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Epicardial Adipose Tissue Volume as a Marker of Coronary Artery Disease Severity in Patients with Diabetes Independent of Coronary Artery Calcium: Findings from the CTRAD study

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Abstract

Aims—The association between epicardial adipose tissue (EAT) volume and coronary artery disease (CAD) severity was evaluated, independent of traditional risk factors and coronary artery calcium (CAC) scores, in patients with diabetes type 2 (DM-2) using cardiac computed tomography angiography (CTA).

Methods—A multivariate analysis was utilized to assess for an independent association after calculating EAT volume, CAD severity, and calcium scores in 92 patients with DM-II from the CTRAD study. We graded CAD severity as none (normal coronaries), mild-moderate (<70% stenosis), and severe (70% or greater stenosis).

Results—A total of 39 (42.3 %) asymptomatic patients with diabetes did not have CAD; 30.4% had mild/moderate CAD; and 27.1% had severe CAD. Mean EAT volume was highest in patients with severe CAD (143.14 cm^3) as compared to mild/moderate CAD (112.7 cm^3), and no CAD (107.5 cm^3) (p= 0.003). After adjustment of clinical risk factors, notably, CAC score, multivariate regression analysis showed EAT volume was an independent predictor of CAD severity in this sample (odds ratio 11.2, 95% confidence interval 1.7 –73.8, p =0.01).

Conclusions—Increasing EAT volume in asymptomatic patients with DM-II is associated with presence of severe CAD, independent of BMI and CAC, as well as traditional risk factors.

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Keywords

EAT; Pericardial fat; Coronary Artery Disease; Multi-detector Computed Tomography; Computed Tomography Angiography; Diabetes; Metabolic Syndrome

INTRODUCTION

It is well known that Diabetes Mellitus (DM) confers a high risk of cardiovascular disease (CVD) (1, 2). Since myocardial ischemia due to multi-vessel atherosclerosis typically occurs asymptomatically and atypically among those with DM, early risk assessment strategies are paramount to improve identification, medical optimization, and to ultimately decrease morbidity and mortality from CVD.

The relationship between central obesity and cardiovascular disease is well established (3–6). Visceral adiposity increases with obesity and is a key component of insulin resistance (7), and may reflect greater accuracy of attendant CVD risk in those with diabetes compared to traditional markers of obesity, such as BMI. Local visceral adiposity, specifically, human epicardial adipose tissue (EAT), has recently garnered much intrigue as it is located perivascularly along large coronary arteries and expands with obesity (8, 9). Predominately, coronaries encased in EAT have been correlated with atherosclerotic intimal lesions (10, 11). These perivascular adipose deposits have been hypothesized to be potentially a metabolically active paracrine organ able to bi-directionally traffic numerous locally released bioactive and inflammatory cytokines or adipokines to the underlying coronary artery adventitia, thus mediating atherogenesis (12).

Additionally, recent studies have correlated the burden of coronary artery disease (CAD) with radiologic measurement of increasing EAT in among others: populations of post-menopausal women (13), patients presenting with angina (5, 14), and more recently, in asymptomatic subjects with multiple CVD risk factors referred for computed tomography (CT) angiography (15). Further, studies quantifying EAT have utilized various imaging modalities including: echocardiography (16), cardiac magnetic resonance (MR) (17), and multi-detector computed tomography (MDCT) (18).

Although prior studies have examined the correlation between EAT thickness (48) or EAT volume (49,50) and CAD severity, they have done so using Asian participants, who may have different thresholds for visceral adiposity than other ethnic groups. Prior studies have also not looked at the independent association of EAT and CAD severity after adjusting for Coronary Artery Calcium (CAC) score. We assessed EAT volume and severity of CAD using CTA imaging in asymptomatic patients with diabetes; a burgeoning cohort which is notoriously afflicted with obesity and has significant CAD risk. We assessed the independent association between the volume of EAT, as detected by CTA, and the presence and severity of CAD in patients with type 2 diabetes.

SUBJECTS, MATERIALS AND METHODS

Patient Selection

CTA scans were used from the CTRAD study (Cardiac CT's Role in Asymptomatic Patients with DM-II) in which consecutive asymptomatic patients (n=203) with type 2 diabetes from three community clinics of the University of California, Irvine, were randomly assigned to either undergo 64-slice CT angiography or continue their usual care. We used data from the 92 patients who were randomized to getting a CTA. Patients with type 2 diabetes were identified by ongoing treatment with diabetic medications or having a fasting blood sugar greater than or equal to 126 mg/dL, or hemoglobin A1C (HgbA1c) greater than or equal to 6.5%, or a physician diagnosis of diabetes. Patients were excluded if they had a history of known coronary artery disease, any prior catheterizations with interventions, cardiac bypass surgery, or if they were currently having ongoing chest pain and undergoing a cardiac work up.

