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Pericardial Fat, Intra-thoracic Fat, and Measures of Left Ventricular Structure and Function: The Framingham Heart Study

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Abstract

Background—Pericardial fat has been implicated in the pathogenesis of obesity-related cardiovascular disease. Whether the associations of pericardial fat and measures of cardiac structure and function are independent of the systemic effects of obesity and visceral adiposity has not been fully explored.

Methods and Results—Participants from the Framingham Heart Study (n=997, 54.4% women) underwent chest and abdominal CT and cardiovascular MRI (CMR) between 2002 and 2005. Pericardial fat, intrathoracic fat, and visceral adipose tissue (VAT) quantified from multidetector computed tomography, along with BMI and waist circumference, were examined in relation to CMR measures of left ventricular (LV) mass, LV end diastolic volume (LVEDV), and left atrial dimension. In women, pericardial fat (r=0.20 to 0.35, p<0.001), intrathoracic fat (r=0.25 to 0.37, p<0.001), VAT (r=0.24 to 0.45, p<0.001), BMI (r=0.36 to 0.53, p<0.001), and waist circumference (r=0.30 to 0.48, p<0.001) were directly correlated with LV mass, LVEDV, and left atrial dimension. In men, pericardial fat (r=0.19 to 0.37, p<0.001), intrathoracic fat (r=0.17 to 0.31, p<0.001), VAT (r=0.19 to 0.36, p<0.001), BMI (r=0.32 to 0.44, p<0.001), and waist circumference (r=0.34 to 0.44, p<0.001) were directly correlated with LV mass and left atrial dimension, but LVEDV was not consistently associated with adiposity measures. Associations persisted after multivariable adjustment, but not

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Short Commentary
Pericardial fat, fat that surrounds the heart, may be associated with obesity-related cardiovascular disease. We explored whether the associations of pericardial fat and measures of cardiac structure and function are linked. We measured pericardial fat in participants from the Framingham Heart Study, as well as measures of cardiac structure and function. We found that multiple, different measures of fat were associated with cardiac measures of structure and function, but none persisted after accounting for overall body weight and visceral abdominal fat, the most metabolically active fat depot. An important exception was the relation of pericardial fat and left atrial dimension in men. These results suggest that the systemic effects of obesity on cardiac structure and function may outweigh the local pathogenic effects of pericardial fat.

after additional adjustment for body weight and VAT, with the exception of pericardial fat and left atrial dimension in men.

Conclusions—Pericardial fat is correlated with CMR measures, but the association is not independent of or stronger than other ectopic fat stores or proxy measures of visceral adiposity. An important exception is left atrial dimension in men. These results suggest that the systemic effects of obesity on cardiac structure and function may outweigh the local pathogenic effects of pericardial fat.

Keywords

pericardial fat; visceral fat; left ventricular mass; left atrial size; obesity; epidemiology; risk factors

Introduction

Pericardial fat is an ectopic fat depot associated with measures of adiposity[1–7] that may exert a paracrine effect on nearby anatomic structures. We have previously shown that pericardial fat, but not intra-thoracic fat, is associated with coronary artery calcification.[7] Local toxic effects of pericardial fat may also manifest as abnormalities of left ventricular (LV) structure and function. Previous small studies have demonstrated that pericardial fat is associated with measures of LV mass,[8–10] left atrial size, impaired diastolic filling,[10;11] and negatively correlated with cardiac index.[12] However, these prior studies are limited by their small sample size, use of echocardiography to estimate the thickness of epicardial fat, and lack of adjustment for important covariates. Therefore, whether the association of pericardial fat and measures of LV structure and function are independent of the systemic effects of obesity have not been fully explored.

Thus, we sought to examine the correlation of pericardial fat, intra-thoracic fat, visceral abdominal fat, and measures of LV structure and function by cardiovascular magnetic resonance (CMR). Given the lack of anatomic contact between intra-thoracic fat and visceral abdominal fat and these measures, we hypothesized that only pericardial fat would be associated with measures of LV structure and function.

Methods

Study Sample

In 1948, the Framingham Heart Study Original Cohort was enrolled, totaling 5209 men women and men, 28 to 62 years. The offspring and spouses of the Original Cohort were enrolled into the Offspring Study in 1971.[13;14] The current analysis is comprised of Offspring cohort participants who participated in both the multi-detector computed tomography (MDCT) and cardiovascular magnetic resonance (CMR) sub-studies.

