Title

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Journal

Academic radiology, 17(12)

ISSN

1878-4046

Authors

Ahmadi, Naser
Nabavi, Vahid
Yang, Eric
et al.

Publication Date

2010-12-13

Peer reviewed

Original Investigation

Increased Epicardial, Pericardial, and Subcutaneous Adipose Tissue Is Associated with the Presence and Severity of Coronary Artery Calcium

Naser Ahmadi, MD, Vahid Nabavi, MD, Eric Yang, MD, Fereshteh Hajsadeghi, MD, Mustapha Lakis, MD, Ferdinand Flores, BS, Irfan Zeb, MD, Manzoor Bevinal, MD, Ramin Ebrahimi, MD, Matthew Budoff, MD

Rationale and Objectives: Epicardial adipose tissue (EAT), pericardial adipose tissue (PAT), and subcutaneous adipose tissue (SAT) are mediators of metabolic risk and may be involved in the pathogenesis of coronary artery disease. The aim of this study was to investigate the association of visceral and subcutaneous fat depots with the presence and severity of coronary artery calcium (CAC) in asymptomatic individuals.

Materials and Methods: One hundred eleven consecutive subjects underwent CAC assessment, and their Framingham risk scores were measured. EAT, total thoracic adipose tissue, and SAT volumes were measured from slice level 15 mm above to 30 mm below the ostium of the left main coronary artery. PAT was calculated as thoracic adipose tissue − EAT. SAT was defined as the volume of fat depot anterior to the sternum and posterior to the vertebra. CAC was defined as 0, 1 to 100, 101 to 400, or ≥400. Relative risk regression analysis was used to assess the association between fat depots and CAC.

Results: There were modest correlations between EAT (r = 0.58), PAT (r = 0.47), SAT (r = 0.34), and CAC (P < .01). EAT, PAT, and SAT increased proportionally with the severity of CAC in both genders (P < .05). After adjustment for cardiovascular risk factors and body mass index, the relative risks for each standard deviation increase in EAT, PAT, and SAT were 3.3 (95% confidence interval, 1.9–5.6), 2.7 (95% confidence interval, 1.6–3.9), and 2.6 (95% confidence interval, 1.5–4.4) for CAC ≥ 100 compared to CAC 0, respectively (P < .05). The area under the receiver-operating characteristic curve to predict CAC ≥ 100 was higher in each fat depot compared to Framingham risk score, and addition of fat depots to Framingham risk score provided maximum prognostication value to detect CAC ≥ 100.

Conclusions: Increased EAT, PAT, and SAT are associated with the severity of CAC independent of risk factors.

Key Words: Epicardial adipose tissue; pericardial adipose tissue; total thoracic adipose tissue; subcutaneous adipose tissue; coronary artery calcium; coronary artery disease; risk factor.

Cardiovascular death has been reduced significantly because of improvements in detection and management of coronary artery disease (CAD) over the past few decades (1,2). However the recent increase in the rate of overweight and obesity, up to two thirds of the US population, may diminish the favorable effect of recent improvements in the diagnosis and treatment of CAD (2–4).

Adipocytes secrete numerous factors that could potentially modulate the development of vascular disease, including proinflammatory cytokines and adipokines, angiogenic molecules, and stem cell homing factors (5,6). Recent evidence indicates that adipose tissue is a functional component, exerting paracrine influences on blood vessel contractility (7,8).

Anthropometric measures such as body mass index (BMI) or waist circumference have traditionally been used to estimate overall adiposity. However, direct measures of region-specific adipose tissue are superior to estimated overall adiposity for the identification and management of high-risk individuals (2–4,9).

Recent studies have documented accurate visceral and subcutaneous adipose tissue (SAT) assessment using nonenhanced computed tomography (10). Previous studies have reported an association between epicardial adipose tissue (EAT) and the severity of CAD (5,11). However the associations between different visceral fat depots, EAT, and pericardial adipose tissue (PAT) as well as SAT with subclinical coronary atherosclerosis are not well studied.

