Pericardial Adipose Tissue and Coronary Artery Calcification in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Objective: To examine the relationship of pericardial adipose tissue (PAT) with coronary artery calcification in the Multi-Ethnic Study of Atherosclerosis.

Design and Methods: The baseline cohort comprised 6,814 Caucasian (38%), African-American (28%), Chinese American (12%), and Hispanic (22%) adults aged 45-84, without known clinical cardiovascular disease. Cardiac CT was used to measure PAT (cm³) and calcification (Agatston score). We examined cross-sectional associations of PAT with the presence (score >0) and severity (continuous score if >0) of calcification using prevalence ratio (PR) (n = 6,672) and linear regression (n = 3,362), respectively. Main models were adjusted for age, age², gender, race/ethnicity, field site, smoking, physical activity, alcohol, and education.

Results: PAT volume (adjusted for age, height, weight, and site) was greatest in Chinese males, whereas Black males had less PAT than all but Black females. PAT was associated with presence [PR per standard deviation (SD): 1.06 (95% CI: 1.04, 1.08)] and severity [difference in log Agatston score per SD: 0.15 (0.09, 0.21)] of calcification, but neither association varied by race/ethnicity. Adjustment for generalized adiposity attenuated but did not eliminate the associations. With further adjustment for traditional risk factors and inflammatory markers, only the association with severity remained statistically significant [PR: 1.02 (1.00, 1.04); difference: 0.10 (0.03, 0.17)]. Heterogeneity by sex was observed for the presence of calcification (PR in men: 1.04; in women: 1.08; P for interaction <0.0001).

Conclusion: PAT was associated with the presence and severity of coronary artery calcification in this cohort, but neither association varied by race/ethnicity.

Introduction

Excess fat deposition within and around tissues and organs may directly impair the functions of those tissues and organs (1) and may therefore be more pathogenic than fat depots in other locations. Both abdominal visceral fat (2) and pericardial fat (visceral fat around the heart) (3,4) have a higher release of free fatty acids and inflammatory cytokines than subcutaneous fat. Because of its location, pericardial adipose tissue (PAT) may constitute an especially harmful fat depot. Recent research has shown that pericardial and epicardial adipose depots are indeed associated with cardiovascular disease risk factors (5) and outcomes (6,7), and these associations appear to persist after adjustment for other adiposity measures such as BMI and waist circumference (8–10). However, most of the studies on PAT done to date have been in small populations (11–13), often with indications for imaging (5,14,15). The few larger studies have not addressed differences across racial-ethnic groups (7,16). Our group’s preliminary analysis (17) in a subset of the Multi-Ethnic Study of Atherosclerosis (MESA) cohort demonstrated the cross-sectional association of pericardial fat with calcified coronary plaque, an indicator of subclinical atherosclerosis (18) that predicts the risk of future coronary heart disease events (19) beyond that

Disclosure: The authors declared no conflict of interest.

Funding Sources: This research was supported by contracts N01-HC-95159 through N01-HC-95169 and by grant R01-HL-085323 from the National Heart, Lung, and Blood Institute.

Received: 20 April 2011 Accepted: 16 August 2012 Published online 5 November 2012. doi:10.1002/oby.20090
predicted by the Framingham Risk Score (20). This work expands that analysis to the entire cohort and allows us to compare associations across racial/ethnic groups. The latter comparisons are of particular interest because studies of coronary calcification in MESA (21) and other populations (22,23) have shown lower prevalence and severity in Blacks than in Whites, even after adjustment for sociodemographic variables and CVD risk factors.

A further limitation to many existing studies of pericardial and epicardial adipose tissues is the use of echocardiography (5,8,15), which produces only a two-dimensional measure of thickness. Computed tomography (CT) scans, which are available in MESA, permit a three-dimensional assessment of volume. Our group developed an efficient method to measure the volume of PAT using cardiac CT scans (24) and has developed and validated a simpler method for use in a larger cohort such as MESA (17).

Methods and Procedures

Study population

The MESA is a prospective study of subclinical markers of cardiovascular disease in a cohort of 6,814 African-American, Caucasian, Asian (largely Chinese), and Hispanic adults aged 45-84 years and free of known cardiovascular disease at baseline (2000-2002) (25). Participants were from six communities in the United States: Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles, CA; New York, NY; and St. Paul, MN. The MESA study was approved by the Institutional Review Board at each field center. Participants gave written informed consent.

