAC, although waist-to-hip ratio was significantly associated with CAC.[30] Another MESA substudy of 398 participants with abdominal CT found that nonsubcutaneous fat was positively associated with CAC, whereas abdominal subcutaneous fat was not.[31]

The lack of association between fat mass measured by BIA, CAC presence, and lnCAC, despite the well-known association between BMI and incident CVD, is surprising but has potential underlying explanations. Because BMI is weight/height squared and weight includes both fat mass and fat-free mass, it is possible that it is fat-free mass, not adipose tissue, that accounts for the relationship between higher BMI and CVD risk. Furthermore, BIA gives an estimate of total

fat mass but does not differentiate by quality of adipose tissue (subcutaneous versus visceral) or describe the distribution of adiposity. Recent studies suggest that centralized rather than generalized body distribution of fat and visceral rather than subcutaneous adipose tissue, neither of which can be discerned by BIA, are likely key variables linking obesity to elevated cardiovascular risk.[12,32] Other factors associated with higher adiposity, such as cholesterol levels, blood pressure, and diabetes, may mediate the relationship between adiposity and CVD, thus accounting for the lack of significant association on multivariable analysis. In addition, it is possible that the association between excess adiposity and coronary artery disease is independent of calcification of coronary plaque and related to coronary endothelial function or inflammation.

Furthermore, although we expected higher fat-free mass to be associated with decreased CAC scores, what we noted was the reverse. This finding is different from several findings from previous studies in other populations. Chung et al[24] noted that individuals with muscle mass 2 SDs below the norm (sarcopenia) by BIA had higher CAC scores than those without sarcopenia; individuals with sarcopenic obesity had the highest CAC scores in this study. In 2 large studies of Korean populations, the lowest quartile of skeletal muscle mass index, calculated using appendicular muscle mass by BIA, was associated with higher CAC scores in both studies.[33,34] Finally, in a study of Brazilian elderly aged >80 years, muscle mass was inversely associated with CAC scores.[35] Interestingly, Wassel et al[36] found the association between muscle mass and CAC score differed significantly by ethnicity in a study of postmenopausal women. Increased muscle mass appeared to be associated with lower CAC scores in Filipina populations, but not Black or non-Hispanic White women. Also, in a previous MESA analysis of 1020 participants who had CT scans with estimation of lean muscle area, there was no association between lean muscle area and CAC.[37] Finally, a study of 570 patients with stable coronary heart disease participating in cardiac rehabilitation showed that higher lean mass index was associated with lower mortality at 3 years.[38]

There are hypotheses to explain our unexpected finding of an association of higher fat-free mass with higher coronary calcium. BIA cannot identify the quality of fat-free mass, and studies suggest that lean muscle, rather than muscle with lipid accumulation, may have cardio-metabolic protective properties. A body composition substudy of MESA using CT scans showed that higher abdominal muscle density, but not higher abdominal muscle area, independently predicted reduced mortality. These results suggest that the quality of muscle, rather than quantity, may be important to health, and indicate that myosteatosis is associated with adverse cardiovascular effects.[39] In fact, weight loss interventions have demonstrated reductions in low-density muscle.[40] Interestingly, studies of high-level, elite athletes, who tend to have higher fat-free mass, have shown significantly higher CAC scores compared with average exercisers, with this relationship predominantly seen in men.[41] In fact, lifelong exercise volume has been positively correlated with CAC prevalence and higher CAC scores. However, despite more calcific plaque, active individuals tend to have less high-risk variants of plaque, such as noncalcified and mixed plaque.[42] Also, fat-free mass by BIA has been shown to correlate with higher blood pressure by ambulatory monitoring, suggesting that muscle mass may have adverse effects on cardiovascular risk factors.[43]

We acknowledge limitations of our study. This is a cross-sectional study and does not assess changes in CAC over time. None of our measures, including fat and lean mass estimates derived from BIA, can fully describe the distribution or quality of muscle and fat, as noted previously. It has now been recognized that adipose tissue itself is quite heterogeneous, with visceral adipose tissue associated with the risk of incident CVD to a much greater degree than subcutaneous fat.[11,44] Also, BIA-derived measures have been criticized as being highly influenced by one's state of hydration, which can be particularly variable in older individuals; however, BIA measurements in this study were done in a standardized fashion under fasting conditions. Furthermore, there has been good correlation between magnetic resonance imaging–derived muscle mass and BIA-derived muscle mass in individuals across the age spectrum.[45] Although CAC by Agatston score is clinically predictive of cardiovascular events and widely used clinically for the detection of subclinical CVD, its limitations are increasingly recognized. The Agatston method scores only above a certain threshold, although important information may exist below the threshold. For this reason, we included the SWCS, which assigns values below the Agatston score threshold. Although we included a large number of potential variables related to CAC in our models, there are likely additional factors that were not collected as part of the MESA study that affect the relationship between fat mass, fat-free mass, and CAC. Finally, these cross-sectional data are limited in contributing to the understanding of the cause–effect relationship between body composition and coronary calcium.

In conclusion, this cross-sectional study found a significant association between higher lean mass by BIA, higher coronary calcium scores, and, to a lesser extent, higher fat mass by BIA. Further research is needed to better understand the role of body composition, specifically the quantity and quality of lean and fat mass, in the initiation and pathophysiology of coronary artery disease. Prospective studies of CVD

development, including more accurate measures and precise measures of body composition and coronary atherosclerosis, as may be attained by CT and magnetic resonance imaging, are warranted to further refine our understanding of obesity and CVD development.

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Disclosures

None.

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