Between 1998–2001, 3539 Offspring cohort participants attended the 7th examination cycle of the Framingham Heart Study. As part of the multi-detector computed tomography (MDCT) sub-study, 1418 (40.1%) underwent MDCT scanning from 2002 to 2005 for coronary and abdominal aortic calcium assessment, of whom 1372 had interpretable pericardial fat measures.[15] In addition, 1794 participants underwent CMR during a similar time period.[16] Of the 1418 participants who underwent MDCT imaging, 1372 had interpretable pericardial fat measures, 1036 also had CMR measures, 1006 of whom attended the 7th examination cycle, and 7 had an incomplete covariate profile, resulting in a total sample size of 997.

The study protocol was approved by the institutional review boards of the Boston University Medical Center, the Massachusetts General Hospital, and the Beth Israel Deaconess Medical

Center. All subjects provided written informed consent. The authors had access to the data and take full responsibility for its integrity.

MDCT scan protocol and Analysis

In a supine position, participants underwent radiographic assessment with 8-slice MDCT (LightSpeed Ultra, General Electric, Milwaukee, WI). The heart was imagined on average with forty-eight contiguous 2.5 mm slices with a prospectively ECG triggered scanning protocol (120 kVp, 400 mA, temporal resolution 330 ms). In addition 25 5 mm thick slices (120 kVp, 400 mA, gantry rotation time 500 ms, table feed 3:1) were acquired covering 125 mm beginning at the level of S1.

Using an offline workstation (Aquarius 3D Workstation, TeraRecon Inc, San Mateo, CA), total-thoracic and pericardial fat tissue volumes (cm^3) were measured. Because absolute Hounsfield Units (HU) pixel values correspond to properties of the imaged tissues, we used a predefined image display setting (window width −195 to −45 HU; window center −120 HU) that identifies pixels that correspond to adipose tissue. Using a semi-automatic segmentation technique, total-thoracic and pericardial fat volumes were measured. Total thoracic fat volume included adipose tissue located in the pericardium and in the thorax from the level of the right pulmonary artery to the diaphragm and the chest wall to the descending aorta. Pericardial fat volume was defined as adipose tissue located within the pericardial sac. Inter-reader reproducibility was excellent (inter-class correlation coefficient for total-thoracic fat 0.98; for pericardial fat 0.95).[7] Intra-thoracic fat was created as a derived variable from the difference between total-thoracic and pericardial fat; this allowed for the creation of two distinct fat depots; this differs from our prior definition of intra-thoracic fat.[7] Visceral adipose tissue volumes (VAT) were quantified with the above-mentioned image display windows;[17] inter-class correlations were 0.99 (inter-class correlations).[17]

Cardiovascular Magnetic Resonance (CMR) Protocol and Analysis

CMR imaging was performed using a 1.5T whole body scanner (Philips Medical Systems, Best, The Netherlands). Short axis cine images encompassing the left ventricle were obtained, using a steady-state free precession (SSFP) sequence[18] with contiguous 10 mm slices and a temporal resolution of 30–35msec.

CMR data were analyzed by a single observer blinded to clinical data observers using a commercial workstation (EasyVision 5, Philips Medical systems, Best, The Netherlands). LV endocardial borders were traced manually at end-systole and end-diastole. LV epicardial borders were traced at end-diastole; LVEDV and LV myocardial volume were calculated using the summation of discs method. LV mass was calculated by multiplying an accepted myocardial density (1.05 g/cm^3) by the calculated volume of myocardium. Left atrial dimension was measured in the AP direction from an axially-oriented image.

Risk Factor and Covariate Assessment

Risk factors were obtained from the 7th Framingham Offspring examination (1998–2001). Waist circumference (WC) was measured at the level of the umbilicus; body mass index (BMI) was defined as weight (kilograms) divided by height-squared (meters). Using fasting morning samples, fasting plasma glucose (FPG), total and HDL cholesterol, and serum triglycerides were measured. Diabetes was defined as FPG ≥ 126 mg/dL or treatment (hypoglycemic agent or insulin). Impaired fasting glucose (IFG) was defined as FPG 100–125 mg/dl in the absence of treatment for DM. Current smokers were defined as those who smoked on average at least one cigarette per day in the past year. Alcohol consumption was quantified via physician-administered questionnaires. Women were considered post-menopausal if menses had stopped

for one year or more. Hypertension was defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or anti-hypertensive treatment.

