Lack of Association Between Epicardial Fat Volume and Extent of Coronary Artery Calcification, Severity of Coronary Artery Disease, or Presence of Myocardial Perfusion Abnormalities in a Diverse, Symptomatic Patient Population: Results from the CORE320 Multicenter Study

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Abstract

Background—Epicardial fat may play a role in the pathogenesis of coronary artery disease (CAD). We explored the relationship of epicardial fat volume (EFV) with the presence and severity of CAD or myocardial perfusion abnormalities in a diverse, symptomatic patient population.

Methods and Results—Patients (n=380) with known or suspected CAD who underwent 320-detector row CT angiography, nuclear stress perfusion imaging, and clinically driven invasive coronary angiography for the CORE320 international study were included. EFV was defined as adipose tissue within the pericardial borders as assessed by CT utilizing semi-automatic software. We used linear and logistic regression models to assess the relationship of EFV with coronary

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calcium score, stenosis severity by quantitative coronary angiography (QCA), and myocardial perfusion abnormalities by SPECT.

Median EFV among patients (median age 62.6 years) was 102 cm^3 [interquartile range 53]. Calcium score   1 was present in 83% of patients with 59% having   1 coronary artery stenosis of   50% by QCA, and 49% having abnormal myocardial perfusion results by SPECT. There were no significant associations between EFV and CACS, presence severity of   50% stenosis by QCA, or abnormal myocardial perfusion by SPECT.

Conclusions—In a diverse population of symptomatic patients referred for invasive coronary angiography, we did not find associations of epicardial fat volume with the presence and severity of coronary artery disease or with myocardial perfusion abnormalities. The clinical significance of quantifying epicardial fat volume remains uncertain but may relate to the pathophysiology of acute coronary events rather than the presence of atherosclerotic disease.

Keywords

epicardial fat; pericardial fat; coronary artery disease; coronary artery calcification; coronary artery stenosis; myocardial ischemia

There is a considerable interest in the reported associations between epicardial fat volume (EFV) and coronary plaque burden, number of coronary arterial stenoses, and presence of provokable myocardial ischemia.[1–16] These relationships appear to remain significant even when adjusting for body-mass-index (BMI) or traditional risk factors.[17] The mechanisms underlying these associations have not been elucidated but current hypotheses implicate the release of free fatty acids and triglycerides from epicardial fat as a source of inflammatory cytokines.[18][19] Specifically, the vasa vasorum in the peripheral arterial wall arising from smaller circular and parallel branches of the epicardial coronary arteries provides a ready source of cytokines which may stimulate inflammation and recruitment of macrophages and B-lymphocytes.[19,20,21] These inflammatory processes are connected to the development of atherosclerosis and adverse clinical events.[19,22]

On the other hand, some clinical studies did not find significant associations between EFV and coronary artery disease (CAD), and other studies revealed results which were no longer significant after adjustment for established risk factors.[23, 24] Furthermore, the majority of clinical studies reporting significant associations of EFV with CAD were derived from community-based patient samples with low risk profiles. Thus, there is conflicting evidence whether EFV indeed is an independent risk factor for CAD.[25]

The purpose of this investigation was to explore the association of EFV with the presence and severity of coronary artery disease as well as myocardial perfusion abnormalities among a diverse, symptomatic population using rigorous methodology.

Methods

Study Population

Three hundred and eighty-one patients who were enrolled for the CORE320 multicenter study were included for this analysis. The details of the CORE320 study design have been

previously described. [26–28] Briefly, patients aged 45 to 85 with suspected or known CAD who were referred for clinically indicated invasive coronary angiography were enrolled at 16 centers in Brazil, Canada, Denmark, Germany, Japan, Netherlands, Singapore, and the USA. All patients underwent 320-row CT for coronary artery calcium scanning (CACS), CT coronary angiography, and nuclear stress myocardial perfusion imaging within 60 days of invasive coronary angiography. All enrolled participants provided informed consent approved by institutional and central review boards.

Covariates

Race, gender, age, and smoking status were reported for all study participants. Hypertension was defined as systolic blood pressure   140 mm Hg, diastolic blood pressure   90 mm Hg, or use of antihypertensive medications. Weight (kg) was measured with the use of a standard balance-beam scale. Body mass index was calculated as weight (kg) divided by height squared (in m^2). Diabetes was defined as a fasting glucose level   126 mg/dL or use of medication for diabetes. Dyslipidemia was defined as total cholesterol >200 mg/dL, low-density lipoprotein cholesterol   130 mg/dL, high-density lipoprotein cholesterol <40 mg/dL for men and high-density lipoprotein cholesterol <50 mg/dL for women, or use of lipid-lowering medications.

CT Imaging and Analysis of Epicardial Fat Volume

Details of CT acquisition and analyses were described elsewhere.[26–28]

Briefly, after obtaining anteroposterior and lateral scanograms CACS imaging was performed using prospective ECG triggering over a single heartbeat with a gantry rotation of 0.35 seconds, 3-mm slice collimation, tube voltage of 120 kV, and tube current adjusted according to body weight. Coronary calcification was quantified using the Agatston method. A calcium score of   1 was defined as abnormal (= categorical outcome). The calcium score was also used as a continuous outcome to assess the relationship between EFV and coronary calcification. We defined epicardial fat as all adipose tissue enclosed by the pericardium, including the epicardial fat surrounding the coronary arteries. Epicardial fat quantification was performed using a dedicated software (Virtual Place Advance, Aze Ltd, Tokyo Japan). Image data were processed as follows: First, the upper heart limit - marked by bifurcation of the pulmonary trunk - and lower slice limit - identified as the last slice containing any portion of the heart - were identified from a visual review of the CT images. Next, an experienced reader (18 years in CT interpretation) scrolled through the slices between upper and lower heart limit and traced the pericardium in a transverse view with the aid of the software (Figure 1). Following the pericardial tracing, epicardial fat quantification occurred automatically based on voxel Hounsfield unit (HU) values. Contiguous voxels between the HU limits of (−195, −45) were defined as fat voxels.[1, 2, 14] EFV was determined by the sum of cross-sectional areas of fat multiplied by slice thickness (3mm) (Figure 1). The operator of the software was blinded to any clinical information or study results. Inter-observer agreement for our method of EFV quantification was tested among two observers in 14 patients who were enrolled for the run-in phase of the CORE320 study revealing a mean difference of 1.5 cm^3 (p=0.61) and no heterogeneity of variance (standard deviation ratio 0.993, p=0.90) by Bland-Altman analysis.

