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Hepatic Steatosis and Subclinical Cardiovascular Disease in a Cohort Enriched for Type 2 Diabetes: The Diabetes Heart Study

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Abstract

OBJECTIVES—To explore mechanisms whereby hepatic steatosis may be associated with cardiovascular risk, we investigated cross-sectional relationships between hepatic steatosis, regional fat accumulation, inflammatory biomarkers, and subclinical measures of atherosclerosis in the Diabetes Heart Study.

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METHODS—The Diabetes Heart Study is a family study of sibling pairs concordant for type 2 diabetes. A subset of 623 randomly selected participants was evaluated for hepatic steatosis, defined as a liver:spleen attenuation ratio of <1.0 by computed tomography. We quantified visceral fat, subcutaneous fat, coronary, aortic, and carotid artery calcium by computed tomography; and carotid atherosclerosis by ultrasound. Associations between the liver:spleen attenuation ratio and these factors were expressed as Spearman correlations.

RESULTS—After adjustment for age, race, gender, body mass index, and diabetes status, the liver:spleen attenuation ratio correlated with visceral fat (r = −0.22, $P < 0.0001$) and subcutaneous fat (r = −0.13, $P = 0.031$). Hepatic steatosis was associated with lower high-density lipoprotein (r = 0.21, $P < 0.0001$), higher triglycerides (r = −0.25, $P < 0.0001$), higher C-reactive protein (r = −0.095, $P = 0.004$), and lower serum adiponectin (r = 0.34, $P < 0.0001$). There were no significant associations between the liver:spleen attenuation ratio and coronary, aortic, or carotid calcium, or carotid intimal thickness.

CONCLUSIONS—This suggests that hepatic steatosis is less likely a direct mediator of cardiovascular disease and may best be described as an epiphenomenon. The strong correlations between pro-atherogenic biomarkers, visceral fat, and elements of the metabolic syndrome suggest that hepatic steatosis reflects more than general adiposity, but represents a systemic, inflammatory, pro-atherogenic adipose state.

INTRODUCTION

Hepatic steatosis (HS) is an increasingly prevalent condition observed in Western nations, presumably due to consumption of a high-fat diet (1). HS may be viewed as a precursor to nonalcoholic steatohepatitis (NASH), which greatly increases the risk of developing hepatic cirrhosis over time (2). In addition to these known risks of progressive liver injury, numerous studies have uncovered a correlation between hepatic steatosis and the metabolic syndrome. HS has been linked to visceral adiposity, low serum HDL, high serum triglycerides, pro-inflammatory biomarkers such as C-reactive protein, and has been shown to be associated with an increased risk of cardiovascular events independent of these other variables in diabetic patients (3–7). While the data linking HS to the metabolic syndrome are compelling, whether HS can be viewed as a risk factor of cardiovascular disease independent of traditional components of the metabolic syndrome remains to be determined.

Increased carotid intimal thickness has also been linked to classic features of the metabolic syndrome including visceral fat accumulation. However, there is conflicting evidence of an independent relationship between hepatic steatosis and measures of subclinical atherosclerosis. An association between hepatic steatosis and carotid intimal medial thickness was found in one cross-sectional study (10), but not in two others (8, 9).

These findings merit further inquiry as to whether hepatic steatosis itself mediates the development of cardiovascular disease and if it could be incorporated into predictive models. Growing evidence suggests that the presence of abnormal coronary, aortic, and carotid calcium deposits as measured by computed tomography (CT) may be an important subclinical predictor of cardiovascular disease (11, 12). The benefits of screening for arterial calcium deposition have been postulated to aid in risk stratification for coronary disease (13). Therefore, an evaluation of associations between hepatic steatosis and vascular calcium affords a novel opportunity to evaluate the role of hepatic steatosis as a participant in the causal pathway for atherosclerosis *versus* simply an epiphenomenon.