Measurements

Coronary artery calcification. Calcified coronary plaque was determined with either an electrocardiogram-triggered (at 80% of the R-R interval) electron-beam CT scanner (Chicago, Los Angeles, and New York field centers; Imatron C-150, Imatron, Tokyo, Japan) or with prospectively electrocardiogram-triggered scan acquisition at 50% of the R-R interval with a multidetector system that acquired four simultaneous 2.5-mm slices for each cardiac cycle in a sequential or axial scan mode (Baltimore, Forsyth County, and St. Paul field centers; LightSpeed, General Electric, Waukesha, WI, or Volume Zoom, Siemens, Erlangen, Germany). Additional details have been published previously (26). Experienced and trained technologists scanned the heart of each participant two times and transmitted the scans over the Internet to the CT Reading Center (Harbor-UCLA Research and Education Institute in Torrance, CA). A cardiologist read all scans in a masked fashion. The Agatston score (27), averaged from the two scans, was used to quantify the amount of calcified coronary plaque. The re-read agreement for the Agatston score was excellent (intraclass correlation coefficient, 0.99) (26). For the presence of calcified coronary plaque (Agatston score >0), agreement between duplicate scans (κ = 0.92) (28) and re-read agreement (κ = 0.93 and 0.90, for intra- and interobserver, respectively) (21) were also high.

Pericardial adipose tissue. Two experienced CT readers, blinded to the measure of calcified coronary plaque, measured PAT volume. Pericardial fat was measured according to a sampling protocol developed by our group (17). The superior extent of the left main coronary artery was identified in a cross-sectional scan. Slices within 15 mm above this slice and 30 mm below this slice were included. The anterior border of the volume was defined by the chest wall and the posterior border by the aorta and the bronchus. Volume Analysis software (GE Healthcare, Waukesha, WI) was used to discern fat from the remaining portions of the heart with a threshold of -190 to -30 Hounsfield units. The volume was the sum of all voxels containing PAT. The sampling protocol was highly correlated (Pearson correlation coefficient: 0.93; P < 0.0001) (17) with the “gold standard” method (24), which measures the entire PAT volume encasing the heart. The intraclass correlation coefficients for intra-reader and inter-reader reliability for the new method were very high (0.999 and 0.997, respectively) (17).

Anthropometrics. Weight was measured with a Detecto Platform Balance Scale (Detecto, Webb City, MO) to the nearest 0.5 kg. Height was measured with an Accu-Hite Measure Device stadiometer with level bubble (Seca, Hamburg, Germany) to the nearest 0.1 cm. BMI was defined as weight in kilograms divided by the square of height in meters. Waist circumference (at the umbilicus) was measured to the nearest 0.1 cm using a steel measuring tape with standard 4 oz tension (Gulick II, 150-cm anthropometric tape).

Covariates. Questionnaires were used to collect information on demographics, smoking status, alcohol use, physical activity, education, medical history, and medication use. Cigarette smoking status was classified as current, former, and never. Alcohol use was defined as current, former, and never. Physical activity was based on MET-minutes of intentional physical activity per week, and was classified as low (<300), moderate (300 to <1,500) and high (≥1,500). Education was defined as less than high school, finished high school, or finished college. Blood pressure was measured in the right arm of the participant after 5 min in a sitting position using a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, Tampa, FL). The second and third of three readings were averaged to obtain the blood pressure levels. Total cholesterol, high-density lipoprotein (HDL)-cholesterol and triglyceride levels were measured in EDTA-treated plasma on a Roche COBAS FARA centrifugal analyzer (Roche Diagnostics, Indianapolis, IN). C-reactive protein was measured using ultra-sensitive ELISA (Quantikine HS Human IL-6 Immunoassay; R&D Systems, Minneapolis, MN). Triglycerides, C-reactive protein and interleukin-6 were log transformed because of non-normality. Glucose levels were measured using rate-reflectance spectrophotometry using thin film adaptation of the glucose oxidase method on the Vitros analyzer (Johnson & Johnson Clinical Diagnostics, Rochester, NY), and diabetes was defined as self-reported diabetes, nonfasting glucose ≥ 11.1 mmol/l (200 mg/dl), fasting glucose ≥ 7.0 mmol/l (126 mg/dl), or use of hypoglycemic medication (29). Lipid medications and antihypertensive medications were coded yes/no based on medications taken during the last two weeks that were brought to the examination.