Invasive Coronary Angiography Data Acquisition and Data Analysis

Invasive coronary angiography was performed using standard angiographic techniques within the 60 days following CT image acquisition and was clinically driven. Coronary angiographic images were saved in digital imaging and communication in medicine (DICOM) format and forwarded to an independent angiographic core laboratory for analysis. The coronary tree segmentation for invasive coronary angiography was previously described.[29, 30] Quantitative coronary angiography (QCA) was performed using edge-detection techniques (CAAS II QCA Research version 2.0.1 software, PIE Medical Imaging, Maastricht, the Netherlands). The most severe stenosis within each coronary segment was analyzed, with quantitative assessment performed for all stenoses which were deemed 30% by visual assessment. Two outcome variables were used: a categorical threshold for significant stenosis defined as 50% diameter stenosis by QCA and stenosis as a continuous outcome. Since no quantitative measurements were made for stenoses <30%, 15% was imputed for values which were visually assessed as 1–29% narrowed and occluded vessels were marked as 100%.

Nuclear Perfusion Imaging

All SPECT cameras used in the study were required to undergo accreditation for quality assurance before commencement and throughout the enrollment period. The SPECT qualification process was multifocal, involving evaluation of both camera physics and image quality. To account for variability in imaging equipment and image-acquisition techniques, the nuclear core laboratory evaluated images for quality control following guidelines of the American Society of Nuclear Cardiology.[31]

Myocardial territories were analyzed by SPECT for rest and stress myocardial perfusion abnormalities with a 4-point severity and reversibility-score using a 13-territory model.[26] The summed stress score (SSS) was defined as the sum of abnormal myocardial segments at stress phase.[32] In the analysis, artifacts did not contribute to the summed stress score (SSS) and therefore a SSS 1 defined an abnormal SPECT study in accordance with methods used for large multicenter studies and independent core laboratories.[33] In addition, SSS was used as a continuous outcome measure to assess the relationship between EFV and myocardial perfusion abnormalities.

Statistical Analysis

Values are presented as median, and the 25th and 75th percentile quartiles (quartiles 1 and 3). Multivariable regression models were generated to evaluate the relationship between EFV with plaque burden, coronary artery stenosis, and ischemia. Because each outcome was positive and highly skewed, we used logistic regression models with clinically meaningful cut points as well as median regression models to assess continuous association. For the logistic regression model outcomes, we defined significant coronary artery stenosis as 50% stenosis by QCA, coronary calcified plaque as Agatston calcium score > 0, and myocardial hypoperfusion as SPECT SSS 1. Each model was fit in three ways: (1) a univariate model with only EFV as a predictor; (2) model 1 adjusted for age, sex and race; and (3) model 2 additionally adjusted for BMI, hypertension, diabetes mellitus, dyslipidemia, smoking status, family history of CAD, and (in calcified plaque and

myocardial hypoperfusion models only) significant coronary artery stenosis. Group comparisons for differences in EFV were performed using Kruskal-Wallis ANOVA. P-value are two-sided and values less than 0.05 were considered statistically significant. No adjustments were made for multiple testing. The statistical analysis was performed with SAS 9.2 (SAS Institute).

Results

Descriptive Results

Clinical characteristics of study patients are listed in Table 1. Of 381 patients in the final CORE320 cohort we had to exclude one individual because of corrupt imaging data resulting in 380 patients for this analysis. The 380 subjects consisted of 251 men (66%) with a median age of 62.0 years (quartiles 1 and 3 of 55.7, 68.4, respectively). The CORE320 study population consists of predominantly intermediate risk patients (67%) with 31% having known CAD or high pretest probability.[32] Median EFV was 102 cm^3 [quartiles 1 and 3 of 78,131, respectively]. Distribution of EFV among patients is shown in Figure 2. Table 2 lists the median EFV for subgroups according to risk factors and ethnicity. Notably, obese patients had higher EFV compared to normal weight patients, and African-Americans had lower EFV than Caucasian or Asian patients.

Relationship of Epicardial Fat Volume with Coronary Artery Calcification

A total of 313 (83%) patients had a coronary calcium score of greater than 0. Univariate and multivariate analyses suggested no association of EFV with the presence of coronary artery calcium (Table 3). Median regression analysis revealed no significant relationship between calcium score and EFV after adjusting for risk factors. A scatterplot with smoothing demonstrates the relationship between calcium score and EFV in Figure 3. The results for median regression models are shown in Table 4.

Relationship of Epicardial Fat Volume with Obstructive CAD

A total of 225 (59%) patients had one or more coronary artery stenosis of at least 50% by QCA. No association between EFV and the presence or absence of obstructive CAD was noted when using QCA as continuous outcome (Figure 4) or on univariate and multivariate analyses using a 50% threshold by QCA for defining a significant stenosis (Table 5). The results for median regression models are shown in Table 6.

Relationship of Epicardial Fat Volume with Myocardial Perfusion Defects

A total of 188 (49%) patients had abnormal myocardial perfusion by SPECT. Univariate and multivariate analyses suggested no association of EFV with myocardial perfusion abnormalities (Table 7). A weak trend for a negative relationship between EFV and SSS is visible in the scatterplot with Lowess smoothing (Figure 5), though median regression analysis did not find this effect statistically significant (Table 8).

Discussion

In contrast to a number of previous studies, we did not find a significant association between EFV and the presence and extent of coronary arterial calcification by CT, presence of obstructive coronary artery disease by cardiac catheterization, or myocardial perfusion abnormalities by SPECT. Accordingly, our results are unexpected and contrary to our hypotheses.

We applied robust methodology and analysis in our study. CT acquisition and assessment for calcification followed standard methods. We used a careful approach to determine EFV with high agreement among observers. Median values as well as distribution of EFV are consistent with those reported in previous studies. We used standard, validated methodology for assessing coronary stenoses and myocardial perfusion. Importantly, all analyses – including statistical evaluations - were performed in independent core laboratories with particular expertise in the respective areas. Strengths of our study also included a solid sample size and the rigorous design structure of a multi-center study.