In the present study, we evaluated (1) the associations of visceral and subcutaneous fat depots with the presence and severity of coronary artery calcium (CAC) in asymptomatic

Acad Radiol 2010; ■:1–7

From the Los Angeles Biomedical Research Institute at Harbor UCLA Medical Center, Torrance, CA (N.A., V.N., E.Y., F.H., M.L., F.F., I.Z., M.B., M.B.); and the Greater Los Angeles VA Medical Center, University of California, Los Angeles, School of Medicine, Los Angeles, CA (R.E.). Received April 28, 2010; accepted August 3, 2010. **Address correspondence to:** N.A. e-mail: nahmadi@labiomed.org

doi:10.1016/j.acra.2010.08.017

individuals, (2) the prognostic value of different fat depots to detect significant subclinical atherosclerosis, and (3) whether the addition of adipose tissue assessment to conventional cardiovascular risk assessment improves risk stratification.

MATERIALS AND METHODS

One hundred eleven consecutive asymptomatic patients who underwent CAC scanning from January to June 2009 were prospectively studied, and their adipose tissues were measured. Subjects with established cardiovascular disease, stroke, diabetic retinopathy, end-stage renal disease, Raynaud syndrome, infection, cancer, immunosuppression, systemic inflammation status, or end-stage liver disease were excluded. BMI, blood pressure, fasting blood glucose, and lipid profile were obtained by standard techniques. Risk factors were determined, and Framingham risk score (FRS) was calculated to assess the risk for developing coronary disease events (myocardial infarction or cardiovascular death) over the next 10 years (12). The study protocol and consent form were approved by the Institutional Review Board Committee of the Los Angeles Biomedical Research Institute at Harbor UCLA Medical Center.

CAC Scanning

CAC was detected using an E-Speed electron beam scanner (GE-Imatron, South San Francisco, CA). The coronary arteries were imaged with 30 to 40 contiguous 3-mm slices from 1 cm below the tracheal bifurcation to the base of the heart, with 100-ms exposure time, 400-mA electron gun current, and 120-kV electron gun voltage, during mid-diastole using electrocardiographic triggering with a 15-second breath hold. Image reconstruction was performed with a 250-mm field of view, 512 × 512 image matrix, and a kernel to achieve a high contrast resolution of 7 line pairs/cm.

Using the Agatston method, CAC was considered present in a coronary artery when a density threshold of >130 Hounsfield units (HU) was detected in ≥3 contiguous pixels (>1 mm^2) overlying that coronary artery and quantified. The region of interest was used to measure the area and peak density of the calcified plaques that were >2 pixels in size (0.5 mm^2).

The calcium score of each lesion was calculated by multiplying lesion area by a density factor derived from maximal HU within this area. The density factor was assigned in the following manner: 1 for lesions for which the maximal density was 130 to 199 HU, 2 for lesions 200 to 299 HU, 3 for lesions 300 to 399 HU, and 4 for lesions ≥400 HU. A total calcium score was determined by summing individual lesion scores at each anatomic site (13).

PAT, Thoracic Adipose Tissue (TAT), and SAT Measurement

Two experienced computed tomography readers, blinded to each other, patient characteristics, and CAC scores, measured