Statistical analysis

Sample means and SDs were computed for the continuous characteristics and proportions were calculated for discrete characteristics by PAT quartiles. P-values for these unadjusted associations were calculated using analysis of variance for continuous variables and overall chi-square tests for categorical variables. Adjusted means for pericardial fat volume and for prevalence and severity of calcification by race and gender were calculated using SAS LSMEANS.

Pericardial adipose tissue was the main exposure variable. For the presence of coronary artery calcification (Agatston score >0)
outcome, we used prevalence ratio (PR) regression (log link) with robust confidence intervals. For severity of calcification (Agatston score among participants with score >0), we log-transformed Agatston score and used linear regression. For comparison, we also examined BMI and waist circumference as exposures in separate models and in combined models with PAT. PRs and differences in

| Pericardial adipose tissue quartiles | 0–49 cm³ | 50–69 cm³ | 70–99 cm³ | ≥100 cm³ | P-value |
|-------------------------------------|----------|-----------|-----------|----------|---------|
| Race/ethnicity, %                   |          |           |           |          | <0.001  |
| Caucasian                           | 36       | 34        | 37        | 47       |         |
| Chinese                             | 10       | 15        | 14        | 8        |         |
| Black                               | 38       | 30        | 25        | 16       |         |
| Hispanic                            | 15       | 21        | 24        | 28       |         |
| Female, %                           | 68       | 60        | 51        | 33       | <0.001  |
| Age, y                              | 59 (10)  | 62 (10)   | 64 (10)   | 65 (10)  | <0.001  |
| Age groups, %                       |          |           |           |          | <0.001  |
| 44–54                               | 43       | 30        | 22        | 18       |         |
| 55–64                               | 26       | 29        | 29        | 27       |         |
| 65–74                               | 22       | 28        | 32        | 36       |         |
| 75–84                               | 9        | 13        | 17        | 19       |         |
| Education, %                        |          |           |           |          | <0.001  |
| Less than high school               | 12       | 17        | 21        | 22       |         |
| Finished high school                | 45       | 47        | 47        | 47       |         |
| Finished college                    | 43       | 36        | 32        | 31       |         |
| Smoking, %                          |          |           |           |          | <0.001  |
| Current                             | 14       | 14        | 13        | 12       |         |
| Former                              | 31       | 33        | 37        | 45       |         |
| Never                               | 56       | 53        | 50        | 43       |         |
| Intentional Physical Activity, %    |          |           |           |          | <0.001  |
| Low (0–299 MET-min/wk)              | 25       | 27        | 31        | 36       |         |
| Moderate (300–1499 MET-min/wk)      | 36       | 39        | 38        | 37       |         |
| High (≥1500 MET-min/wk)             | 39       | 35        | 31        | 27       |         |
| Alcohol use, %                      |          |           |           |          | <0.001  |
| Current drinker                     | 58       | 55        | 51        | 58       |         |
| Former heavy drinker                | 4        | 5         | 6         | 8        |         |
| Former light drinker                | 17       | 19        | 20        | 18       |         |
| Never drinker                       | 21       | 22        | 23        | 16       |         |
| Systolic blood pressure, mm Hg      | 121 (21) | 126 (22)  | 128 (21)  | 131 (20) | <0.001  |
| HDL-cholesterol, mmol/L             | 1.5 (0.4)| 1.4 (0.4)| 1.3 (0.3)| 1.2 (0.3)| <0.001  |
| Triglycerides, mmol/L               | 1.2 (0.7)| 1.4 (0.9)| 1.6 (1.1)| 1.8 (1.1)| <0.001  |
| Taking lipid-lowering medication, % | 11       | 15        | 18        | 21       | <0.001  |
| Taking antihypertensive medication, | 26       | 33        | 42        | 47       | <0.001  |
| Diabetic, %                         | 7        | 11        | 15        | 20       | <0.001  |
| C-reactive protein, nmol/L          | 28 (49)  | 34 (58)   | 40 (58)   | 42 (56)  | <0.001  |
| Interleukin-6, pg/mL                | 1.2 (1)  | 1.4 (1)   | 1.6 (1)   | 1.9 (1)  | <0.001  |
| Pericardial adipose tissue, cm³     | 38 (8)   | 60 (6)    | 83 (8)    | 137 (37) | <0.001  |
| BMI, kg/m²                          | 25 (4)   | 27 (5)    | 29 (5)    | 32 (6)   | <0.001  |
| Waist, cm                           | 88 (12)  | 95 (12)   | 101 (12)  | 109 (13) | <0.001  |
| Agatston score (positives only)     | 214 (428)| 283 (543)| 283 (571)| 365 (600)| <0.001  |
| Presence of coronary calcification (Agatston score >0), % | 34       | 45        | 54        | 66       | <0.001  |