Possible explanations for the lack of association of EFV with metrics of CAD disease prevalence may be found in our patient population: ethnic diversity, geographical variations, and cardiovascular risk profile. Our patients were referred for cardiac catheterization with clinical suspicion of obstructive coronary artery disease, placing our patients in an intermediate-high risk group in contrast to lower risk populations in community samples.[1, 2] Fat distribution in general - and EFV in specific - varies among ethnic groups with African Americans having lower average EFV than Caucasians and Asians – as also shown in our study.[34, 35] At the same time, African Americans are at greater risk of adverse events compared to other ethnic groups.[36] It is conceivable that by combining patients with different EFV and risk patterns, the associations of EFV with disease markers were diminished. On the other hand, we did not find trends among our data that this indeed was the case.

We noted that increased EFV was associated with BMI 30 as previously described.[1,37] Despite the lack of association between EFV and CAD in our study, we found a trend for greater calcium scores in obese compared to normal weight individuals, consistent with other reports.[38, 39] Since the relationship between obesity and coronary artery disease severity is modest, it is possible that such association is weakened for a marker of obesity, i.e., EFV. It is critical to emphasize that we did not investigate the association of EFV with clinical outcome, but rather with coronary artery disease severity. There is strong evidence for an association between obesity and CAD outcome.[40, 41] Similarly, recent data provided evidence from large patient cohorts that greater EFV is associated with increased risk of myocardial infarction though it remains uncertain if this association is truly independent from traditional risk factors.[42] It is conceivable that the effects of EFV are more important in influencing vascular functions, particularly, in response to plaque alterations,[43] rather than directly contributing to atherosclerotic disease burden. As patient outcome is more important than the presence of disease, our results should not lend themselves to disregard the potential significance of EFV for clinical management.

We acknowledge the limitations of our study. The CORE320 patient cohort was enrolled for a separate study design. Accordingly, sample size calculation for our present study was not considered for CORE320 enrollment. While our sample size is larger than many clinical studies of similar design, it is conceivable that some results did not reach statistical significance because of insufficient power. However, the widths of confidence intervals for our main analyses support the strengths of our results. Estimation of EFV is subject to error. We used analytic methods of EFV which were validated in previous studies[1, 2, 14] yet variability may occur. Median EFV reported in our study, however, is in agreement with other reports[2, 14] from similar populations. In addition, interobserver agreement for EFV was high for our method aided by the semi-automatic nature of EFV analysis. Lastly, we did not differentiate between epicardial and perivascular fat nor did we differentiate between fat types, e.g., brown fat vs. other, which may have different implications for disease associations and patient outcome.[18,44]

In conclusion, we neither found a significant association of epicardial fat volume with the presence and extent of coronary artery disease as assessed by coronary calcium scannind and invasive coronary angiography, nor with myocardial perfusion abnormalities by SPECT in this diverse, intermediate-high risk population. Our results are in disagreement with some prior reports and they may point to a more complex relationship between epicardial fat volume and coronary artery disease risk. While the current value of assessing epidcardial fat volume for clinical management remains unclear, its evaluation may help predicting future CAD events rather than describing baseline disease burden.

Acknowledgments

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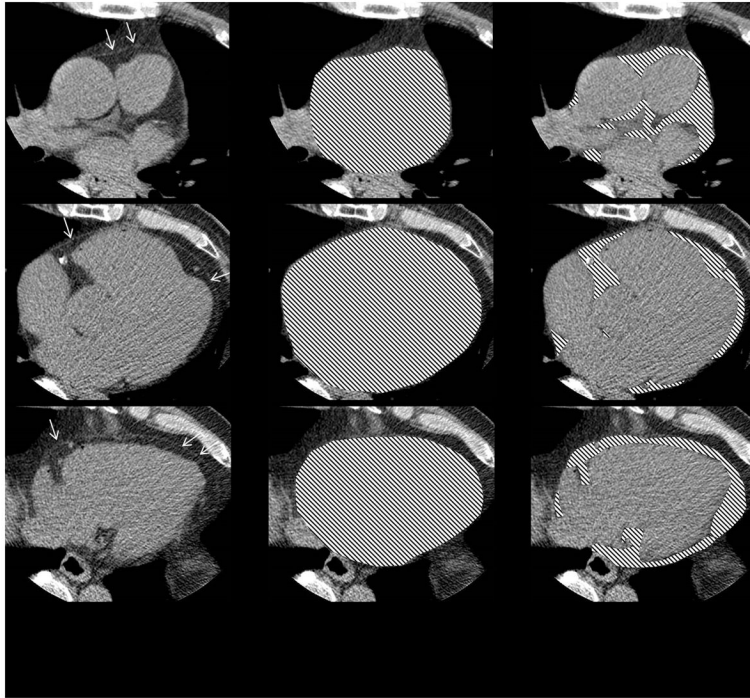
Figure 1. Epicardial Fat Volume Quantification

The figure illustrates our method of epicardial fat volume quantification using a semi-automated software. After manually tracing the pericardial borders, fat volume is derived based on Hounsfield unit attenuation within the region of interest.

Left: The white arrows point to the pericardial sac as a thin band enveloping the heart.

Middle: The pericardial sac is traced by an expert observer.