We have undertaken a cross-sectional analysis of diabetic individuals enrolled in the Diabetes Heart Study (DHS) to assess relationships between hepatic steatosis and proatherogenic biomarkers, regional fat measurements, elements of the metabolic syndrome,

and subclinical cardiovascular disease as measured by carotid intimal thickness and carotid, aortic, and coronary calcium.

METHODS

Study Population and Selection

The DHS is a family study in which siblings concordant for type 2 diabetes as well as unaffected family members were recruited from Internal Medicine and Endocrinology clinics in western North Carolina. The DHS study design has been described in detail previously (14–16). To summarize, entry criteria required index cases diagnosed with type 2 diabetes mellitus after age 34 and no historical evidence of diabetic ketoacidosis. At least one type 2 diabetic sibling was recruited for each index case enrolled. Additional non-diabetic family members were also enrolled when possible. The study was approved by the Institutional Review Board at the Wake Forest University School of Medicine and all subjects provided comprehensive informed consent for all study protocols. From this existing DHS cohort, 623 individuals were randomly selected to participate in a sub-study of regional fat distribution. These patients underwent additional measurements including abdominal computed tomography to quantify hepatic density and visceral and subcutaneous fat, neck, and chest computed tomography to measure arterial calcium, and B-mode carotid ultrasound to measure carotid intimal thickness.

Demographic Variables

Study participants were evaluated between 1999 and 2005 at the General Research Center of Wake Forest University School of Medicine. Comprehensive interviews focusing on medical history and health behaviors were obtained from all patients. Participants were questioned about smoking history. Pack-years were quantified among all participants as the average number of packs per day × the total number of years smoked. Newer smokers (those who reported having smoked less than 100 cigarettes in their lifetime) were coded as having zero pack-years.

Measurements of weight and height to the nearest 0.5 cm and 0.1 kg were obtained during the visits, and resting blood pressure was measured. Hypertension was defined as the current use of any anti-hypertensive medication or a resting systolic blood pressure greater than 140 mmHg or resting diastolic blood pressure greater than 90 mmHg.

Fasting laboratory assays for total cholesterol, high-density lipoprotein cholesterol, triglycerides, glucose, and hemoglobin A1c were obtained. Low-density lipoprotein concentration was calculated using the Freidewald equation and results were considered valid for subjects whose triglycerides were less than 796 mg/dL (17).

Radiographic Imaging Techniques

Non-contrast enhanced computed tomography is a valid tool for measuring the fat content of the liver (18, 19), and therefore provides a useful method to describe the presence and severity of hepatic steatosis. The CT attenuation of the liver was measured as the average measurement from three regions of interest, one from each hepatic lobe. The attenuation of the spleen, recorded from a single homogenous region, was used as an internal control to correct the hepatic attenuation. In this study, the presence of hepatic steatosis was defined as liver to spleen attenuation ratio (L:SAR) of <1.0. An alternative method of defining hepatic steatosis is a liver attenuation of <40 Hounsfield units (18). Data from both methods are included, but the L:SAR serves to eliminate variance by providing an internal control.

Calcified plaque was measured in the aorta, carotid arteries, and coronary arteries with single and multidetector CT systems using a standardized protocol (20). Images were obtained during a breath-hold with ECG gating at 50% of the RR interval. During the scans, a calibration standard (Image Analysis, Columbia, KY) was placed underneath each participant. In addition to the daily calibrations, biweekly calibration checks for measurement of calcium hydroxyapatite were performed and recorded.

CT exams were analyzed by experienced analysts producing an Agatston score corrected for slice thickness on a GE Advantage Windows Workstation using the SmartScores software package (General Electric Medical Systems, Waukesha, WI). The reproducibility of coronary artery calcification (CAC) scores in our hands obtained from the duplicate scans and inter and intra-observer variability were all >0.96.

Visceral and subcutaneous fat measurements at the level of L4-L5 were obtained using a 4-slice Multi-Detector CT system (Light Speed; General Electric Healthcare, Waukesha, WI).