HDL, high-density lipoprotein.
P-values are from analysis of variance (ANOVA) (continuous variables), indicating whether the means are different, or overall chi-square tests (categorical variables), indicating whether the cell percents are different than expected.
TABLE 2 Pericardial adipose tissue by race and gender

| Both genders | Women | Men |
|--------------|-------|-----|
|               | N     | Mean/% (95% CI) | N     | Mean/% (95% CI) | N     | Mean/% (95% CI) |
| Crude pericardial adipose tissue, cm³ | 6,727 | 80 (79, 81) | 3,558 | 69 (68, 70) | 3,169 | 92 (90, 93) |
| All           |       |               |       |               |       |               |
| White         | 2,586 | 85 (83, 87) | 1,346 | 70 (68, 72) | 1,240 | 101 (99, 104) |
| Chinese       | 792   | 74 (72, 76) | 408   | 70 (67, 72) | 384   | 78 (75, 82)   |
| Black         | 1,862 | 67 (66, 69) | 1,033 | 61 (59, 63) | 829   | 75 (73, 78)   |
| Hispanic      | 1,487 | 88 (86, 91) | 771   | 76 (74, 79) | 716   | 101 (98, 105) |
| Adjusted¹ pericardial adipose tissue, cm³ | 6,727 | 80 (79, 81) | 3,558 | 72 (71, 74) | 3,169 | 92 (91, 93) |
| All           |       |               |       |               |       |               |
| White         | 2,586 | 85 (84, 87) | 1,346 | 74 (73, 76) | 1,240 | 97 (95, 100)  |
| Chinese       | 792   | 94 (91, 97) | 408   | 91 (88, 95) | 384   | 97 (94, 100)  |
| Black         | 1,862 | 60 (58, 61) | 1,033 | 51 (49, 53) | 829   | 69 (67, 72)   |
| Hispanic      | 1,487 | 87 (85, 89) | 771   | 75 (73, 78) | 716   | 100 (97, 102) |

¹Adjusted for age, height, weight, and study site, and for race or gender where not stratified.

log Agatston score ($\beta$-coefficient) were reported per SD of PAT (42 cm³), BMI (5 kg/m²), and waist circumference (14 cm). Covariates for the main models included demographic characteristics (age, age-squared, race/ethnicity, field site, and gender), behavioral factors (smoking, alcohol use, physical activity), and education as a measure of socioeconomic status. We also examined models adjusted for traditional cardiovascular risk factors and inflammatory markers that are believed to mediate the association between general obesity and cardiovascular disease: diabetic status, systolic blood pressure, total and HDL-cholesterol, triglycerides, C-reactive protein, interleukin-6, and use of antihypertensive or lipid-lowering medications. For both presence and severity of calcified plaques, we evaluated statistical interactions of PAT with gender and race/ethnicity.

For the analyses using presence of calcification as the outcome, we excluded participants missing PAT data ($n = 32$), BMI or waist circumference ($n = 2$), or covariates ($n = 53$), for a total sample of 6,727. For the analyses of severity of calcification, we excluded participants with an Agatston score of 0 ($n = 3,416$) and those missing PAT data ($n = 13$), BMI or waist circumference ($n = 1$), or covariates ($n = 22$), for a total sample of 3,362. For the models that adjusted for traditional cardiovascular risk factors and markers of inflammation, we further excluded participants missing values of those variables, for total samples of 6,510 for the presence of calcification analysis and 3,247 for severity.