Right: The overlay represents epicardial fat enclosed by the pericardium.
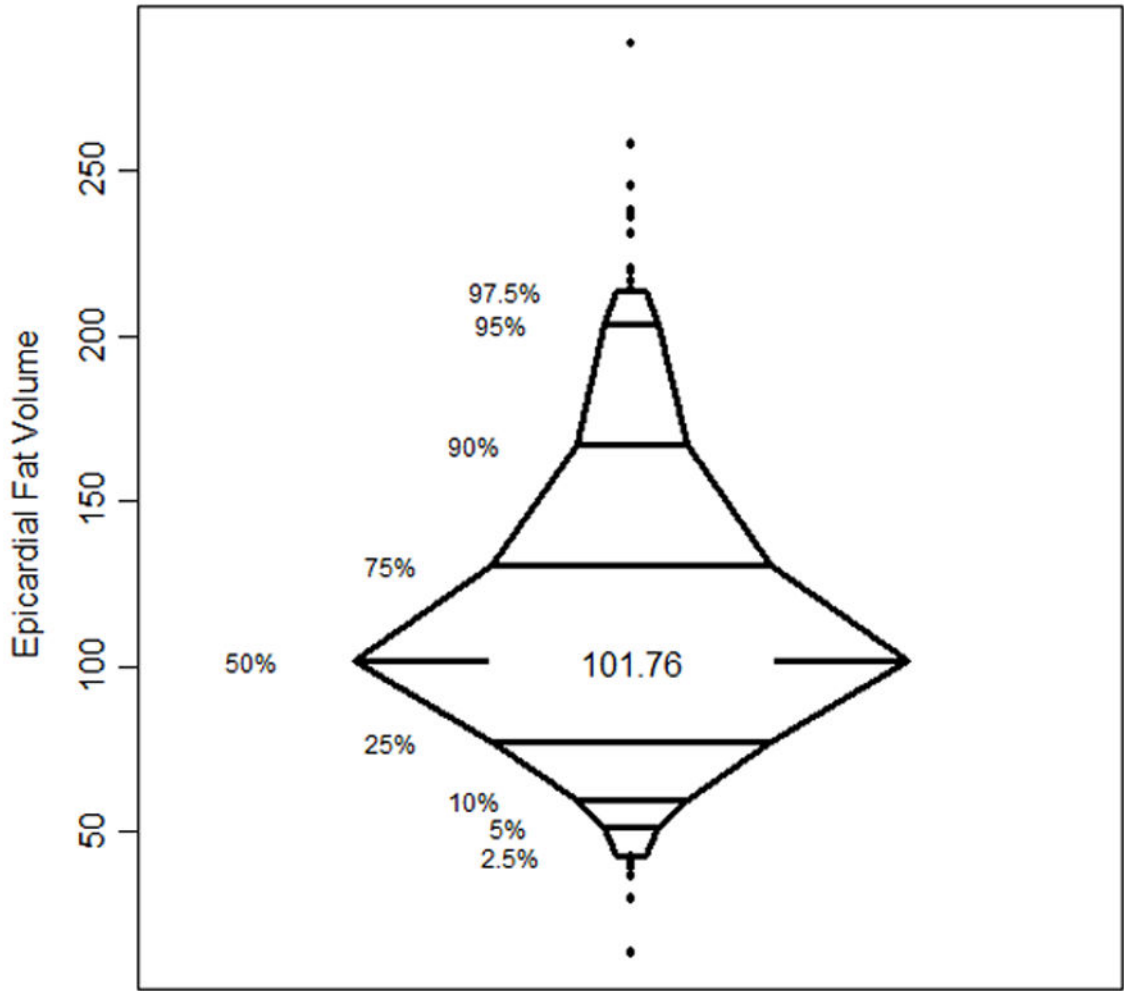
Figure 2. Distribution of Epicardial Fat Volume in the Study Population
The percentile box plot shows the distribution of epicardial fat volume among the 380 study participants.
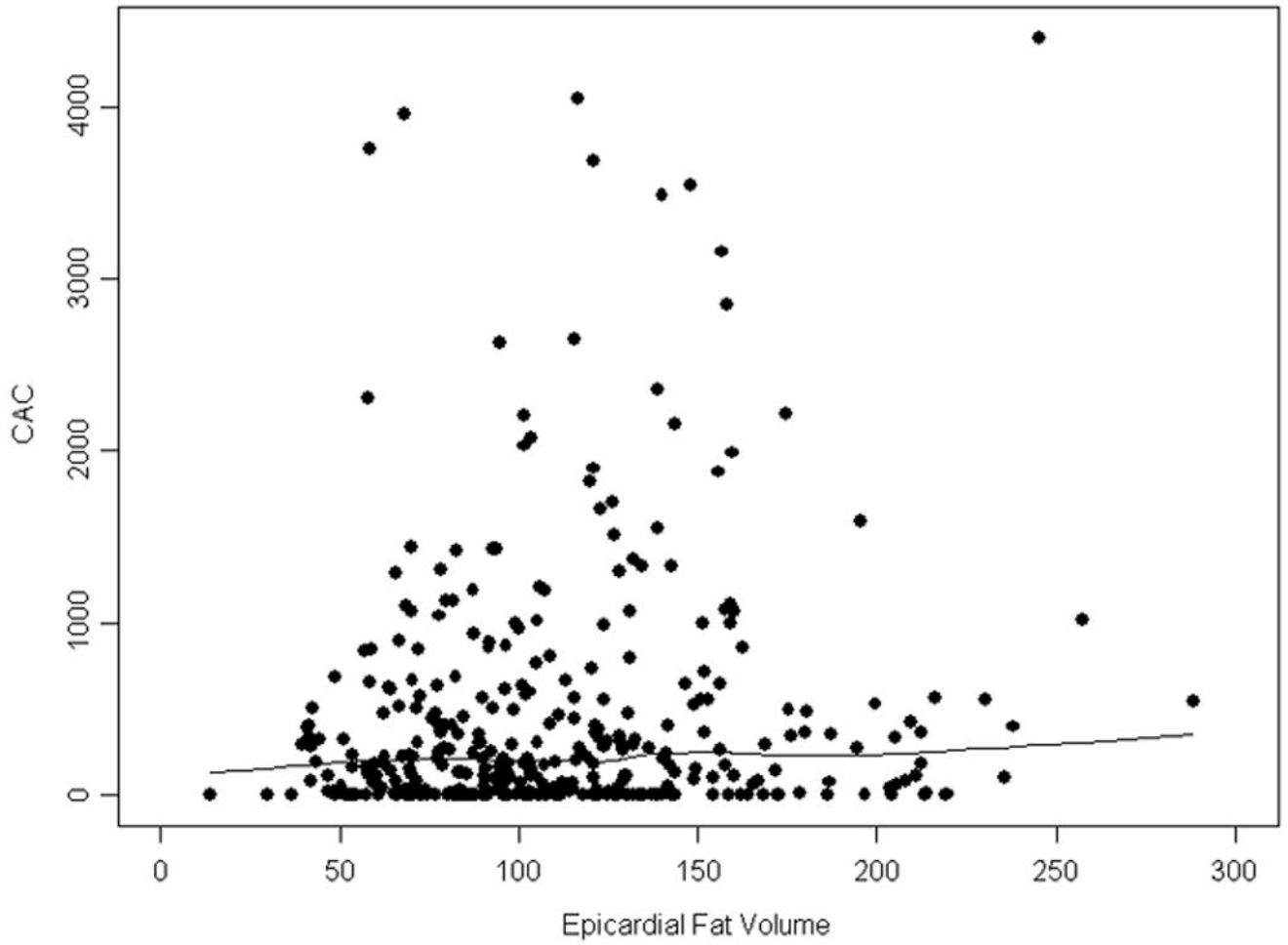
Figure 3. Relationship between Epicardial Fat Volume and Coronary Calcium Score
Shown is a scatterplot and Lowess smoothing of epicardial fat volume (EFV) and coronary
artery calcium score (CACS) revealing no significant association.
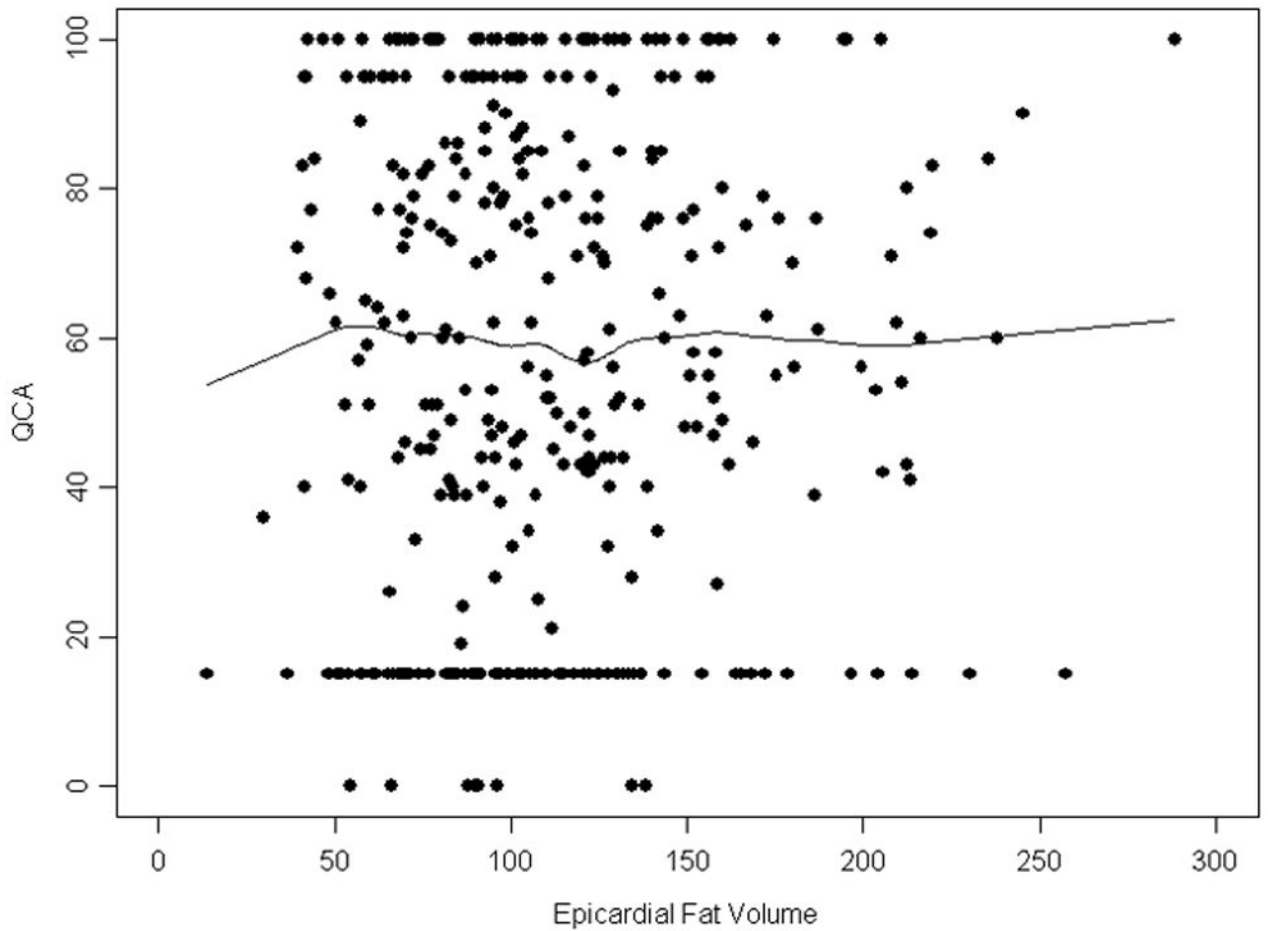
Figure 4. Relationship between Epicardial Fat Volume and Coronary Artery Stenoses