Carotid intimal thickness was measured using procedures previously described (21). High-resolution B-mode carotid ultrasonography was performed by using a 7.5-MHz transducer and a Biosound Esaote (AU5) ultrasound machine, and B-mode images were recorded on an S-VHS videocassette. Scans were performed on both the right and left extracranial carotid arteries by trained and certified ultrasound technicians. A preliminary exploratory transverse scan was performed to assess the participant's anatomy and to detect the presence of significant atherosclerotic disease. A second exploratory longitudinal scan was then performed on the common carotid, the bulb, and the internal carotid to assist in interpreting the presence of significant disease. Standardized longitudinal images were then acquired of the near and far walls of the distal 10-mm portion of the common carotid artery at five predefined interrogation angles spaced 30° apart on each side. The mean value of intimal medial thickness (IMT) was then measured offline in a total of 20 arterial segments, including both sides of the neck. The mean value of up to 20 mean common carotid IMT values is expressed as carotid intimal thickness in this study.

Statistical Analyses

The sample means and standard deviations were computed for the continuous characteristics and the measures of subclinical cardiovascular disease (coronary, carotid, and aorta artery calcified plaque and carotid IMT). For the discrete demographic characteristics, the numbers and proportions were calculated. To better approximate the distributional assumptions of conditional normality and homogeneity of variance, the transformation for each measurement was carefully examined using Box-Cox transformations (22).

Associations between HS and measures of interest such as regional body fat, pro-atherogenic biomarkers, and measures of subclinical cardiovascular disease were determined using Spearman's correlation (without adjusting for other covariates) and partial correlation coefficients (after adjusting for covariates). It should be appreciated that in addition to the usual possible confounding covariates, correlations between individual subjects in our data set who are members of the same family have potential to confound the results. We used generalized estimating equations (GEE) to adjust for these familial correlations (23). A series of GEE models assuming exchangeable correlation and using the empirical estimate of the variance to adjust for familial correlation were used to compare the characteristics between those with and without HS (24). Standard regression diagnostic for collinearity and influence were computed for each model. All statistical analyses were performed using SAS version 9.1.3 (SAS, Cary, NC).

RESULTS

Of the 623 subjects from 243 families enrolled in the study, 431 (69.2%) were found to have a normal liver and 192 (30.8%) had HS as defined by L:SAR of <1.0. Subjects with a normal liver are compared to those with HS in Table 1. No statistically significant associations were detected between HS and smoking history or number of years as a diabetic. On average, subjects with HS had a higher body mass index (BMI) with an adjusted mean BMI of 31.8 in the normal liver group *versus* an adjusted mean BMI of 34.4 in the HS group (*P* value <0.0001). Hemoglobin A1C was higher in the HS group (8.1 ± 0.14% vs. 7.6 ± 0.12%, *P* value 0.0006) indicating less stringent diabetic control among those with hepatic steatosis. The prevalence of hypertension, coronary artery disease, and stroke did not differ between those with and without HS.

As expected, biomarkers that are associated with hyperlipidemia and the metabolic syndrome correlated with hepatic steatosis. Adjusted mean serum triglycerides were significantly higher in the HS group (216 ± 11.1 mg/dL *vs.* 148 ± 5.1 mg/dL, $P < 0.0001$) and serum HDL was significantly lower in the HS group (42.5 ± 1.1 mg/dL *vs.* 48.1 ± 0.8 mg/dL, $P < 0.0001$). Serum LDL levels were not significantly different between the two groups, and statin therapy was not associated with presence or absence of HS. Although alcohol use was slightly greater in the HS group, there was not a statistically significant correlation between alcohol use and HS in this study. Mean serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT) were slightly higher in the HS group, but only SGPT demonstrated statistical significance (SGPT 33.2 *vs.* 25.77, $P = 0.0268$).