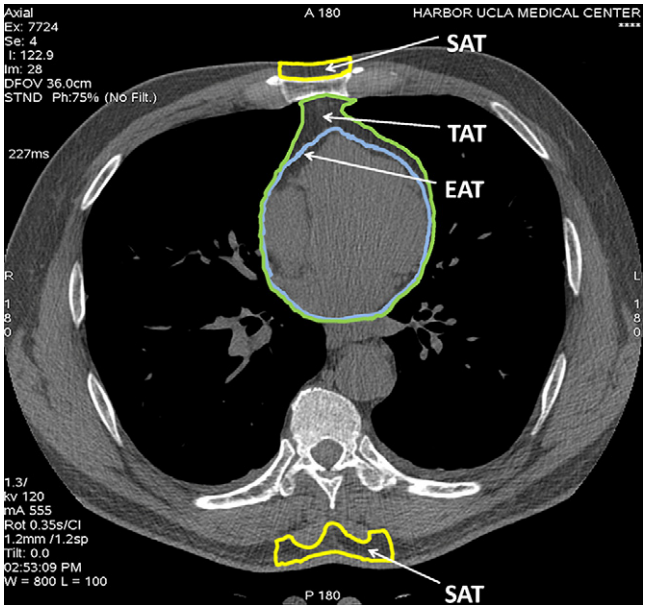

Figure 1. Adipose tissue was measured in axial images starting 15 mm above the superior extent of the left main coronary artery (LM) to 30 mm below that slice. Adipose tissue inside pericardial sac defined as epicardial adipose tissue (EAT; inside blue line). Combined inside and outside pericardial sac adipose tissue was defined as total thoracic adipose tissue (TAT; inside green line). Subcutaneous adipose tissue (SAT) was defined as the volume of fat depot anterior to the sternum and posterior to the vertebra (inside yellow line).

EAT, TAT, and SAT. Adipose tissue was measured in axial images starting 15 mm above the superior extent of the left main coronary artery to 30 mm below that slice. Volume Analysis software (GE Healthcare, Waukesha, WI) was used to discern adipose tissue on the basis of a corresponding HU threshold of −190 to −30 HU (mean, −120 HU) (10). Adipose tissue volumes were measured by a semiautomatic segmentation technique in each slice with the above display settings. The reader was required to manually trace the EAT, TAT, and SAT. The adipose tissue volume of each fat depot is the sum of all voxels (cubic centimeters) containing adipose tissue across 45 mm in length from 15 mm above to 30 mm below the left main coronary artery ostium.

Adipose tissue inside the pericardial sac defined as EAT. Combined inside and outside pericardial sac adipose tissue was defined as total TAT. PAT was calculated as TAT − EAT. SAT was defined as the volume of fat depot anterior to the sternum and posterior to the vertebra (Fig 1).

Statistical Analysis

All statistical analyses were performed using PASW version 18.0 (SPSS, Inc, Chicago, IL). CAC was classified according to the calcium score groupings of 0, 1 to 100, 101 to 400, and ≥400. All continuous data are presented as mean ± standard deviation, and all categorical data are reported as percentages or absolute numbers. Kruskal-Wallis tests and analyses of variance were used to assess differences between groups. The

TABLE 1. Cardiovascular Risk Factors, Adipose Tissue Volume, and Severity of CAC

Variable	CAC 0 (n = 33)	CAC 1–100 (n = 24)	CAC 101–400 (n = 20)	CAC ≥ 400 (n = 34)	P
Age (years)	56 ± 11	61 ± 10	64 ± 11	68 ± 11	.0001
Men	14	11	16	23	.01
Current smokers	0	13%	0	3%	.10
Hypertension*	30%	50%	40%	41%	.50
Hypercholesterolemia†	42%	54%	70%	53%	.30
Diabetes mellitus‡	6%	13%	5%	24%	.10
Family history of CHD§	58%	46%	65%	62%	.60
SBP (mm Hg)	125 ± 17	125 ± 18	133 ± 19	123 ± 16	.40
DBP (mm Hg)	77 ± 10	74 ± 8	77 ± 7	73 ± 8	.20
BMI (kg/m^2)	26.7 ± 3.4	26.9 ± 2.8	27.8 ± 3.8	28.2 ± 3.9	.20
Total cholesterol (mg/dL)	189 ± 31	190 ± 33	164 ± 34	173 ± 46	.50
HDL-C (mg/dL)	53 ± 18	56 ± 15	46 ± 9	46 ± 11	.30
LDL-C (mg/dL)	112 ± 40	103 ± 34	96 ± 28	94 ± 42	.60
Triglycerides (mg/dL)	119 ± 41	120 ± 44	114 ± 40	124 ± 47	.80
BMI (kg/m^2)	29.7 ± 4.1	30.3 ± 4.6	30.3 ± 4.6	30.4 ± 3.9	.30
FRS (%)	6.8 ± 3.9	9.5 ± 4.1	11.6 ± 4.3	14.7 ± 4.4	.001
EAT (cm^3)	68.3 ± 35.6	79.3 ± 38.5	102.1 ± 47.9	108.6 ± 38.8	.0001
PAT (cm^3)	57.3 ± 49.5	66.7 ± 46.1	83.7 ± 49.9	107.9 ± 49.3	.0001
SAT (cm^3)	53.9 ± 28.9	64.2 ± 32.1	83.4 ± 32.2	86.5 ± 40.1	.0001
Total TAT (cm^3)	125.6 ± 68.6	146.1 ± 59.1	185.7 ± 66.4	216.5 ± 65.5	.0001

Data are expressed as mean ± SD or as percentages.