Shown is a scatterplot and Lowess smoothing of epicardial fat volume (EFV) and presence of a 50% stenosis by quantitative coronary angiography (QCA) stenosis revealing no significant association. Please note clustering of data points at the extreme ranges due to imputation of values less than 30% and at 100%.
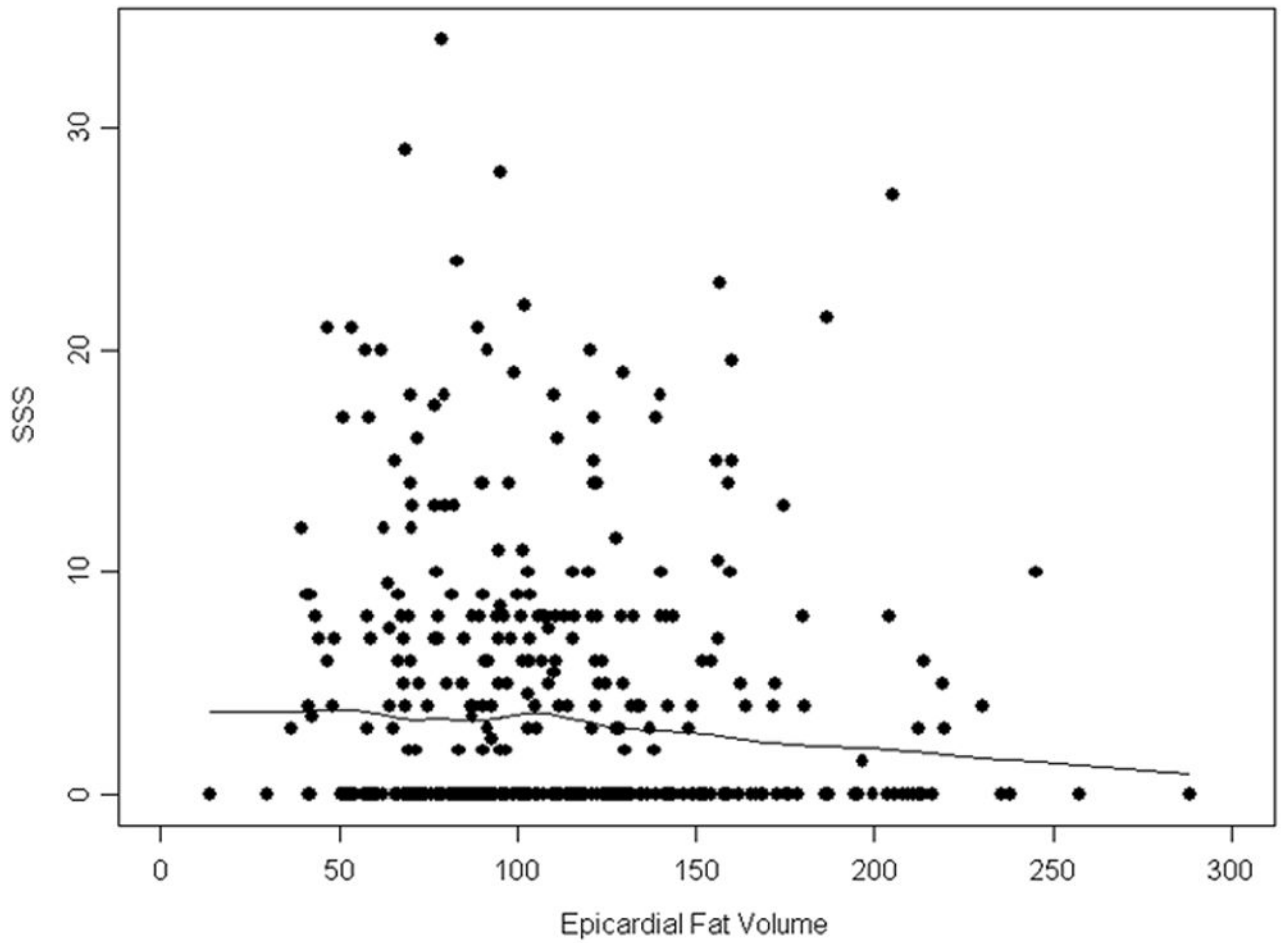
Figure 5. Relationship between Epicardial Fat Volume and Myocardial Perfusion Abnormalities
Shown is a scatterplot and Lowess smoothing of epicardial fat volume (EFV) and presence
of myocardial perfusion abnormalities using summed stress score (SSS) by SPECT
revealing no significant association.