Institutional Board Review (IRB) Approval

Our study was approved by the IRB of our institution and was compliant with Health Insurance Portability and Accountability Act (HIPAA) regulations.

CT Scan Parameters and Acquisition

Oral or intravenous metoprolol was used to achieve a heart rate of less than 65 beats per minute (bpm). In addition, sublingual nitroglycerin (0.4–0.8 mg tablet) was given to the patient 1 minute prior to image acquisition unless contraindicated.

Using a prospectively ECG-gated (mid-diastole) technique, pre-contrast 3 mm non-spiral images were obtained from above the level of tracheal bifurcation to the diaphragm to cover the entire heart. Sequential images were obtained without overlap for measurement of EAT volume.

For contrast enhancement, each patient received 64–93 ml (mean 74.9 ± 3.3 ml) of Iohexol (Omnipaque 350 mg/mL, Amersham Health, Cork, Ireland), which was injected at a rate of 4–5 ml/sec, followed by an injection of 50 ml of saline at 5 ml/sec through an 18-gauge catheter. Routine coronary CT angiography (CTA) was performed using a 64-slice MDCT (Toshiba Aquilion, Tustin, CA) with a technique described in previous publications (19). A retrospective ECG-gated volumetric data set was acquired during a single breath-hold. The mean scan time was 9.1 ± 1.4 seconds (range was between 8–13 seconds). Datasets were reconstructed based on a relative-delay strategy at 10% of R-R intervals. Reconstructed images were then transferred to a remote workstation (Vitrea 2, Vital Images Inc., Minnetonka, Minnesota) where the images could be evaluated by two independent and blinded clinicians, who are both level III certified in cardiac CTA interpretation. Calcium score was routinely obtained with the application of Vitrea software and an overall Agaston score was registered for each patient (20). Coronary artery assessment is described in the following section.

CAD Assessment

The CTA datasets were evaluated by two independent, cardiac CTA level III certified clinicians who were blinded to the EAT volume measurements. They used dedicated remote workstations to which all the reconstructed images were transferred (Vitrea 2, Vital Images Inc., Minnetonka, Minnesota). Calcium score was assessed using the Agaston method (20). The presence or absence of coronary plaque was performed using reconstructed data sets, which were evaluated at different ECG-phases for diagnostic image quality and from which the optimal data set was chosen. Plaques were then categorized as none, mild/ moderate or severe if there were no visible atherosclerotic plaques, less than 50%, 50–70%, or greater than 70% luminal narrowing, respectively. CAD was diagnosed if there were moderate or severe plaques present

Volumetric Measurements of EAT

EAT was defined as fat density (attenuation values between −30 to −190 HU) (21, 22) observed within the parietal pericardium boundary (23). Volumetric analysis was performed on all 92 patients by two separate blinded clinicians who had been trained in measuring EAT volume. We utilized the same non-enhanced images used for calcium scoring analysis. Total volume was measured using axial non-contrast data set during the mid-diastolic phase. Starting from the lower margin of the aortic arch and advancing images toward the inferior cardiac border by 6 mm, the area of every observed epicardial fat pocket located between the myocardial surface and the pericardium was manually traced. The sum of measured areas for each slice was multiplied by the slice thickness (3 mm, range 35 to 40 slices per heart)) to achieve the volume of the slice in mm^3. Coronary vessels were included in measured areas (24, 25). Figure 1 shows the examples of EAT from our patients, including assessment of EAT in someone with higher volume (Figure 1a) and in someone with lower volume (Figure 1b).

Statistical Analysis

Continuous data were presented as mean values ± SD and categorical variables were reported as percentages. The continuous data such as EAT volume, age and BMI were examined for normality before analyses and were found to be normally distributed. Univariate analyses described the clinical characteristics of the study participants. Bivariate Analysis was performed using chi-square and ANOVA. Chi square for independence was used to explore the association between each of categorical variable and the CAD severity variable with three categories. ANOVA was used to assess the distribution of the continuous variables across the three categories of CAD severity and distribution of EAT volume across the categories of clinical variables such as BMI, Calcium score and CAD severity.