Statistical Analysis

Due to differences in the distribution of pericardial fat and CMR variables, all analyses were sex-stratified. All adiposity measures were standardized to a mean of 0 and a standard deviation of 1, within each sex, to facilitate comparison of regression coefficients between different fat depots. We considered a full panel of adiposity traits in relation to CMR variables: BMI, WC, VAT, pericardial fat, and intra-thoracic fat. In particular, because intra-thoracic fat is not in direct anatomic contact with the myocardial structures examined here, it was used as a natural control. Sex-specific age-adjusted Pearson correlations between all adiposity measures and LA dimension, LVEDV, and LV mass were calculated. Next, multivariable regression models were constructed with each adiposity variable as the exposure and the CMR variables modeled as the outcomes. Two models were considered: 1) the multivariable-adjusted model, which included adjustment for age, smoking, alcohol, menopause, hormone replacement therapy, systolic blood pressure, hypertension treatment, and height; 2) a second model which was additionally adjusted for body weight. Due to the inclusion of body weight in body surface area calculations, we did not index our measures to body surface area. Models using BMI as an exposure did not additionally adjust for height. Formal sex interactions were tested in the first model.

Several secondary analyses were performed. Models examining intra-thoracic and pericardial fat in relation to CMR variables were additionally adjusted for 1) VAT; 2) diabetes and cardiovascular disease (CVD); 3) in models excluding prevalent CVD.

SAS version 8.0 was used to perform all computations; a two-tailed p-value<0.05 was considered significant.[19]

Results

Study Sample Characteristics

Overall, the study sample comprised 542 women and 455 men with a mean age of 60 years. Overall, 26.3% of women and 27.0% of men were obese. Additional study sample characteristics can be found in Table 1.

Correlations

All adiposity measures were correlated to CMR measures in women, with correlations ranging from 0.28 to 0.53 (LA dimension), 0.20 to 0.36 (LVEDV), and 0.35 to 0.48 (LV mass) (Table 2). Similar correlations were observed in men, with the exception of LVEDV, which was not correlated with VAT, pericardial fat, or intra-thoracic fat.

Multivariable Models

In women, all adiposity measures were associated with LA dimension (Table 3). Per standard deviation increase in pericardial fat, LA dimension was 1.18 cm larger (p<0.0001). In contrast, per standard deviation increase in intra-thoracic fat, LA dimension was 1.37 cm larger (p<0.0001; p-value for difference between pericardial and intra-thoracic fat=0.22). After adjustment for body weight, all associations between fat depots and LA dimension were attenuated (all p-values>0.18). Among men, per SD increase in pericardial fat, LA dimension was 1.74 cm larger (p<0.0001), compared to 1.47 cm larger per SD increase in intra-thoracic fat (p<0.0001; p-value for difference between pericardial and intra-thoracic fat=0.12). After adjustment for body weight, only the association between pericardial fat and LA dimension remained significant (p=0.002).

All measures of adiposity were associated with LVEDV in women. In particular, per 1 SD increase in BMI, LVEDV was 6.88 cm^3 larger ($p<0.0001$). Both pericardial and intra-thoracic fat were associated with LVEDV; the regression coefficient was larger for intra-thoracic (3.73) as compared to pericardial fat (3.01), although the p-value for the difference between pericardial and intra-thoracic fat was not significant ($p=0.29$). In men, neither VAT, pericardial fat, nor intra-thoracic fat was associated with LVEDV.

All measures of adiposity were associated with LV mass in women. Pericardial fat and intra-thoracic fat had similar associations with LV mass (4.33 vs 4.48 g per 1 SD increase in fat; p-value for difference between pericardial and intra-thoracic fat=0.85). After adjustment for body weight, pericardial fat remained associated with LV mass ($p=0.01$), although the magnitude of the association was decreased. In men, all measures of adiposity were associated with LV mass. Similar to women, there was no difference in the magnitude of association between pericardial fat, intra-thoracic fat and LV mass (3.83 vs 3.75 g per 1 SD increase in fat; p-value for difference between pericardial and intra-thoracic fat=0.98).

Secondary analyses

Models examining the relation between pericardial fat and intra-thoracic fat in relation to CMR measurements were additionally adjusted for VAT (Table 4). After adjustment for VAT, nearly all associations were attenuated, with the exception of the association between pericardial fat and LA Dimension in men ($p=0.0004$).

When models were additionally adjusted for diabetes and CVD, results were not materially different (Table 4). Similarly, when analyses first excluded individuals with CVD, results were similar (Table 4).