Table 1

Baseline Characteristics

Characteristic	Non-obese (BMI< 30)	Obese (BMI=>30)	Overall
Median (Q1, Q3) or N (%)	**N=284**	**N=96**	**N=380**
Age, in years	62.6 (55.7,68.8)	60.0 (55.3, 66.6)	62.0 (55.7, 68.4)
Male Gender	195 (69)	56 (58)	251 (66)
Race			
Asian	113 (40)	12 (13)	125 (33)
African American	27 (10)	16 (17)	43 (11)
Caucasian	144 (51)	68 (71)	212 (56)
Coronary Risk Factor			
Hypertension	212 (75)	84 (88)	296 (78)
Diabetes	95 (33)	35 (36)	130 (34)
Dyslipidemia	190 (68)	63 (68)	253 (68)
Previous myocardial infarction	80 (28)	23 (24)	103 (27)
Smoking Status			
Current Smoker	53 (20)	11 (12)	64 (18)
Former Smoker	106 (39)	26 (28)	132 (36)
Never Smoker	111 (41)	56 (60)	167 (46)
Family history of coronary artery disease	115 (43)	46 (50)	161 (45)
Epicardial Fat Volume	96.0 (72.0,126.0)	122.0 (92.0,160.0)	102.0 (78.0,131.0)
CACS[*] and CT angiography (CTA)			
Positive Calcium Score (CACS[*]>0)	235 (84)	78 (82)	313 (83)
Coronary artery plaque with stenosis (CTA 50%)	195 (69)	54 (56)	249 (66)
Invasive angiography			
Coronary artery stenosis (QCA[†] 50%)	183 (64)	45 (47)	228 (60)
Coronary artery severe stenosis (QCA[†] 70%)	138 (49)	35 (36)	173 (46)
Coronary artery occlusion (QCA[†]=100%)	54 (19)	12 (13)	66 (17)
Single photon emission computed tomography			
Myocardial hypo-perfusion (SSS[‡]>0)	142 (50)	46 (48)	188 (49)
Myocardial ischemia (SDS[§] >0)	217 (76)	62 (65)	279 (73)

[*] CACS: coronary artery calcium score

[†] QCA: quantitative coronary angiography

[‡] SSS: summed Stress score

[§] SDS: summed difference score

Table 2

Epicardial Fat Volume by Risk Factors and Ethnicity

Group	N	Epicardial Fat Volume (Median [Q1, Q3])	p-value[**]
All patients	380	101.76 [77.58, 131.02]	
Diabetes			
Yes	130	100.02 [71.88, 127.89]	0.34
No	250	103.12 [79.07, 134.53]	
Smoking			
Never	167	96.81 [77.61, 123.70]	0.053
Former	132	108.69 [84.29, 140.13]	
Current	64	96.95 [71.03, 132.45]	
Hypertension			
Yes	296	103.60 [80.55, 132.05]	0.01
No	82	90.67 [68.44, 127.60]	
Dyslipidemia			
Yes	253	101.80 [78.41, 130.77]	0.74
No	119	101.58 [71.81, 132.47]	
Family History of CAD[*]			
Yes	161	101.12 [80.40, 130.95]	0.98
No	196	102.72 [74.94, 131.33]	
Previous MI			
Yes	103	104.83 [76.89, 140.09]	0.41
No	277	100.76 [77.61, 130.95]	
BMI			
Normal (<25)	127	94.10 [68.70, 126.15]	<0.0001
Overweight (25–<30)	157	99.28 [78.78, 126.78]	
Obese (30)	96	122.04 [92.10, 159.52]	
Race			
Caucasian	212	103.33 [81.56, 134.76]	0.01
Asian	125	103.10 [77.55, 138.66]	
African-American	43	84.30 [68.44, 111.96]	