After adjusting for age, gender, race, and diabetes status, measurements of visceral intra-abdominal fat by computed tomography negatively correlated with L:SAR, thus indicating positive correlation with HS ($r = -0.2236$, $P < 0.001$). Correlations between L:SAR and measurements of subcutaneous fat were weaker, but present ($r = -0.1332$, $P = 0.0031$, Table 2). Body mass index was also significantly correlated with L:SAR in adjusted models ($r = -0.1931$, $P < 0.0001$).

As shown in Table 3, L:SAR directly correlated with serum adiponectin levels ($r = 0.3372$, $P < 0.0001$), and inversely correlated with serum CRP ($r = -0.0946$, $P = 0.0040$). Serum triglycerides were inversely associated with L:SAR, signifying a higher triglyceride level among those with HS ($r = -0.2454$, $P < 0.0001$). In contrast, serum HDL was directly correlated with L:SAR, signifying lower levels of HDL in those with HS ($r = 0.2055$, $P < 0.0001$).

In the unadjusted models, aortic calcium and carotid intimal thickness were significantly associated with L:SAR. However, after adjusting for age, gender, race, diabetes status, pack-year smoking history, visceral adiposity, and CRP, the relationship disappeared (Table 4).

These relationships were also investigated using an alternative definition of hepatic steatosis, defined as liver attenuation <40 Hounsfield units. The correlations remained the same as the comparisons using L:SAR.

DISCUSSION

This cross-sectional cohort study of diabetic families from the DHS utilized an existing database of serum biomarkers and radiographic imaging to investigate the link between hepatic steatosis and subclinical cardiovascular disease as measured by coronary, aortic, and carotid calcium levels and carotid intimal thickness. Numerous studies have consistently demonstrated a link between hepatic steatosis and a pro-atherogenic, pro-inflammatory

biomarker profile (low HDL, high triglycerides, high CRP, and low adiponectin), but no study had investigated whether the presence of hepatic steatosis was independently associated with subclinical cardiovascular disease as measured by arterial calcium deposition.

While we did identify a significant association between L:SAR and aortic calcium and carotid intimal thickness in the unadjusted models, these associations appeared to be mediated through metabolic factors. Upon adjustment for these factors, the associations were eliminated. Similar relationships were noted when using the alternative definition of hepatic steatosis of liver attentuation <40 Hounsfield units.

The expected correlations demonstrated between HS and visceral adiposity, increased BMI, low HDL, high triglycerides, low adiponectin, and high CRP are consistent with the large body of evidence which links hepatic steatosis to the metabolic syndrome as a systemic inflammatory state. Additionally, these findings help to validate our measurement of hepatic steatosis. Interestingly, hepatic steatosis did not demonstrate a statistically significant link between history of prevalent coronary disease, stroke, or hypertension in this study.

Some potential limitations of this study include the pre-ponderance of diabetics among the sample population and the nature of the DHS as a family study. While a diabetic population will invariably have a skewed representation of many pro-atherogenic variables, collecting data from diabetic individuals has added utility, as they are at higher risk for metabolic syndrome and subclinical cardiovascular disease. In spite of this, no convincing link could be made between subclinical cardiovascular disease as measured by arterial calcium and hepatic steatosis. The possibility remains that the considerable extent of subclinical atherosclerosis in this diabetic cohort may actually limit our ability to observe a graded relationship with HS.

Our data are suggestive that HS is less likely to be a direct mediator of subclinical cardiovascular disease and may instead represent an epiphenomenon. The strong correlations that we observed between pro-atherogenic biomarkers and the elements of the metabolic syndrome suggest that hepatic steatosis reflects more than general adiposity, but represents a systemic, inflammatory, pro-atherogenic adipose state.

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STUDY HIGHLIGHTS

What Is Current Knowledge

- Hepatic steatosis is associated with inflammation and the metabolic syndrome.
- Inflammation and metabolic syndrome are associated with coronary disease.
- Data directly linking hepatic steatosis and coronary disease exist but are limited.