Discussion

Principal Findings

In this community-based study of nearly 1000 participants undergoing contemporaneous CMR and MDCT examinations, we found that pericardial fat volume is associated with LV mass, LVEDV, and LA dimension in women and with LV mass and LA dimension in men. These associations persist after multivariable adjustment, but not after accounting for body weight or VAT, with the exception of LA dimension in men. There is a similar pattern of association of intra-thoracic fat with LV structure and function after multivariable adjustment, but not after adjustment for body weight or VAT. Finally, BMI and WC are also associated with CMR measures after multivariable adjustment. These results suggest that any potential local pathologic effect of pericardial fat on LV structure and function are overwhelmed by the systemic effects of obesity. Our findings do not suggest that pericardial fat is a better correlate of cardiac structure and function than VAT or other more easily conducted anthropometric measures of adiposity.

In the Context of the Current Literature

Pericardial fat has been found to correlate with LV mass across a range of BMI values[8–10] and with impaired diastolic filling and atrial enlargement in morbid obesity.[11] It has been proposed that the direct anatomic proximity of pericardial fat to the myocardium allows for a paracrine interaction that may affect cardiac morphology and function. Such local effects are hypothesized to render pericardial fat a stronger correlate of cardiac structure and function than more general measures of adiposity.[20] In the present study, we confirmed that pericardial fat is associated with CMR measures, but observed that it is no more correlated as compared to other ectopic fat depots and proxy measures of adiposity. We additionally found that the association between pericardial fat and CMR measures is attenuated once VAT is taken into

account. These data suggest this may not be the case for pericardial fat and that the systemic effects of generalized adiposity may overwhelm the local effects of pericardial fat.

Mechanisms

Adiposity may affect LV structure and function via mechanical, paracrine, and systemic processes. Compression of the heart by pericardial or intrathoracic fat deposits may decrease LV diastolic filling, leading to atrial dilation. The presence of impaired diastolic function and increased LA dimension without LV hypertrophy in uncomplicated obesity suggests a possible mechanical role for regional adiposity in cardiac structure and function independent of systemic obesity-related disorders such as diabetes and hypertension.[21] Our finding that pericardial fat remained a significant correlate of LA dimension in men after adjusting for body weight and VAT supports this notion. We did not, however, observe an association between pericardial fat and LVEDV in men.

Direct contact between adipose tissue and the myocardium may impact LV structure and function via paracrine secretion. Pericardial fat lies directly on the myocardium and shares the same coronary blood supply, with no fascia separating the two layers.[22] Samples of pericardial fat from 42 patients undergoing coronary artery bypass graft surgery showed increased mRNA and protein levels of chemokine (MCP-1) and inflammatory cytokines (IL-1β, IL-6, IL-6sR, and TNF-α) relative to subcutaneous fat and independent of obesity, diabetes, and statin or ACE inhibitor use.[23] Another coronary artery bypass graft study found pericardial fat to be a source of adiponectin and resistin in addition to MCP-1, IL-6, IL-6sR, and TNF-α.[24] However, pericardial fat concentrations of inflammatory biomarkers in coronary artery bypass graft patients did not correlate with plasma concentrations, suggesting that the release of such markers by pericardial fat, a relatively small fat depot, is not great enough to be detected systemically.[23]

Pericardial fat has also been found to correlate with coronary artery calcification after multivariable and VAT adjustment, suggesting that fat depots in anatomic contact with the vasculature may exert local pathologic effects.[7] In light of our findings in the present study that associations between pericardial fat and CMR measures do not generally persist after adjustment for body weight and VAT, and that pericardial fat, which is in direct anatomic contact with myocardium, is no more correlated with measures of LV structure and function than intrathoracic fat, it appears that the paracrine effects of pericardial fat may be more pronounced for coronary artery calcification than for general measures of LV structure and function.

In comparison to the possible mechanical and paracrine effects of pericardial fat, the systemic effects of obesity on cardiac structure and function have been well described. Obesity is strongly associated with diabetes, hypertension, dyslipidemia, and cardiovascular disease.[25; 26] Hypertension is an independent risk factor for LV hypertrophy and increased LV mass, but cardiac hypertrophy is observed even in normotensive obese patients.[27] This may be due to hemodynamic changes resulting from the increased blood volume and flow required to adequately perfuse increased body mass.