BMI, body mass index; CAC, coronary artery calcium; CHD, coronary heart disease; DBP, diastolic blood pressure; EAT, epicardial adipose tissue; FRS, Framingham risk score; HDL-C, high-density lipoprotein cholesterol; LDL-C, high-density lipoprotein cholesterol; PAT, pericardial adipose tissue; SAT, subcutaneous adipose tissue; SBP, systolic blood pressure; TAT, thoracic adipose tissue.

CAC Coronary Artery Calcium Score; SBP Systolic Blood Pressure; DBP Diastolic Blood Pressure.

*Self-reported diagnosis of hypertension, prescribed medication for hypertension, or current SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg (≥130/80 mm Hg if diabetic).

†Self-reported diagnosis of high cholesterol, prescribed medication for high cholesterol, or current total cholesterol > 200 mg/dL.

‡Self-reported diagnosis of diabetes (type 1 or 2) or prescribed medication for diabetes.

§First-degree relative, female aged < 65 years, male aged < 55 years.

association of each fat depot with CAC was analyzed by univariate (models I to V) and multivariate (models VI and VII) linear regression analysis. Relative risk regression analyses were used to assess the association of each standard deviation increase in each fat depot and significant CAC (CAC ≥ 100). These analyses were adjusted for demographics, age, sex, and traditional cardiac risk factors. The results are reported as relative risk per standard deviation increase for the relative risk regression. SAS version 9.2 (SAS Institute Inc, Cary, NC) was used to compare receiver-operating characteristic curve areas. Nonparametric comparisons of areas under correlated receiver-operating characteristic curves (AUCs) were used to assess the differences between the AUCs (14).

RESULTS

Characteristics of the study population are highlighted in Table 1 according to the severity of CAC among 111 consecutive participants (mean age, 60 ± 10 years; range, 36–76 years; 64 men). CAC was present in 70% of subjects (78 of 111; 24 with CAC 1–100, 20 with CAC 101–400, and 34 with CAC ≥ 400). There were no significant statistical differences between cohorts in hypertension, hypercholesterolemia, diabetes, smoking status, family history of premature coronary heart disease, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, blood urea nitrogen, creatinine, BMI, and systolic and diastolic blood pressure. FRS increased significantly with increasing severity of CAC (Table 1).

Adipose Tissue and CAC

There were moderate correlations between EAT (r = 0.58), PAT (r = 0.47), and TAT (r = 0.51) and CAC (P < .05). SAT was correlated weakly with CAC (r = 0.34, P = .0001). The volume of each fat depot progressively increased as the severity of CAC increased (Table 1).

SAT increased in both genders as CAC increased (Fig 2a). In univariate linear regression analysis, SAT was statistically significant increased with the presence and severity of CAC (Table 2). Multivariate relative risk regression analysis revealed that SAT was independently associated with significant CAC (Table 3).

Visceral adipose tissues, measured as EAT, PAT, and TAT, increased significantly with increasing CAC in both genders.