A multivariate logistic analysis was performed to assess the relationship between presence of severe coronary artery disease (CAD) (stenosis of 70% or more in at least one segment of the coronary arteries) and EAT. EAT volume was also dichotomized with EAT value >120 cm3 as a cut off. This cutoff was based on the distribution of our data EAT value of close to 75th percentile. We first ran staged models, with the first model adjusting for age, gender, race, hgbA1c, and use of medications including; anti-hypertensives, statins, and insulins. The second model additionally adjusted for BMI and the third model also adjusted for CAC

scores. Statistical significance was defined as p-value < 0.05. All statistical analyses were performed using SAS 9.3. (SAS institute, Cary, North Carolina).

RESULTS

Clinical characteristics of patients

Table 1 lists the clinical characteristics of 92 study participants. The sample included 39% males and 53% females and the mean age of all participants was 56.2 ± 9.4. With respect to race demographics, 63% of the sample were of Hispanic descent. The average Hemoglobin A1C (HgbA1c) was 7.94 % ± 1.7. The mean body mass index (BMI) was 32 ±7.5 and the mean EAT volume was 118.27± 42.24. Sixty-four percent of the participants were hypertensive, 84% had dyslipidemia and only 9% were smokers. Additionally, 19% were on insulin, 54% on statins, 58% on other anti-lipemics and 69% on anti-hypertensives.

Clinical characteristics of patients for three categories of CAD severity

A total of 39 (42.3%) asymptomatic patients in our sample had normal coronary arteries (Table 1). We found mild/moderate CAD in 28 (30.4%) of these asymptomatic patients and severe CAD in 25(27.1%) asymptomatic patients. As expected mean age was higher across increasing severity of CAD (p<0.001). The mean age for patients with absent CAD was 50.6 ± 6,9, for patients with mild/moderate CAD, mean age was 59± 8.53 and for those with severe CAD, mean age was 61.7 ± 9.44 (p<0.001). Thirty-four percent of asymptomatic female patients with diabetes did not have CAD; compared with only 7.6 % of asymptomatic male patients who had no evidence of CAD; we found a statistically significant difference in the gender distribution across the three categories of CAD severity (p< 0.001). There was a noted difference across stages of CAD severity between Hispanics and Non-Hispanics (p< 0.0001). Notably, there was no significant difference in HgbA1c or mean BMI across the categories of CAD severity (p=0.42 and p=0.70, respectively).

Mean EAT volumes compared across patient's characteristics

Table 2 shows the relationship between clinical characteristics of patients and mean EAT volume. Men tended to have higher EAT volumes as compared to women (130.3 ± 48.5 vs. 110 ± 36.6; p=0.02). Subjects older than 60 years old had higher EAT volumes (131.1 ± 41.53) as compared to those aged 35–60 (112 ± 42.67; p=0.05). EAT volumes were the highest among Caucasians (136.1 ±37.55), as compared to Asians (135.0 ± 43.80), and Hispanics (113.8 ± 42.57) who had the lowest EAT values (p= 0.03). EAT was higher in patients with the BMI category 30–39 compared to those with less than 25 to 29 BMI, (131.6 ± 44.64 cm3 vs 103.6 ± 37.5 cm3, p=0.01). Patients with higher CAC score (>400) had higher EAT volume (141.30 ± 42.5 cm3) as compared to those with CAC between 1–100 (121.07 ± 47.09 cm3) (p=0.03), however the relationship between EAT volume and CAC was not linear. The EAT volume was the highest in patients with severe CAD (143.14 ± 46.0) as compared to those with no CAD (107.5 ± 39.4) or mild/moderate CAD (112.7 ± 37.23) (p= 0.003).

Association between EAT volume and presence of severe CAD

As seen in table 3, all three models showed EAT to be an independent predictor of presence of severe CAD. The odds of severe CAD were increased with higher EAT [odds ratio (OR) 9.2, 95% confidence interval (CI): 1.97 –43.56; p =0.005] after further adjustment for BMI in addition to age, gender, race, hgbA1c, and the use of anti-hypertensives, statins, and insulin. The estimated associated between EAT and severe CAD increased with additional adjustment for calcium score (OR = 11.20, CI: 1.70–73.88; p= 0.01).