Results

Sample characteristics (unadjusted) are shown in Table 1 by quartiles of PAT. Participants with higher volumes of pericardial fat were slightly older, with higher BMIs and waist circumferences. They had higher mean systolic blood pressure, triglycerides, C-reactive protein and interleukin-6 levels, and lower mean HDL-cholesterol. They were more likely to be male, to be taking lipid or blood pressure medications, and to be diabetic, and they had higher Agatston scores. Pericardial fat was also associated with education, smoking, drinking, and physical activity.

Table 2 shows crude and adjusted mean PAT volume by race and gender. Adjusted for age, height, weight, and study site, pericardial fat volumes were substantially lower in women than in men and in Blacks than in other race/ethnic groups, regardless of gender. Among women, Chinese had higher levels than Hispanics and Whites. Among men, Chinese, Whites, and Hispanics did not differ. Notably, Black men had less pericardial fat than all groups other than Black women.

Table 3 shows associations of both presence (PRs) and severity (differences in log Agatston score) of coronary calcification per one SD increment in PAT. Associations with BMI and waist circumference (modeled separately) are also shown for comparison. In unadjusted models (not shown), PAT was associated with both presence [PR = 1.19 (1.16, 1.21)] and severity [difference in log Agatston score = 0.27 (0.21, 0.33)] of calcification. These associations were attenuated by adjustment for demographic factors (“basic adjusted model”), but were not further attenuated by adjustment for behavioral and sociodemographic factors (“main models”). Additional adjustment for BMI or waist circumference (“mutually adjusted models”) further attenuated but did not eliminate the associations. Adjustment for traditional cardiovascular risk factors and inflammatory markers (diabetic status, systolic blood pressure, total and HDL-cholesterol, triglycerides, use of antihypertensive or lipid-lowering medications, C-reactive protein, and interleukin-6) also attenuated but did not eliminate the associations. When models were adjusted for BMI plus traditional cardiovascular risk factors and inflammatory markers, only the association with severity remained statistically significant (although the lower confidence limit of 1.00 for the PR suggests an association, albeit very weak, remains for presence of calcification as well).

Race- and gender-stratified results (using the main model) are shown in Table 4. We found no statistically significant heterogeneity by
Pericardial Fat and Calcification

McClain et al.

TABLE 3 Association of pericardial adipose tissue with the presence and severity of coronary artery calcification

|                | Presence |                  | Severity |      |
|----------------|----------|------------------|----------|------|
|                | Prevalence ratio (95% CI) (N = 6,727) | P-value | Difference in log Agatston score (β) (95% CI) (N = 3,362) | P-value |
| Basic adjusted modelsa | PAT (42 cm³) 1.06 (1.04, 1.08) | <0.0001 | 0.15 (0.09, 0.20) | <0.0001 |
|                | BMI (5 kg/m²) 1.07 (1.05, 1.09) | <0.0001 | 0.11 (0.05, 0.17) | 0.0002 |
|                | Waist circumference (14 cm) 1.07 (1.05, 1.10) | <0.0001 | 0.13 (0.07, 0.19) | <0.0001 |
| Main modelsb | PAT (42 cm³) 1.06 (1.04, 1.08) | <0.0001 | 0.15 (0.09, 0.21) | <0.0001 |
|                | BMI (5 kg/m²) 1.08 (1.05, 1.10) | <0.0001 | 0.12 (0.06, 0.18) | <0.0001 |
|                | Waist circumference (14 cm) 1.07 (1.05, 1.10) | <0.0001 | 0.13 (0.07, 0.20) | <0.0001 |
| Mutually adjustedc (PAT and BMI) main model | PAT (42 cm³) 1.03 (1.01, 1.05) | 0.0017 | 0.12 (0.06, 0.19) | 0.0004 |
|                | BMI (5 kg/m²) 1.06 (1.03, 1.08) | <0.0001 | 0.05 (−0.02, 0.12) | 0.1587 |
| Mutually adjustedc (PAT and waist) main model | PAT (42 cm³) 1.03 (1.01, 1.05) | 0.0008 | 0.12 (0.05, 0.19) | 0.0007 |
|                | Waist circumference (14 cm) 1.05 (1.03, 1.08) | <0.0001 | 0.06 (−0.01, 0.14) | 0.0908 |
| Main models adjusted for CVD risk factorsd | PAT (42 cm³) 1.03 (1.01, 1.05) | 0.0013 | 0.11 (0.05, 0.17) | 0.0007 |
|                | BMI (5 kg/m²) 1.04 (1.02, 1.06) | 0.0008 | 0.07 (0.01, 0.14) | 0.0340 |
|                | Waist circumference (14 cm) 1.04 (1.02, 1.06) | 0.0011 | 0.08 (0.01, 0.15) | 0.0327 |
| Mutually adjustedd (PAT and BMI) main model adjusted for CVD risk factorsd | PAT (42 cm³) 1.02 (1.00, 1.04) | 0.1039 | 0.10 (0.03, 0.17) | 0.0068 |
|                | BMI (5 kg/m²) 1.03 (1.00, 1.06) | 0.0265 | 0.02 (−0.05, 0.10) | 0.5470 |
| Mutually adjustedd (PAT and waist) main model adjusted for CVD risk factorsd | PAT (42 cm³) 1.02 (1.00, 1.04) | 0.0886 | 0.10 (0.03, 0.17) | 0.0070 |
|                | Waist circumference (14 cm) 1.03 (1.00, 1.06) | 0.0251 | 0.02 (−0.05, 0.10) | 0.5389 |