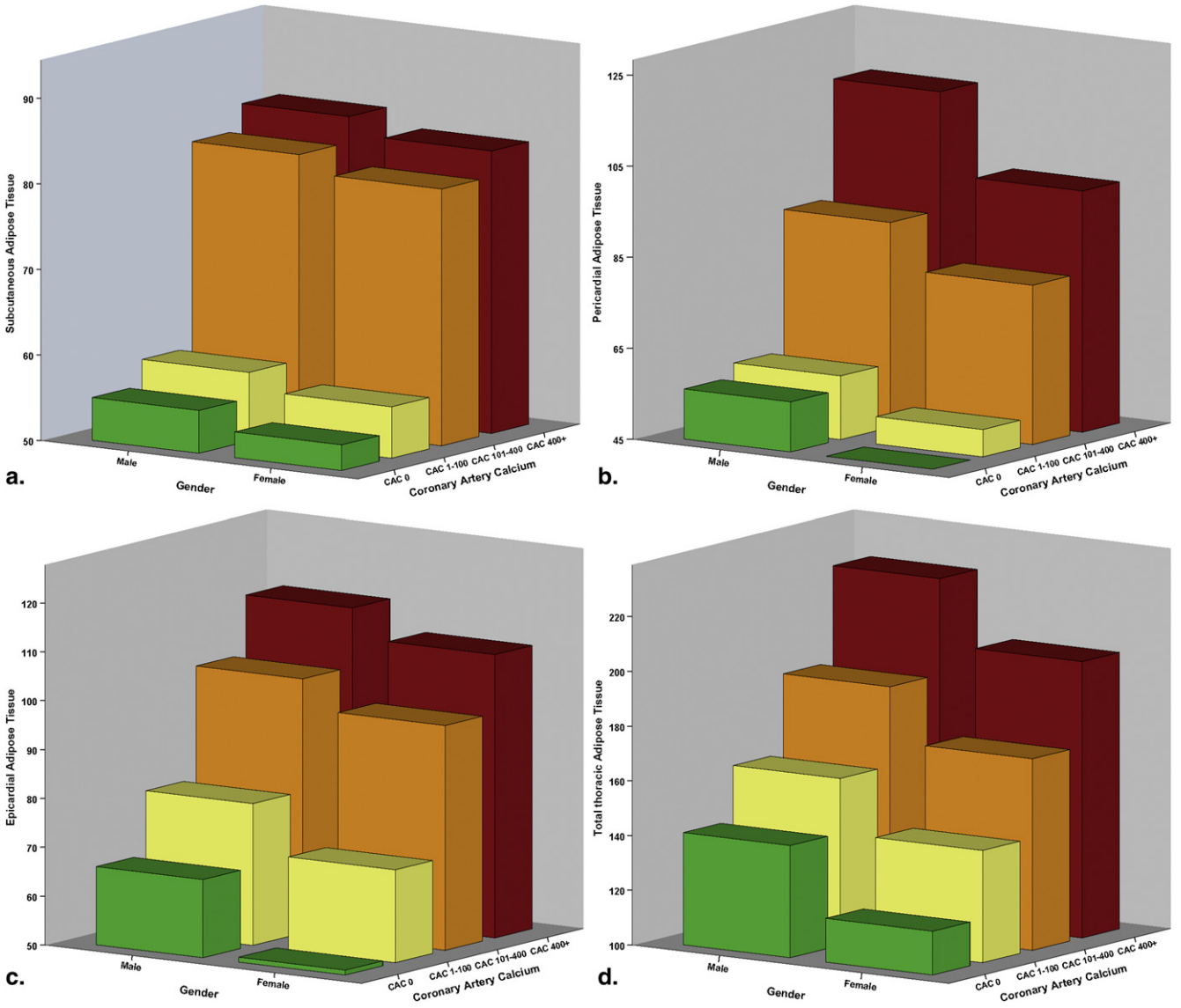

Figure 2. **(a)** Subcutaneous adipose tissue increased proportionally with the severity of coronary artery calcium (CAC) in both genders. **(b)** Pericardial adipose tissue increased proportionally from CAC 0 to ≥400 in both genders. **(c)** Epicardial adipose tissue increased proportionally with the severity of CAC in both genders. **(d)** Total thoracic adipose tissue increased with the severity of coronary artery calcium in both genders.

The maximum adipose tissue was noted in men with CAC ≥ 100 (Figs 2b–2d) Univariate linear regression analysis revealed that EAT, PAT, and TAT, but not BMI, were significantly associated with the presence and severity of CAC (Table 2). Multivariate relative regression analysis showed that PAT, EAT, and TAT were independent predictors of significant CAC (Table 3). After adjustment for age, gender, conventional cardiovascular risk factors, and BMI using relative risk regression analysis, the risks for each standard deviation increase in EAT, PAT, and TAT were 3.3 (95% confidence interval [CI], 1.9–5.6, $P = .0001$), 2.7 (95% CI, 1.6–3.9, $P = .0001$), and 3.1 (95% CI, 1.87–5.03, $P = .0001$) for CAC ≥ 100 compared to CAC 0, respectively (Table 3).