What Is New Here

- The association between hepatic steatosis and cardiovascular disease is likely an epiphenomenon.
- Arterial calcium and carotid intimal thickness did not correlate with hepatic steatosis.
- Hepatic steatosis was more strongly associated with visceral fat than subcutaneous fat.

Table 1

Comparison of Demographic Characteristics between Those With and Without Hepatic Steatosis

Variable	Categories	Raw Values All (N = 623)	GEE Model-Based Means and *P* Values		
			Normal Liver (N = 431)	Fatty Liver (N = 192)	*P* Value
Age (yrs)	Mean (SE)	61.2 (8.8)	62.1 (9.1)	59.0 (7.8)	<0.001
Male	Yes (%)	278 (44.6%)	201 (46.6%)	77 (40.1%)	0.1555
Female	Yes (%)	345 (55.4%)	230 (53.4%)	115 (59.9%)	0.1555
White	Yes (%)	480 (77.1%)	316 (73.3%)	164 (85.4%)	0.0015
Black	Yes (%)	143 (23.0%)	115 (26.7%)	28 (14.6%)	0.0015
Smoking	Never (%)	243 (39.1%)	168 (39.2%)	75 (39.0%)	0.5241
	Former (%)	251 (40.4%)	175 (40.8%)	76 (39.6%)	0.5241
	Current (%)	127 (21.4%)	86 (20.0%)	41 (21.4%)	0.5241
Percent alcohol *	Mean (SE)	0.87 (3.94)	0.8 (3.52)	1.02 (4.77)	0.5851
Pack-years smoking (pack-yrs)	Mean (SE)	19.4 (26.0)	18.7 (1.2)	19.2 (2.0)	0.832
BMI (kg/m^2)	Mean (SE)	31.9 (6.4)	31.8 (0.38)	34.4 (0.54)	<0.0001
Diabetes	Yes (%)	516 (82.8%)	343 (79.6%)	173 (90.1%)	<0.0001
Years with diabetes (yrs)	Mean (SE)	10.3 (7.3)	10.9 (0.43)	10.2 (0.59)	0.2005
Hemoglobin A1c (%)	Mean (SE)	7.4 (1.8)	7.6 (0.1)	8.1 (0.1)	0.0006
Hyperlipidemia	Yes (%)	353 (59.6%)	256 (61.1%)	97 (56.1%)	0.2632
Statin therapy	Yes (%)	251 (40.3%)	181 (42.0%)	70 (36.5%)	0.3453
SGPT (ALT)	Mean (SE)	25.77 (36.05)	22.56 (12.93)	33.2 (62.05)	0.0268
SGOT (AST)	Mean (SE)	28.07 (24.85)	26.58 (11.06)	31.48 (41.73)	0.1284
Serum triglycerides (mg/dL)	Mean (SE)	183 (117)	148 (5.1)	216 (11.1)	<0.0001
Serum HDL (mg/dL)	Mean (SE)	45.7 (13.9)	48.1 (0.79)	42.5 (1.1)	<0.0001
Serum LDL (mg/dL)	Mean (SE)	108 (32)	111 (2.1)	105 (2.9)	0.0606
Serum CRP (mg/dL)	Mean (SE)	0.65 (0.96)	0.61 (0.05)	0.75 (0.09)	0.1206
Serum adiponectin (mg/L)	Mean (SE)	11.5 (7.8)	12.6 (0.50)	8.6 (0.54)	<0.0001
Hypertension	Yes (%)	524 (84.1%)	368 (85.4%)	156 (56.1%)	0.8676
Systolic blood pressure (mmHg)	Mean (SE)	139 (19.1)	140 (1.2)	141 (1.4)	0.8315
Diastolic blood pressure (mmHg)	Mean (SE)	72.7 (10.0)	73.1 (0.52)	74.8 (0.80)	0.0445
History of cardiovascular disease **	Yes (%)	246 (42.4%)	171 (42.8%)	75 (41.7%)	0.5693
History of stroke	Yes (%)	56 (9.2%)	39 (9.2%)	17 (8.9%)	0.7252
Coronary calcium (Agatston score)	Mean (SE)	1669 (2945)	1622 (137)	1894 (226)	0.225
Carotid calcium (Agatston score)	Mean (SE)	336 (702)	348 (39.1)	263 (43.6)	0.065
Aortic calcium (Agatston score)	Mean (SE)	11468 (16111)	11077 (804)	10173 (1093)	0.3997
Carotid intimal thickness (mm)	Mean (SE)	0.69 (0.13)	0.70 (0.01)	0.70 (0.01)	0.2389