DISCUSSION

Our study found an independent association between EAT volumes with severity of CAD in an asymptomatic cohort of patients with Diabetes type 2 after adjustment of traditional risk factors, BMI, and CAC scores. Although EAT volumes correlated with increasing coronary artery calcium (CAC) scores, an established surrogate marker of CAD (26–28), our study shows that EAT volumes predicted presence and severity of CAD independent of CAC. As such, anatomical identification of EAT represents an objective imaging marker in the assessment of CAD severity in those with diabetes. In tandem, the findings of an association of EAT with CAD independent of CAC scores, which are typically attained with CT, offers powerful prognostic potential for the use of a more practically available imaging modalities with no radiation burden associated with measurement of EAT, such as echocardiography.

Further, our unique cohort represents a diverse population of asymptomatic patients with DM-II in whom CTA is normally not performed, giving insight into the contributors of CAD severity in this group of patients. Prior studies correlating CAD and EAT have done so in a population that was referred for CTA, usually due to symptoms or suspicion of CAD and therefore may have had selection bias.

Additionally, although recent studies have been completed which describe the association of EAT and CAD in DM cohorts (48–50), these studies were completed exclusively in homogenous Asian populations. In contrast, the current analysis occurred in a diverse and heterogeneous cohort reflective of population demographics of the United States (US). Although we did not have sufficient power to perform subanalysis by ethnicity, we found that Hispanics, who represented 63% of our study participants had lower EAT volumes than Causaians or Asians. Future studies could further explore if lower EAT volume could possibly be a contributing mechanism underlying the Hispanic paradox in cardiovascular disease, in which Hispanics despite paradoxically greater prevalence of obesity and diabetes, actually have lower CVD events compared to Causaians with similar risk factors.

Moreover, we showed that obesity measured using BMI has potential limitations. Although there was an association of EAT with BMI, EAT volume remained a predictor of CAD, independent of conventional cardiac risk factors including, most notably BMI. In fact, there was a non-significant correlation of BMI with severity of CAD, confirming the non-linear relationship of BMI to CAD (29–31). In conjunction with these finding, the long held association between central obesity, a characterization which includes populations with Diabetes, and CVD may be more accurately described by the effects of visceral fat (as measured in this study by EAT) as opposed to BMI, which also measures the less

metabolically active subcutaneous fat. The association of EAT and CAD, independent of BMI may legitimize the plausible "local" paracrine metabolism of perivascular adipose tissue, an extension of visceral adiposity.

Although previously thought to have a possible protective role, including allowance for coronary wall expansion in early atherosclerotic plaque generation of up to 40% luminal obstruction; recent studies are implicating EAT as a potent mediator of atherosclerotic disease via a dynamic bi-directional cytokine trafficking system influenced by both endocrine and inflammatory response processes (32–35). Within the local coronary environment increased pathogenic epicardial adipocyte expression of certain deleterious cytokines such as: tumor necrosis factor –alpha, interleukin -6, interleukin-16, visfatin, and leptin, have been shown to be coupled with decreased expression of vaso-protective adipokines such as adiponectin (9,36,37). Further, free molecular trafficking and communication across and through the coronary wall layers may be facilitated by the coronary microcirculation, as the local vaso vasorum exhibits increased neovascularization preceding overt endothelial dysfunction in at risk patient populations (25,38). Further, recent data using animal models have revealed resection of coronary EAT decreased the progression of CAD, suggesting that EAT may exacerbate coronary atherosclerosis (39). These insights have prompted further studies which have attempted to correlate EAT measurements to the extent of CAD (40–44).

Moreover, cohort studies such as the Framingham Heart Study (45, 46) and the Multi-Ethnic Study of Atherosclerosis (MESA) study (8) have reported EAT measurements as an independent predictor of high coronary artery calcium score. However, these studies did not have subgroup analysis of populations with Diabetes nor did they directly visually assess the severity of the coronary artery plaque. The findings of the current study show that the association between EAT and severity of CAD is also present in those with DM; further, this association exists independent of CAC. Incident cardiovascular events in populations associated with EAT, such as the DM population in question, have yet to be established, and represents a topic where future research may be focused.

The advantages of quantifying EAT using CTA as opposed to alternative imaging modalities include higher reproducibility than measurement by echocardiography (14, 47). Nevertheless, as we have reported an association of EAT with CAD, independent of CAC, and since echocardiography is a more utilized imaging modality with no radiation burden to the patient,, assessing EAT thickness via echocardiography maybe a valuable parameter to add to standard reporting if future studies show that CTA and echocardiographic measures of EAT are strongly correlated.