As shown in Tables 2 and 3, EAT correlated more with the presence and severity of CAC than PAT and SAT, as well as FRS ($P < .05$). The addition of SAT and visceral adipose tissue to FRS resulted in higher predictive power for CAC ≥ 100. Maximum prognostic value to detect the presence and severity of CAC was observed ($R^2 = 0.54$) after the addition of adipose tissues to the clinical variables (Table 2).

Receiver-operating characteristic curves were constructed to assess the independent as well as incremental diagnostic value of study variables to predict CAC ≥ 100. As shown in Table 4, FRS exhibited the lowest AUC (0.63; 95% CI, 0.58–0.73). The AUC to predict CAC ≥ 100 was higher in each fat depot compared to FRS. Combination of visceral adipose tissue and SAT provided more robust prognostic value than either alone. Also, the addition of fat depots to FRS provided maximum prognostication value to detect CAC ≥ 100 (AUC, 0.88; 95% CI, 0.81–0.91; $P = .0001$).

TABLE 2. Linear Regression Analysis of the Association Between Cardiovascular Risk Factors and CAC

Model	R	R^2	β	95% CI	P
Single variables					
I: EAT	0.58	0.34	0.21	0.11 to 0.62	.0001
II: PAT	0.47	0.22	0.15	0.05 to 0.22	.0001
III: SAT	0.34	0.12	0.11	0.02 to 0.21	.0001
IV: TAT	0.51	0.27	0.19	0.07 to 0.32	.0001
V: BMI	0.17	0.03	0.02	−0.01 to 0.03	.10
Combination variables					
VI					
SAT			0.08	0.03 to 0.11	.01
+					
PAT			0.10	0.03 to 0.14	.001
+	0.65	0.45			
EAT			0.16	0.08 to 0.23	.0001
+					
FRS			0.09	0.02 to 0.12	.03
VII					
SAT			0.06	0.01 to 0.11	.01
+					
PAT			0.08	0.02 to 0.15	.01
+					
EAT			0.13	0.03 to 0.32	.001
+					
Age			0.02	0.01 to 0.08	.001
+					
Gender (male)			0.15	0.02 to 0.35	.02
+	0.74	0.55			
Hypercholesterolemia			0.12	−0.02 to 0.19	.10
+					
Diabetes mellitus			0.17	−0.01 to 0.21	.10
+					
Hypertension			0.08	−0.03 to 0.15	.30
+					
Smoking status			0.05	−0.02 to 0.11	.10
+					
Family history of CHD			0.03	−0.05 to 0.15	.50
+					
BMI			0.02	−0.01 to 0.06	.10

Dependent variable: CAC.

BMI, body mass index; CAC, coronary artery calcium; CHD, coronary heart disease; CI, confidence interval; EAT, epicardial adipose tissue; FRS, Framingham risk score; PAT, pericardial adipose tissue; SAT, subcutaneous adipose tissue; TAT, thoracic adipose tissue.

DISCUSSION

The current study demonstrates that (1) both SAT and visceral TAT were associated with the presence and severity of CAC; (2) each fat depot was an independent predictor of significant CAC, even after adjustment for age, gender, BMI, and cardiovascular risk factors; (3) each fat depot had more prognostic value to detect CAC ≥ 100 than FRS; (4) EAT was correlated more with the presence and severity of CAC compared to PAT and SAT as well as FRS; and (5) the addition of fat depots to clinical variables resulted in maximum prognostic value in detecting significant subclinical atherosclerosis.