[**] p-values calculated by Kruskal-Wallis ANOVA

[*] CAD: Coronary artery disease

Table 3

Odds Ratios for Calcified Atherosclerosis (Calcium score >0)

Logistic Regression Models	Odds ratio	Lower CL	Upper CL	p
Model 1: Unadjusted				
Epicardial fat volume (EFV)	1.005	0.999	1.012	0.1259
Model 2: includes age, gender and race				
Age	1.111	1.065	1.159	<.0001
Gender (male vs. female)	3.254	1.790	5.918	0.0001
Race (Caucasian vs. Asian)	0.929	0.455	1.895	0.8388
Race (African-American vs. Asian)	0.572	0.225	1.455	0.2410
Epicardial fat volume (EFV)	0.999	0.992	1.006	0.8106
Model 3: all predictors				
Age	1.117	1.058	1.179	<.0001
Gender (male vs. female)	2.205	1.042	4.664	0.0386
Race (Caucasian vs. Asian)	0.875	0.346	2.214	0.7780
Race (African-American vs. Asian)	0.441	0.131	1.488	0.1871
BMI[*] (obese [BMI 30] vs. normal [BMI<25])	2.373	0.797	7.068	0.1207
BMI (overweight [BMI 25–29] vs. normal [BMI<25])	1.656	0.673	4.074	0.2718
Hypertension	2.989	1.255	7.116	0.0134
Dyslipidemia	1.036	0.466	2.301	0.9308
Family History of coronary artery disease	1.431	0.685	2.988	0.3405
Previous myocardial infarction	1.657	0.566	4.857	0.3571
Diabetes mellitus	1.206	0.539	2.698	0.6491
Smoking (current vs. never)	2.407	0.890	6.508	0.0834
Smoking (former vs. never)	1.390	0.587	3.288	0.4537
Coronary artery disease (QCA[†] 50)	9.842	4.009	24.159	<.0001
Epicardial fat volume (EFV)	0.997	0.987	1.007	0.5412

Odds ratios relate to 1 unit change of EFV.

[*] BMI: body mass index

[†] QCA: quantitative coronary angiography

Table 4

Median Regression for Coronary Calcium Score

Median Regression Models	Estimate	Lower CL	Upper CL	p
Model 1: Unadjusted				
Epicardial fat volume (EFV)	1.4991	0.1635	2.8347	0.0279
Model 2: includes age, gender and race				
Age	7.4310	3.1887	11.6733	0.0006
Gender (male vs. female)	177.5607	120.7255	234.3959	<.0001
Race (Caucasian vs. Asian)	4.8345	−58.8501	68.5191	0.8814
Race (African-American vs. Asian)	−40.8245	−111.636	29.9867	0.2577
Epicardial fat volume (EFV)	0.1528	−0.5923	0.8980	0.6870
Model 3: all predictors				
Age	3.1339	−0.5691	6.8368	0.0969
Gender (male vs. female)	77.0303	24.6408	129.4197	0.0041
Race (Caucasian vs. Asian)	4.0177	−60.9330	68.9683	0.9032
Race (African-American vs. Asian)	−42.0501	−118.457	34.3563	0.2797
BMI (obese [BMI 30] vs. normal [BMI<25])	29.1242	−38.1791	96.4275	0.3952
BMI (overweight [BMI 25–29] vs. normal [BMI<25])	0.8471	−58.4900	60.1842	0.9776
Hypertension	32.4875	−29.8496	94.8247	0.3060
Dyslipidemia	24.0807	−24.7714	72.9329	0.3329
Family History of coronary artery disease	30.7022	−18.9112	80.3155	0.2243
Previous myocardial infarction	−21.7638	−104.540	61.0119	0.6053
Diabetes mellitus	−0.5811	−61.9160	60.7539	0.9851
Smoking (current vs. never)	12.1613	−48.8039	73.1266	0.6950
Smoking (former vs. never)	−12.4693	−71.5221	46.5835	0.6781
Coronary artery disease ([†] QCA 50)	255.4947	187.1849	323.8045	<.0001
Epicardial fat volume (EFV)	0.0972	−0.6022	0.7965	0.7848

Median calcium score for 1 unit change of EFV.

[*] BMI: body mass index;

[†] QCA: quantitative coronary angiography

Table 5

Odds Ratios for Obstructive Coronary Artery Disease (1 Stenosis 50% by QCA[*])

Logistic Regression Models	Odds ratio	Lower CL	Upper CL	p
Model 1: Unadjusted				
Epicardial fat volume (EFV)	1.002	0.997	1.006	0.4903
Model 2: includes age, gender and race				
Age	1.027	1.000	1.055	0.0533
Gender (male vs. female)	3.188	2.026	5.016	<.0001
Race (Caucasian vs. Asian)	0.783	0.478	1.281	0.3299
Race (African-American vs. Asian)	0.528	0.246	1.132	0.1006
Epicardial fat volume (EFV)	0.998	0.993	1.003	0.5009
Model 3: all predictors				
Age	1.033	0.999	1.067	0.0582
Gender (male vs. female)	3.219	1.885	5.498	<.0001
Race (Caucasian vs. Asian)	1.062	0.569	1.985	0.8492
Race (African-American vs. Asian)	0.582	0.234	1.450	0.2455
BMI[*] (obese [BMI 30] vs. normal [BMI<25])	0.507	0.235	1.094	0.0834
BMI (overweight [BMI 25–29] vs. normal [BMI<25])	1.133	0.609	2.107	0.6939
Hypertension	1.644	0.844	3.203	0.1437
Dyslipidemia	1.952	1.110	3.431	0.0201
Family History of coronary artery disease	1.323	0.787	2.225	0.2908
Previous myocardial infarction	2.970	1.532	5.759	0.0013
Diabetes mellitus	1.539	0.897	2.641	0.1173
Smoking (current vs. never)	0.856	0.427	1.715	0.6615
Smoking (former vs. never)	0.986	0.551	1.765	0.9616
Epicardial fat volume (EFV)	1.000	0.993	1.006	0.9740

Odds ratios relate to 1 unit change of EFV.