Strengths and Limitations

Compared to earlier work on pericardial fat and measures of LV structure and function, strengths of this study include the large sample size that includes a wide BMI range, reducing the risk of ascertainment bias. Additional strengths include detailed longitudinal assessment of covariates, minimizing the risk of misclassification, and the quantification of pericardial fat volumes, rather than fat thickness. Some limitations warrant discussion. In particular, the cross-sectional study design limits inferences of causality, and the predominantly white study sample

may limit generalizability to other ethnic groups. Unmeasured factors such as sleep apnea may partially account for our findings. Lastly, because CT scanning was performed without heart rate control, it is possible that measurements of pericardial fat may have been effected by motion artifacts.

Conclusions

Pericardial fat is correlated with measures of LV structure and function, but not independent of or more strongly than other ectopic fat stores and proxy measures of visceral adiposity. An important exception is left atrial dimension in men. These results suggest that the systemic effects of obesity on cardiac structure and function may outweigh the local pathogenic effects of pericardial fat.

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Table 1

Study sample characteristics among participants with both pericardial fat, VAT, and CMR measures who have not undergone open-heart surgery. Data represent mean (SD) or percents (n)

	Women (n=542)	**Men (n=455)**
Age (years)	59.8 (8.8)	60.1 (9.3)
Pericardial Fat (cm^3)	108.0 (41.0)	136.5 (54.4)
Intra-thoracic Fat (cm^3)	81.9 (41.4)	147.5 (64.1)
Visceral adipose tissue (cm^3)	1579 (853)	2558 (1072)
Body mass index (kg/m^2)	27.6 (5.5)	28.5 (4.3)
Waist circumference (cm)	96 (15)	102 (11)
Height (inches)	63.6 (2.4)	68.8 (2.6)
Left atrial Dimension (mm)	28.4 (4.4)	31.7 (5.1)
LV end diastolic volume (mm)	108.2 (20.1)	144.6 (29.3)
LV Mass (g)	86.1 (16.5)	127.1 (24.2)
Obesity (%)	26.3 (142)	27.0 (123)
Current smoking (%)	9.0 (49)	8.8 (40)
Alcohol (oz/week)	1.6 (2.2)	3.5 (4.4)
Post menopausal status (%)	82.9 (449)	-
Hormone replacement therapy (%)	38.4 (208)	-
Systolic Blood Pressure (mm Hg)	123.2 (18.2)	126.2 (16.1)
Hypertension Treatment (%)	24.5 (133)	29.0 (132)
Hypertension (%)	34.6 (187)	40.9 (186)
Diabetes (%)	7.0 (38)	10.3 (47)
Cardiovascular Disease (%)	7.8 (42)	13.6 (62)

LV=left ventricular

Table 2

Age-adjusted Pearson correlations between the adiposity and CMR measures

	Women			Men		
	LA Dimension	**LVEDV**	**LV Mass**	**LA Dimension**	**LVEDV**	**LV Mass**
BMI	0.53***	0.36***	0.48***	0.44***	0.10*	0.32***
WC	0.48***	0.30***	0.45***	0.44***	0.14**	0.34***
VAT	0.42***	0.24***	0.45***	0.36***	−0.06	0.19***
Pericardial Fat	0.28***	0.20***	0.35***	0.37***	0.07	0.19***
Intra-thoracic fat	0.33***	0.25***	0.37***	0.31***	−0.02	0.17***

* p<0.05

** p<0.01

*** p<0.001

BMI=body mass index; VAT=visceral adipose tissue; LV=left ventricular; EDV=end diastolic volume

Table 3

Sex-specific, multivariable* adjusted regressions (standard error) between the adiposity and CMR measures. Data expressed per 1 standard of each adiposity measure, after standardization to a mean of 0 and standard deviation of 1.