Although our study is the largest to date on assessing EAT and CAD in asymptomatic patients with CAD, due to the relatively smaller sample size and cross sectional nature of this study, the generalizability and causal association of this study is limited. Additionally, the index analysis may have yielded a still more powerful and interesting result with a comparison to control groups, including asymptomatic patients without type 2 diabetes and symptomatic type 2 patients. As such, prospective research is warranted to establish the

causal relationship between EAT and development of cardiovascular events in this population.

CONCLUSION

Increasing EAT volume as measured by cardiac 64-slice CTA in patients with DM-II is found be a significant predictor of presence of severe CAD, independent of BMI and CAC, as well as traditional risk factors including: hypertension, dyslipidemia. The anatomical proximity of EAT to the coronary arteries, and the evidence indicating that EAT is an active metabolic fat depot suggest that EAT may contribute to the pathogenesis of diabetic coronary atherosclerosis.

Abbreviations

BMI	Body Mass Index
CAC	Coronary Artery Calcium
CAD	Coronary Artery Disease
CTA	Computed Tomography Angiography
DM2	Diabetes Mellitus Type 2
EAT	Epicardial Adipose Tissue
ECG	Electrocardiogram
HDL	High Density Cholesterol
HgbA1c	Hemoglobin A1c
HU	Hounsfield units
LDL	Low Density Cholesterol
MACE	Myocardial infarction, cardiac death, stroke, late revascuarization
MDCT	Multi-detector Computed Tomography
MRI	Magnetic Resonance Imaging
NCEP-ATP III	National Cholesterol Education Program -Adult Treatment Panel III
TG	Triglycerides

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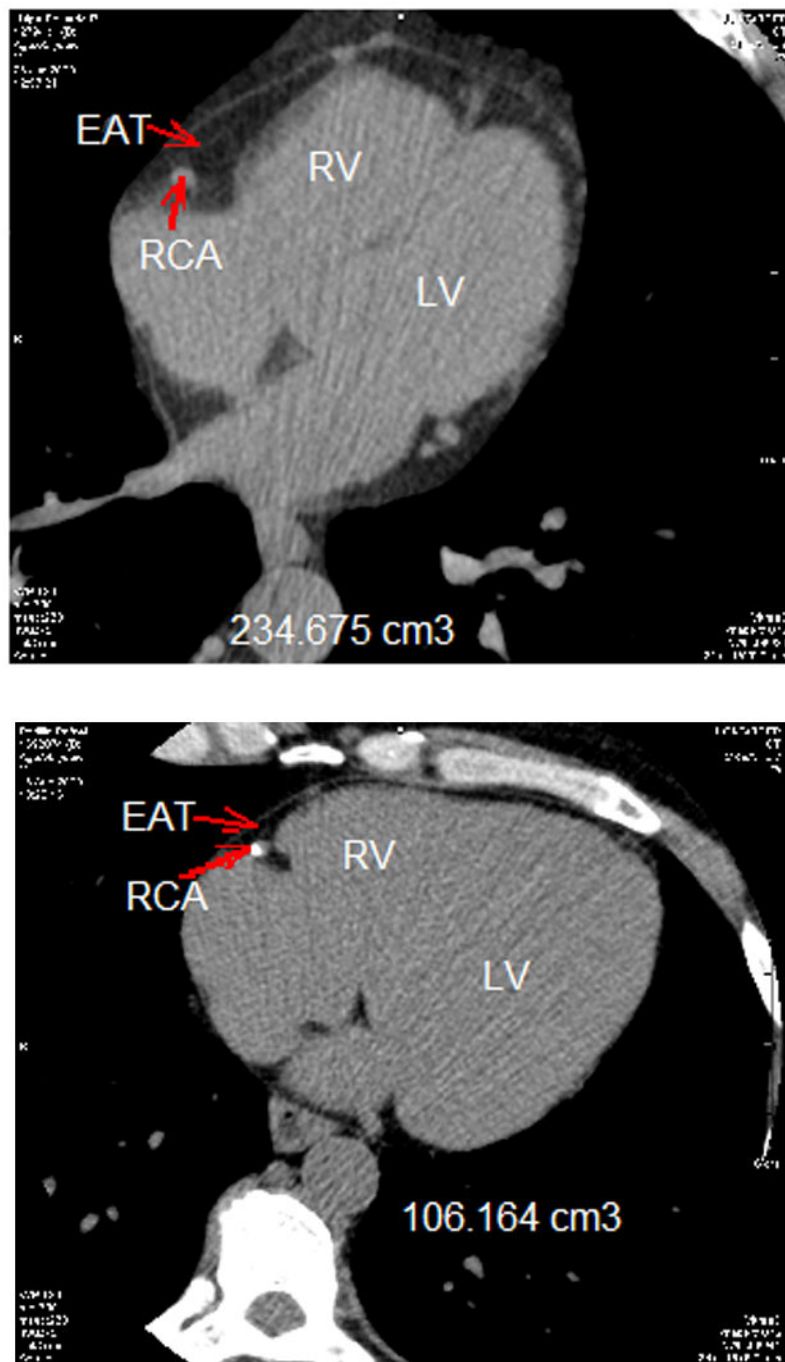
Figure 1.
Epicardial adipose tissue (EAT) total volume measurement. Segmentation of EAT was achieved by isolating the EAT by manually tracing the pericardium in the axial view. After segmentation, a threshold of −190 to −30 Hounsfield units was applied to isolate the adipose tissue.
(A) EAT in someone with higher volume