Estimates are per standard deviation (in the full cohort) increment: 42 cm³ of pericardial adipose tissue (PAT), 5 kg/m² of BMI, and 14 cm of waist circumference. PAT, BMI and waist are modeled separately except in “mutually adjusted” models. CI indicates confidence interval. Boldface indicates that the 95% CI does not include the null.
aAdjusted for study site, age, age squared, gender, and race/ethnicity. 
bFurther adjusted for smoking, physical activity, alcohol, and education. 
cMutually adjusted models contain pericardial adipose tissue and either BMI or waist circumference in the same model and are adjusted for study site, age, age squared, gender, race/ethnicity, smoking, physical activity, alcohol, and education. 
dMain models plus CVD risk factors are additionally adjusted for systolic blood pressure, total and HDL-cholesterol, triglycerides, lipid-lowering medications, antihypertensive medications and diabetic status, interleukin-6, and C-reactive protein. These models have a reduced N compared with the main models because of missing CVD risk factor observations for some participants: N = 6,510 for presence of CAC and N = 3,247 for difference in Agatston score. We checked main models in these subsamples; estimates did not change.

race/ethnicity in the association of pericardial fat with either presence or severity of calcification. Nor were there differences by gender in the association with severity. The PR for presence of calcification was larger in women than in men (P for interaction < 0.0001), but the absolute differences in prevalence across quartiles of pericardial fat (results not shown) were similar between men and women.

We ran several additional analyses in which we varied the definitions of our outcome and exposure (results not shown). These analyses used main model covariates. We defined presence of calcification using several different cutpoints. Using an Agatston score of 10 or more versus <10, there was little change in the PR for pericardial fat [1.07 (95% CI: 1.05, 1.09)]. Using 100 or more versus <100, the PR was 1.11 (1.08, 1.15). Using the ethnic-specific 75th percentile of calcification (49 for Blacks, 66 for Chinese, 61 for Hispanics and 159 for Whites), the overall PR was 1.11 (1.07, 1.14), and, as with the main analysis of >0 vs 0, we found no interaction by race/ethnicity. We also repeated the main model analysis using ethnic-specific standard deviations as the increment in pericardial fat (Whites: 46 cm³, Chinese: 32 cm³, Blacks: 35 cm³, Hispanics: 44 cm³) and again found no interaction by race/ethnicity [PR for Whites: 1.06 (1.04, 1.09), Chinese: 1.07 (1.01, 1.14), Blacks: 1.06 (1.02, 1.10), Hispanics: 1.04 (1.00, 1.08); p for interaction: 0.94].

Discussion
Consistent with other studies (7,12,13,16,30–32), including a sub-study of MESA data by our group (17), we found that PAT was associated with both the presence and severity of coronary artery calcification.
Our study found substantial differences in the volume of pericardial fat by race/ethnicity. Notably, Blacks in MESA had substantially less pericardial fat than the other groups despite having higher BMIs. Divers et al (35) compared European Americans to African-Americans in the African American Diabetes Heart Study and found between-group differences like those shown here, with Blacks having less pericardial fat despite having higher BMIs (overall pericardial fat volumes were higher than in MESA). A study of 150 echocardiography patients also found that Black men had substantially less pericardial fat than White men (41), and Blacks have been shown to have less visceral adipose tissue than Whites in other studies (36,37). Other racial/ethnic groups also differ in the distribution of body fat (38,39).