All GEE models are adjusted for age, race, and gender.

For quantitative variables, means and (standard errors) are reported.

For categorical variables, raw counts and (raw percentages) are reported.

Self-reported history of myocardial infarction.

Q-wave abnormality on EKG (Minnesota code 1.1, 1.2 (except 1.28), 1.3. 4.1, 4.3, 5.1, or 5.3).

Self-reported history of coronary artery bypass graft (CABG).

Self-reported history of percutaneous transluminal coronary angioplasty.

Self-reported history of stroke.

Self-reported history of carotid endarterectomy.

Self-reported history of angina pectoralis.

Self-reported history of any vascular procedure.

* Definition of percent alcohol—estimated percent of a participant's daily energy consumption (in kcal), which is made up by alcohol.

** Definition of cardiovascular disease—any one of the following are true:

Table 2

Correlations between Measures of Hepatic Steatosis (L:SAR and Liver Attenuation) and Regional Body Fat

	Model	Number	Spearman r	GEE-adjusted *P* Value
BMI to L:SAR	0	623	−0.2296	<0.0001
BMI to L:SAR	1	623	−0.1931	<0.0001
BMI to liver attenuation	0	623	−0.3137	<0.0001
BMI to liver attenuation	1	623	−0.2813	<0.0001
Subcutaneous fat at L4/L5 to L:SAR	0	596	−0.1267	0.0002
Subcutaneous fat at L4/L5 to L:SAR	1	596	−0.1332	0.0031
Subcutaneous fat at L4/L5 to liver attenuation	0	596	−0.2181	<0.0001
Subcutaneous fat at L4/L5 to liver attenuation	1	596	−0.2109	0.0005
Intra-abdominal fat at L4/L5 to L:SAR	0	598	−0.3166	<0.0001
Intra-abdominal fat at L4/L5 to L:SAR	2*	598	−0.2236	<0.0001
Intra-abdominal fat at L4/L5 to liver attentuation	0	598	−0.3598	<0.0001
Intra-abdominal fat at L4/L5 to liver attentuation	2*	598	−0.2335	<0.0001

Model 0: Unadjusted.

Model 1: Adjusted for age, gender, race, diabetes status, pack-years smoking history, and intra-abdominal fat.

Model 2: Adjusted for age, gender, race, diabetes status, and pack-years smoking history.

*Model 2 was used here because intra-abdominal fat cannot be adjusted for itself and yield a meaningful result.

Table 3

Correlations between Measures of Hepatic Steatosis (L:SAR and Liver Attenuation) and Inflammatory Markers and Lipoprotein Concentrations