	Women				Men				
	MV adjusted	**p-value**	**+additional adjustment for body weight**	**p-value**	**MV adjusted**	**p-value**	**+additional adjustment for body weight**	**p-value**	**P-value for sex interaction in MV model**
LA Dimension									
BMI**	2.28 (0.18)	<0.0001	-	-	2.12 (0.22)	<0.0001	-	-	0.84
WC	2.00 (0.18)	<0.0001	−0.27 (0.39)	0.50	2.15 (0.22)	<0.0001	0.96 (0.56)	0.09	0.23
VAT	1.66 (0.19)	<0.0001	0.18 (0.25)	0.48	1.68 (0.24)	<0.0001	0.48 (0.30)	0.11	0.31
Pericardial	1.18 (0.20)	<0.0001	0.20 (0.20)	0.32	1.74 (0.23)	<0.0001	0.80 (0.26)	0.002	0.015
Intra	1.37 (0.19)	<0.0001	0.27 (0.20)	0.18	1.47 (0.23)	<0.0001	0.45 (0.25)	0.08	0.27
LVEDV									
BMI**	6.88 (0.82)	<0.0001	-	-	3.71 (1.38)	0.008	-	-	0.04
WC	4.79 (0.80)	<0.0001	−6.73 (1.71)	<0.0001	3.57 (1.33)	0.007	−6.28 (3.45)	0.07	0.42
VAT	3.51 (0.80)	<0.0001	−2.23 (1.10)	0.04	−2.33 (1.38)	0.09	−7.84 (1.68)	<0.0001	0.0003
Pericardial	3.01 (0.80)	0.0002	0.09 (0.84)	0.92	0.80 (1.37)	0.56	−2.19 (1.55)	0.16	0.14
Intra	3.73 (0.80)	<0.0001	0.33 (0.89)	0.71	−1.39 (1.35)	0.30	−4.88 (1.50)	0.001	0.001
LV Mass									
BMI**	6.93 (0.65)	<0.0001	-	-	8.03 (1.09)	<0.0001	-	-	0.24
WC	5.83 (0.64)	<0.0001	−2.04 (1.38)	0.14	7.49 (1.06)	<0.0001	−4.08 (2.74)	0.14	0.12
VAT	5.86 (0.63)	<0.0001	2.03 (0.87)	0.02	4.31 (1.14)	0.0002	−1.57 (1.36)	0.25	0.33
Pericardial	4.33 (0.64)	<0.0001	1.66 (0.66)	0.01	3.83 (1.13)	<0.0001	−0.87 (1.23)	0.48	0.76
Intra	4.48 (0.65)	<0.0001	1.27 (0.71)	0.07	3.75 (1.12)	0.0009	−0.71 (1.20)	0.55	0.67

* MV adjustment refers to age, smoking, alcohol, menopause, HRT, SBP, HTN Rx, and height

** BMI models are not adjusted for height due to collinearity

BMI=body mass index; VAT=visceral adipose tissue; LV=left ventricular; EDV=end diastolic volume, MV=multivariable

Table 4

Sex-specific, multivariable adjusted* regressions additionally adjusted for VAT (top panel), diabetes and CVD (middle panel), and excluding prevalent CVD (lower panel)

	Women		Men	
	MV adjusted	**p-value**	**MV adjusted**	**p-value**
VAT Adjustment				
LA Dimension				
Pericardial	0.17 (0.24)	0.48	1.07 (0.30)	0.0004
Intra	0.09 (0.28)	0.76	0.37 (0.34)	0.29
LVEDV				
Pericardial	0.72 (1.03)	0.48	3.07 (1.82)	0.09
Intra	1.53 (1.23)	0.21	−0.63 (1.99)	0.75
LV Mass				
Pericardial	1.26 (0.80)	0.12	1.06 (1.51)	0.48
Intra	−0.15 (0.96)	0.88	0.33 (1.65)	0.84
DM, CVD Adjustment				
LA Dimension				
Pericardial	1.12 (0.20)	<0.0001	1.66 (0.23)	<0.0001
Intra	1.33 (0.19)	<0.0001	1.36 (0.23)	<0.0001
LVEDV				
Pericardial	3.04 (0.81)	0.0002	0.45 (1.36)	0.74
Intra	3.78 (0.81)	<0.0001	−1.85(1.35)	0.17
LV Mass				
Pericardial	4.23 (0.65)	<0.0001	3.68 (1.14)	0.0014
Intra	4.40 (0.65)	<0.0001	3.58 (1.13)	0.0016
Excluding Prevalent CVD				
LA Dimension				
Pericardial	1.10 (0.21)	<0.0001	1.57 (0.24)	<0.0001
Intra	1.35 (0.20)	<0.0001	1.50 (0.25)	<0.0001
LVEDV				
Pericardial	2.88 (0.83)	0.0006	−0.08 (1.40)	0.95
Intra	3.39 (0.83)	<0.0001	−2.27 (1.42)	0.11
LV Mass				
Pericardial	4.35 (0.66)	<0.0001	3.57 (1.21)	0.0035
Intra	4.13 (0.66)	<0.0001	4.35 (1.23)	0.0005

* MV adjustment refers to age, smoking, alcohol, menopause, HRT, SBP, HTN Rx, and height

BMI=body mass index; VAT=visceral adipose tissue; LV=left ventricular; EDV=end diastolic volume, MV=multivariable