TABLE 3. Multivariate Relative Risk Regression Analysis of the Association Between Adipose Tissues and CAC

Model	CAC 0	CAC ≥ 100	P
Unadjusted			
SAT	1 (reference)	1.76 (1.22–2.54)	.003
PAT	1 (reference)	1.88 (1.22–7.92)	.004
TAT	1 (reference)	2.25 (1.43–4.91)	.0001
EAT	1 (reference)	2.98 (1.92–4.62)	.0001
Adjusted for age and gender			
SAT	1 (reference)	1.95 (1.58–4.79)	.0001
PAT	1 (reference)	2.16 (1.41–3.32)	.0001
TAT	1 (reference)	2.69 (1.55–4.66)	.0001
EAT	1 (reference)	3.04 (1.78–5.18)	.0001
Adjusted for age, gender, and BMI			
SAT	1 (reference)	2.46 (1.49–4.15)	.001
PAT	1 (reference)	2.50 (1.51–3.64)	.0001
TAT	1 (reference)	2.94 (1.57–5.51)	.0001
EAT	1 (reference)	3.17 (1.72–5.47)	.0001
Adjusted for age, gender, hypertension, hypercholesterolemia, diabetes mellitus, family of history of CHD, smoking status, and BMI			
SAT	1 (reference)	2.57 (1.48–4.45)	.001
PAT	1 (reference)	2.72 (1.64–3.94)	.0001
TAT	1 (reference)	3.06 (1.87–5.03)	.0001
EAT	1 (reference)	3.32 (1.95–5.62)	.0001

Relative risk (95% confidence interval) of SAT, TAT, and PAT per standard deviation increase.

BMI, body mass index; CAC, coronary artery calcium; CHD, coronary heart disease; EAT, epicardial adipose tissue; PAT, pericardial adipose tissue; SAT, subcutaneous adipose tissue; TAT, thoracic adipose tissue.

Pathophysiology

Adipose tissue includes lipid-filled adipocytes, endothelial cells (forming an extensive vasculature), pericytes (which have the potential to become adipocytes), fibroblasts (providing structural support), preadipocytes (which are partially committed to an adipocyte fate), mast cells (which influence angiogenesis and remodeling), and immune cells (resident macrophages and T cells). Expansion and uncontrolled remodeling of adipose tissue is associated with increased inflammation, insulin resistance, dyslipidemia, obesity, cardiovascular risk factors, metabolic dysfunction, and CAD (15,16).

Regional heterogeneity of lipid metabolism, insulin sensitivity, balance of proinflammatory and anti-inflammatory adipokine, and cytokine expression are reported in different adipose tissue depots on the basis of their anatomic locations (17,18). Visceral adipocytes have higher lipolytic capacity and lower antilipolytic activity of insulin and are more sensitive to adrenergic stimulation than subcutaneous adipocytes (19).

TABLE 4. C Statistics to Assess the Diagnostic Accuracy of Regional Adipose Tissues and Clinical Variables for the Detection of Significant CAC

Variable	AUC ± SE	95% CI	*P*	Comparison *P* with FRS
FRS	0.63 ± 0.04	0.58-0.73	.0001	—
SAT	0.69 ± 0.03	0.58-0.81	.0001	.05
PAT	0.77 ± 0.03	0.65-0.83	.0001	.01
EAT	0.83 ± 0.02	0.67-0.87	.0001	.004
SAT + PAT + EAT	0.86 ± 0.02	0.78-0.92	.0001	.0001
SAT + PAT + EAT + FRS	0.88 ± 0.02	0.81-0.91	.0001	.0001

AUC, area under the receiver-operating characteristic curve; CAC, coronary artery calcium; CI, confidence interval; EAT, epicardial adipose tissue; FRS, Framingham risk score; PAT, pericardial adipose tissue; SAT, subcutaneous adipose tissue; SE, standard error.

In contrast to subcutaneous preadipocytes, which secreting significant amounts of anti-inflammatory adiponectin and very little interleukin-8 or monocyte chemoattractant protein–1 (MCP-1) during adipocytic differentiation, perivascular adipocytes (EAT, PAT, and TAT) release substantial amounts of proinflammatory interleukin-6, interleukin-8, and MCP-1 and very little adiponectin while exhibiting reduced adipocytic differentiation (20). These suggest that perivascular adipocytes modulate insulin sensitivity and cellular function in an autocrine or paracrine manner while attracting macrophages to the depot, further exacerbating inflammation and adipocyte dysfunction (20,21).