	Model	Number	Spearman r	GEE-Adjusted *P* Value
log(serum C-reactive protein) to L:SAR	0	608	−0.1557	<0.0001
log(serum C-reactive protein) to L:SAR	2	608	−0.0946	0.004
log(serum C-reactive protein) to liver attenuation	0	608	−0.2224	<0.0001
log(serum C-reactive protein) to liver attenuation	2	608	−0.1398	0.0004
log(serum adiponectin) to L:SAR	0	588	0.357	<0.0001
log(serum adiponectin) to L:SAR	2	588	0.3372	<0.0001
log(serum adiponectin) to liver attenuation	0	588	0.292	<0.001
log(serum adiponectin) to liver attenuation	2	588	0.2852	<0.001
Total serum cholesterol to L:SAR	0	621	−0.0394	0.678
Total serum cholesterol to L:SAR	2	621	−0.0213	0.6863
Total serum cholesterol to liver attenuation	0	621	−0.0877	0.2286
Total serum cholesterol to liver attenuation	2	621	−0.0614	0.8569
log(serum triglycerides) to L:SAR	0	621	−0.3048	<0.0001
log(serum triglycerides) to L:SAR	2	621	−0.2454	<0.0001
log(serum triglycerides) to liver attenuation	0	621	−0.2632	<0.0001
log(serum triglycerides) to liver attenuation	2	621	−0.1869	<0.0001
Serum HDL to L:SAR	0	621	0.2543	<0.0001
Serum HDL to L:SAR	2	621	0.2055	<0.0001
Serum HDL to liver attenuation	0	621	0.1775	<0.0001
Serum HDL to liver attenuation	2	621	0.1374	<0.0001
Serum LDL to L:SAR	0	592	0.018	0.2069
Serum LDL to L:SAR	2	592	0.3336	0.1032
Serum LDL to liver attenuation	0	592	−0.0397	0.6734
Serum LDL to liver attenuation	2	592	−0.0280	0.4224

Model 0: Unadjusted.

Model 2: Adjusted for age, gender, race, diabetes status, and pack-years smoking history.

Table 4

Sequential Multivariable Models of Correlation between Measures of Hepatic Steatosis (L:SAR and Liver Attenuation) and Vascular Calcium

	Model	Number	Spearman r	GEE-Adjusted *P* Value
log(coronary calcium) to L:SAR	0	606	0.0479	0.4289
log(coronary calcium) to L:SAR	2	606	0.086	0.1626
log(coronary calcium) to L:SAR	3	574	0.0799	0.2015
log(coronary calcium) to liver attenuation	0	606	0.0693	0.2628
log(coronary calcium) to liver attenuation	2	606	0.1093	0.0741
log(coronary calcium) to liver attenuation	3	574	0.109	0.0573
log(carotid calcium) to L:SAR	0	605	0.0859	0.2127
log(carotid calcium) to L:SAR	2	605	0.0853	0.3104
log(carotid calcium) to L:SAR	3	573	0.0844	0.3098
log(carotid calcium) to liver attenuation	0	605	0.0939	0.2172
log(carotid calcium) to liver attenuation	2	605	0.1019	0.2888
log(carotid calcium) to liver attenuation	3	573	0.1004	0.2143
Aortic calcium to L:SAR	0	599	0.1207	0.0081
Aortic calcium to L:SAR	2	599	0.0951	0.0607
Aortic calcium to L:SAR	3	575	0.1022	0.1444
Aortic calcium to liver attenuation	0	599	0.1063	0.013
Aortic calcium to liver attenuation	2	599	0.0674	0.0943
Aortic calcium to liver attenuation	3	575	0.0606	0.1302
Carotid intimal thickness to L:SAR	0	598	0.0818	0.0255
Carotid intimal thickness to L:SAR	2	598	0.0319	0.3376
Carotid intimal thickness to L:SAR	3	565	0.0347	0.3901
Carotid intimal thickness to liver attenuation	0	598	0.0675	0.0234
Carotid intimal thickness to liver attenuation	2	598	0.0056	0.3994
Carotid intimal thickness to liver attenuation	3	565	0.0006	0.5287

Model 0: Unadjusted.

Model 2: Adjusted for age, gender, race, diabetes status, and pack-years smoking history.

Model 3: Adjusted for age, gender, race, diabetes status, pack-years, visceral adipose tissue, and CRP.