(B) EAT in someone with lower volume

Table 1

Clinical Characteristics of study participants(n=92)

Characteristics	Overall	Coronary Artery Disease (CAD) severity			p-value
		None	Mild & Moderate	Severe	
Age (years)	56.2 ± 9.4	50.6 ± 6.9	59.0 ± 8.53	61.7 ± 9.44	0.0004 ‖§
Males	42.4 (39)	7.6 (7)	15.2 (14)	19.6 (18)	< 0.0001‖‡
Females	57.6 (53)	34.8 (32)	15.2 (14)	7.6 (7)	
Race					
White	18.5 (17)	5.4 (5)	4.3 (4)	8.7 (8)	
Hispanic	68.5 (63)	34.8 (32)	22.8 (21)	10.9 (10)	0.02
Asian	9.8 (9)	1.1 (1)	2.2 (2)	6.5 (6)	
Others	3.3 (3)	1.1 (1)	1.1 (1)	1.1 (1)	
Ethnicity					
Hispanic	68.5 (63)	34.8 (32)	22.83 (21)	10.9 (10)	0.001 ¶‖‡
Non-Hispanic	31.5 (29)	7.6 (7)	7.6 (7)	16.3 (15)	
A1C	7.94 ± 1.7	8.01 ± 1.7	8.15 ± 1.8	7.57 ± 1.45	0.42
Glucose	162.74 ± 58.0	166.6 ± 65.7	164.5 ± 61.1	154.7 ± 40.3	0.72
BMI numeric	32.0 ± 7.5	32.7 ± 9.0	31.6 ± 4.9	31.1 ± 7.6	0.7
Body Mass Index (kg/m2)					
Less than 25	15.2 (14)	6.5 (6)	2.2 (2)	6.5 (6)	0.25 ‡
25 to 29.9	27.2 (25)	12.0 (11)	9.8 (9)	5.4 (5)	
30 to 39.9	46.7 (43)	16.3 (15)	17.4 (16)	13.0 (12)	
Greater than 40	10.9 (10)	7.6 (7)	1.1 (1)	2.2 (2)	
Hypertension *	69.6 (64)	27.2 (25	22 (23.9)	17 (18.5)	0.44 ‡
Dyslipidemia †	91.3 (84)	37.0 (34)	29.4 (27)	25.0 (23)	0.41 ‡
Smoking	9.8 (9)	5.4 (5)	1.1 (1)	3.3 (3)	0.41 ‡
Insulin	20.7 (19)	10.9 (10)	3.3 (3)	6.5 (6)	0.29
Statin	58.7 (54)	22.8 (21)	18.5 (17)	17.4 (16)	0.7

Characteristics	Overall	Coronary Artery Disease (CAD) severity			
		None	Mild & Moderate	Severe	p-value
Anti-lipemic	63.0 (58)	25 (23)	19.6 (18)	18.5 (17)	0.77
Anti-hypertensive	75 (69)	28.3 (26)	22.8 (21)	23.9 (22)	0.16

Values are expressed as mean ± standard deviation for continuous variables or % (n) for dichotomous variables

*
Defined as a persistent diastolic blood pressure above 80 mm Hg or systolic blood pressure above 130 mm Hg for people with diabetes

†
For diabetes patients, defined as (Low Density Cholesterol) LDL > 100, (Tri Glycerides)TG > 150, (High Density Cholesterol) HDL <40 for men and <50 for women.