Despite these marked differences by race/ethnicity in pericardial fat volume and well-established differences by race in calcification (21–23), our study found no difference in the association of pericardial fat with calcification across race/ethnic groups. In the Divers analysis (n = 1,136), an association between PAT and coronary calcified plaque was observed in African-Americans, but not in European Americans (35), but the finding of no association in Whites is inconsistent with other analyses (10,31) in a variety of samples (7,16), including our own. Racial differences have been observed in the association of other body size variables with atherosclerotic disease, including the association of BMI with coronary heart disease in other large cohorts (40). However, in the MESA cohort, Bild et al (21) found the association of BMI with CAC was similar across the four race/ethnic groups, though it was only significant in Whites.

The consistency of the association between pericardial fat and calcification across race/ethnic groups suggests that the mechanism for the association may not differ by race. More information from other populations would be helpful, but unless future studies find substantially larger associations between pericardial fat and coronary calcification than those observed in MESA, it is unlikely that a finding of between-group differences, even if statistically significant, would have important clinical applications.

Statistically significant heterogeneity by sex was observed for the PRs, though, as noted, the absolute difference in prevalence associated with pericardial fat was similar between men and women. The observed heterogeneity may therefore not be very meaningful. Indeed, for our severity analysis, in which a difference measure was used, no interactions were found. In the Framingham cohort, Rosito et al (7) found no sex interaction in the association of pericardial fat with coronary calcification despite significant heterogeneity for associations of pericardial fat with most of the other CVD risk factors they examined.

The pericardial fat-calcification associations seen here were independent of BMI and waist, which suggests that pericardial fat may be a more specific risk factor than generalized obesity in the pathogenesis of CVD. There has been little research on interventions...
targeting PAT, but pericardial fat has been shown to decrease with weight loss, and changes in left ventricular mass with weight loss may be more associated with changes in PAT than with changes in body mass or waist circumference (11).

This study has several strengths. PAT was assessed by multi-slice CT, allowing the use of a volumetric measure. The large diverse cohort allowed comparison across race/ethnic groups. We used PRs, which are more appropriate than odds ratios when the outcome (presence of calcification in this case) has a high prevalence. Our PRs were, as expected, smaller in magnitude than the odds ratios reported in similar analyses, so we repeated our analyses using logistic regression for comparison and obtained odds ratios similar to those seen in other studies. The relatively weak associations found here could also be influenced by the use of PAT, comprising both the epicardial adipose tissue (within the pericardium and therefore in direct contact with the coronary vessels) and the paracardial adipose tissue (outside the pericardium). The epicardial tissue may be more important in any causal mechanism, but is more difficult to measure because of the difficulty in accurately defining the pericardium. This could be considered a limitation of this study. The principal limitation of this research was its cross-sectional nature. Cross-sectional analyses can suffer from survival bias and prevent examination of temporality. Studies using longitudinal data may find larger associations. A major limitation of this analysis is the inability to compare pericardial fat to visceral adipose tissue. It is likely that adjustment for visceral fat would attenuate the associations more than did BMI or waist circumference, but the visceral fat data are not yet available in MESA.

We used SDS as the units for our variables to facilitate comparison of pericardial fat to BMI and waist. Such a comparison may not translate to other populations in which the SDSs of these variables may differ substantially from this cohort. However, in the present analysis, the difference in log Agatston score was much larger for pericardial fat (0.12 per SD) than for BMI or waist (0.05 and 0.06, respectively, in the mutually adjusted models). It is unlikely that the SDSs in other populations would differ from the MESA population enough to eliminate or reverse this finding. Pericardial fat may be a more specific risk factor than generalized obesity. Results from this study suggest that it may also be a consistent risk factor across racial/ethnic groups.

Acknowledgments

We thank the other investigators, the staff, and the participants of the MESA for their valuable contributions. A complete list of participating MESA investigators and institutions can be found at mesanhbi.org.

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