EAT and PAT are visceral fat depots, and epicardial fat shares a common embryonic origin with abdominal visceral fat (22). In fact, EAT and PAT are associated with multiple markers of inflammation, vascular dysfunction, and oxidative stress, including C-reactive protein, fibrinogen, intracellular adhesion molecule–1, interleukin-6, MCP-1, P-selectin, tumor necrosis factor receptor–2, and urinary isoprostanes, vascular endothelial growth factor, and plasminogen activator inhibitor–1 (23–25). Increased levels of the chemokine MCP-1 in visceral adipose tissue attract more monocytes and macrophages, inducing a self-sustaining inflammatory cycle (26,27).

Bourlier et al (28) reported that adipose tissue macrophages in subcutaneous fat depot are composed of distinct macrophage subsets from lean to overweight individuals. These adipose tissue macrophages are active players in the process of adipose tissue development by extending capillary network, genesis of obesity-associated pathologies, systemic inflammation, insulin resistance, and endotoxemia (28).

Adipose Tissue and Coronary Atherosclerosis

Fox et al (29) analyzed SAT and visceral adipose tissue in individuals without known CAD and found that SAT and VAT were significantly associated with blood pressure, fasting plasma glucose, triglycerides, and high-density lipoprotein, with increased odds of hypertension, impaired fasting glucose, and metabolic syndrome in both genders. VAT was more strongly correlated with most metabolic risk factors than was SAT.

Ding et al (10) evaluated the association of TAT (EAT and PAT) with the incidence of coronary heart disease in 998 participants of the Multi-Ethnic Study of Atherosclerosis, which remained significant even after adjustment for BMI, age, gender, and cardiovascular disease risk factors (hazard ratio, 1.26; 95% CI, 1.01–1.59). Furthermore, Rosito et al (16) examined 1155 participants without known CAD from the Framingham Heart Study offspring cohort and compared their computed tomography–measured EAT, PAT, and visceral abdominal adipose tissue with coronary and aortic calcium. They found that EAT, but not PAT, was associated with CAC after multivariate and visceral abdominal adipose tissue adjustment. PAT, but not EAT, was associated with abdominal aortic calcium. Mahabadi et al (30) also demonstrated that EAT and visceral abdominal adipose tissue, but not PAT, were significantly associated with prevalent CAD and remained significant after adjustment for age and gender. However, only EAT remained significant after further adjustment for BMI and waist circumference. Finally recent studies have shown that an increase in EAT is associated with the presence of CAC (31) and the severity of CAD (11).

The present findings reconfirm previous studies and provide evidence that EAT and PAT are independently associated with the presence and severity of CAC. This study is the first trial reporting the direct linkage of visceral adipose tissue and SAT with the severity of subclinical atherosclerosis after adjustment for conventional risk factors and BMI.

Implications

Recent studies have shown that adipose tissue assessment using nonenhanced computed tomography is highly reproducible (10,30), and this can be used for risk stratification, to monitor response to therapy, and to follow up at-risk individuals (32,33). The association of visceral adipose tissue and SAT with the presence and severity of CAC documents the systemic and localized effect of various adipose tissues on subclinical coronary atherosclerosis, in which EAT had the highest association. Furthermore, the present study provides evidence of associations of SAT and PAT with CAC, highlighting the region-specific adipose tissue effect on atherosclerosis. Finally, the addition of visceral adipose tissue and SAT to conventional risk factor assessment significantly improves the prognostication value to detect significant

subclinical atherosclerosis, and in particular, the superior independent and incremental value of each fat depot over FRS to predict significant CAC, support the potential additive role of adipose tissue assessment for early detection and management of subclinical atherosclerosis.

Limitations

The present study had several limitations. First, only asymptomatic individuals who underwent CAC were included. Second, the study sample size was relatively small; however, the results of the present study have clearly demonstrated the association of visceral adipose tissue and SAT with CAC. Additional studies, including outcome studies, are needed to evaluate whether measuring visceral adipose tissue and SAT can provide additive value to predict outcomes and improve patient management.

CONCLUSIONS

Increased EAT, PAT, and SAT are associated with coronary subclinical atherosclerosis measured by CAC, independent of age, gender, BMI, and conventional cardiovascular risk factors. The addition of visceral adipose tissue and SAT to FRS provides incremental value for the detection of significant subclinical atherosclerosis, highlighting the localized and systemic effect of adipose tissues in the subclinical burden of atherosclerosis.

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