‡
Chi-Square test of Independence for categorical variables

§
ANOVA for continuous variables

//
p-value < 0.001

¶
p-value < 0.05

Table 2

Relationship Between Clinical Characteristics of Patients and Mean Epicardial fat Volume

Characteristics	Mean Epicardial Fat [*] Volume (cm^3)	P - Value
Overall	118.57 ± 43.02	
Gender [†]		
Men	130.3 ± 48.5	0.02
Women	110.0 ± 36.6	
Age[†]		
35–60	112.2 ± 42.67	0.05
>60	131.1 ± 41.53	
Race		
White	136.1 ± 37.55	
Hispanic	113.8 ± 42.57	0.03
Asian	135.0 ± 43.80	
Others	69.4 ± 29.5	
Ethnicity		
Hispanic	113.8 ± 42.6	0.11
Non-Hispanic	128.9 ± 42.9	
Body Mass Index (kg/m^2) [‡]		
Less than 25	97.65 ± 38.0	0.01 [§]
25 to 29.9	103.6 ± 37.5	
30 to 39.9	131.6 ± 44.64	
Greater than 40	129.2 ± 36.49	
A1C[†]		
< 7.0	131 ± 43.51	
>=7.0 and <9	112.35 ± 37.33	0.12
>=9.0	112.08 ± 50.7	
Hypertension [†]		
Yes	122.2 ± 39.7	0.22
No	110.4 ± 49.60	
Dyslipidemia [†]		
Yes	119.7 ± 41.13	0.4
No	106.4 ± 61.73	
Smoking [†]		
Yes	130.7 ± 44.1	0.4
No	117.3 ± 43.0	

Characteristics	Mean Epicardial Fat [*] Volume (cm³)	P - Value
Insulin		
Yes	114.3 ± 52.0	0.63
No	119.7 ± 40.7	
Statin		
Yes	116.3 ± 37.7	0.54
No	121.8 ± 50.0	
Anti-hypertensive medication		
Yes	121.5 ± 43.1	1.00
No	109.7 ± 42.60	
Calcium Score [‡]		
Zero	106.55 ± 38.44	0.03
1–100	121.07 ± 47.09	
101–400	118.9 ± 38.90	
> 400	141.30 ± 42.5	
CAD Severity [‡]		
None	107.5 ± 39.4	0.003 [§]
Mild/Moderate	112.7 ± 37.23	
Severe	143.14 ± 46.0	

Values are expressed as mean ± standard deviation

[*] Epicardial fat (Epicardial Adipose Tissue), defined as fat density (attenuation values between −30 to −190 HU) observed within the parietal pericardium boundary. Total volume was measured using axial non-contrast data set during the mid diastolic phase.

[†] t-test for continuous variables

[‡] ANOVA for categorical variables

[§] p-value < 0.01

Table 3

Multivariate Logistic Regression analyses showing association of Epicardial Fat ($>120cm^3$) with the presence of Coronary Artery Disease in patients with diabetes

Age, Gender and Race, A1C, Ant-hypertensives, Statin, Insulin	6.26 (1.64–23.82)	0.007
Age, Gender, Race, BMI A1C, Anti-hypertensives, Statin, Insulin	9.2 (1.97– 43.56)	0.005
Age, Gender, Race, BMI, A1C, Anti-hypertensives, Statin, Insulin, and Calcium score	11.20 (1.70– 73.88)	0.01 ¶

[*] Percicardial fat (Epicardial Adipose Tissue), defined as fat density (attenuation values between −30 to −190 HU) observed within the parietal pericardium boundary. Total volume was measured using axial non-contrast data set during the mid diastolic phase.

[†] Defined as a persistent diastolic blood pressure above 80 mm Hg or systolic blood pressure above 130 mm Hg for people with diabetic

[‡] For diabetes patients, defined as (Low Density Cholesterol) LDL > 100, (Tri Glycerides)TG > 150, (High Density Cholesteol) HDL <40 for men and <50 for women

[§] Race:Included races such as Caucasian, Hispanic, Asian, African-American

[||] Calcium score categories defined as <=99 and >100

[¶] p-value < 0.05