[*]
BMI: body mass index

Table 6

Median regression for Obstructive Coronary Artery Disease

Median Regression Models	Estimate	Lower CL	Upper CL	p
Model 1: Unadjusted				
Epicardial fat volume (EFV)	−0.0156	−0.1316	0.1004	0.7913
Model 2: includes age, gender and race				
Age	0.4134	−0.1582	0.9851	0.1558
Gender (male vs. female)	31.8158	23.2695	40.3621	<.0001
Race (Caucasian vs. Asian)	0.6680	−9.5785	10.9145	0.8981
Race (African-American vs. Asian)	−20.6831	−34.1101	−7.2560	0.0026
Epicardial fat volume (EFV)	−0.0642	−0.1750	0.0467	0.2558
Model 3: all predictors				
Age	0.2490	−0.2838	0.7817	0.3586
Gender (male vs. female)	30.0674	20.3262	39.8085	<.0001
Race (Caucasian vs. Asian)	3.0629	−7.7204	13.8463	0.5767
Race (African-American vs. Asian)	−8.7321	−25.1360	7.6717	0.2957
BMI[*] (obese [BMI 30] vs. normal [BMI<25])	−8.0159	−21.5971	5.5653	0.2464
BMI (overweight [BMI 25–29] vs. normal [BMI<25])	4.2220	−6.4752	14.9193	0.4380
Hypertension	19.9254	8.5336	31.3172	0.0007
Dyslipidemia	10.2237	0.1095	20.3378	0.0476
Family History of coronary artery disease	9.0070	0.3296	17.6845	0.0420
Previous myocardial infarction	14.0616	4.6043	23.5189	0.0037
Diabetes mellitus	6.2628	−3.4387	15.9644	0.2050
Smoking (current vs. never)	−3.0321	−14.8693	8.8051	0.6146
Smoking (former vs. never)	5.0142	−4.8388	14.8672	0.3175
Epicardial fat volume (EFV)	−0.0885	−0.1876	0.0106	0.0799

Median calcium score for 1 unit change of EFV.

[*] BMI: body mass index.

Table 7

Odds Ratios for Abnormal Myocardial Perfusion (SPECT SSS[*]>0)

Logistic Regression Models	Odds ratio	Lower CL	Upper CL	p
Model 1: Unadjusted				
Epicardial fat volume (EFV)	0.996	0.992	1.001	0.1341
Model 2: includes age, gender and race				
Age	0.976	0.951	1.001	0.0621
Gender (male vs. female)	2.282	1.454	3.582	0.0003
Race (Caucasian vs. Asian)	1.517	0.950	2.422	0.0810
Race (African-American vs. Asian)	1.172	0.561	2.451	0.6727
Epicardial fat volume (EFV)	0.996	0.991	1.001	0.0972
Model 3: all predictors				
Age	0.967	0.936	0.999	0.0431
Gender (male vs. female)	1.706	0.991	2.938	0.0541
Race (Caucasian vs. Asian)	1.807	0.974	3.354	0.0607
Race (African-American vs. Asian)	1.532	0.621	3.783	0.3548
BMI[†](obese [BMI 30] vs. normal [BMI<25])	0.749	0.348	1.610	0.4591
BMI (overweight [BMI 25–29] vs. normal [BMI<25])	0.604	0.327	1.116	0.1071
Hypertension	1.447	0.738	2.838	0.2817
Dyslipidemia	0.703	0.398	1.242	0.2251
Family History of coronary artery disease	1.161	0.700	1.924	0.5629
Previous myocardial infarction	3.153	1.679	5.921	0.0004
Diabetes mellitus	1.537	0.907	2.604	0.1100
Smoking (current vs. never)	0.711	0.355	1.425	0.3361
Smoking (former vs. never)	1.022	0.581	1.797	0.9411
Coronary artery disease (QCA[‡] 50)	2.899	1.687	4.981	0.0001
Epicardial fat volume (EFV)	0.995	0.989	1.001	0.1197

Odds ratios relate to 1 unit change of EFV.

[*]SSS: summed Stress score;

[†]BMI: body mass index;

[‡]QCA: quantitative coronary angiography

Table 8

Median Regression for Abnormal Myocardial Perfusion

Median Regression Models	Estimate	Lower CL	Upper CL	p
Model 1: Unadjusted				
Epicardial fat volume (EFV)	−0.0144	−0.0324	0.0037	0.1178
Model 2: includes age, gender and race				
Age	−0.0810	−0.1525	−0.0096	0.0263
Gender (male vs. female)	3.3608	2.2005	4.5210	<.0001
Race (Caucasian vs. Asian)	0.9842	−0.4308	2.3991	0.1722
Race (African-American vs. Asian)	−0.1906	−2.0793	1.6981	0.8428
Epicardial fat volume (EFV)	−0.0103	−0.0238	0.0032	0.1346
Model 3: all predictors				
Age	−0.0996	−0.1601	−0.0392	0.0013
Gender (male vs. female)	0.9544	−0.0432	1.9520	0.0607
Race (Caucasian vs. Asian)	1.6921	0.4589	2.9252	0.0073
Race (African-American vs. Asian)	0.5532	−1.4414	2.5478	0.5857
BMI[*] (obese [BMI 30] vs. normal [BMI<25])	−0.3259	−1.9246	1.2728	0.6886
BMI (overweight [BMI 25–29] vs. normal [BMI<25])	−0.6627	−1.9812	0.6559	0.3235
Hypertension	0.9793	−0.3532	2.3119	0.1492
Dyslipidemia	−0.8929	−2.0679	0.2820	0.1358
Family History of coronary artery disease	−0.0794	−1.1940	1.0353	0.8887
Previous myocardial infarction	3.3575	1.4069	5.3081	0.0008
Diabetes mellitus	1.1218	−0.1656	2.4093	0.0874
Smoking (current vs. never)	−1.4779	−2.8058	−0.1501	0.0293
Smoking (former vs. never)	−0.6715	−1.8462	0.5033	0.2616
Coronary artery disease (QCA[†] 50)	2.4005	1.1199	3.6811	0.0003
Epicardial fat volume (EFV)	−0.0124	−0.0259	0.0010	0.0690

Median Summed stress score for 1 unit change of EFV.

[*] BMI: body mass index;

[†] QCA: quantitative coronary angiography