

# Intrathoracic Fat Measurements Using Multidetector Computed Tomography (MDCT): Feasibility and Reproducibility

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**Key Words:** epicardial fat volume, intrathoracic fat, MDCT, feasibility, reproducibility

**Abbreviations:** Cardiovascular disease (CVD), body mass index (BMI), coronary artery disease (CAD), multidetector computed tomography (MDCT), computed tomography (CT), coronary CT angiography (CCTA), epicardial fat volume (EFV), region of interest (ROI), Advantage Workstation (AW), Hounsfield Unit (HU)

## ABSTRACT

Intrathoracic fat volume, more specifically, epicardial fat volume, is an emerging imaging biomarker of adverse cardiovascular events. The purpose of this work is to show the feasibility and reproducibility of intrathoracic fat volume measurement applied to contrast-enhanced multidetector computed tomography images. A retrospective cohort study of 62 subjects free of cardiovascular disease (55% females, age =  $49 \pm 11$  years) conducted from 2008 to 2011 formed the study group. Intrathoracic fat volume was defined as all fat voxels measuring  $-50$  to  $-250$  Hounsfield Unit within the intrathoracic cavity from the level of the pulmonary artery bifurcation to the heart apex. The intrathoracic fat was separated into epicardial and extrapericardial fat by tracing the pericardium. The measurements were obtained by 2 readers and compared for interrater reproducibility. The fat volume measurements for the study group were  $141 \pm 72$  cm<sup>3</sup> for intrathoracic fat,  $58 \pm 27$  cm<sup>3</sup> for epicardial fat, and  $84 \pm 50$  cm<sup>3</sup> for extrapericardial fat. There was no statistically significant difference in intrathoracic fat volume measurements between the 2 readers, with correlation coefficients of 0.88 ( $P = .55$ ) for intrathoracic fat volume and  $-0.12$  ( $P = .33$ ) for epicardial fat volume. Voxel-based measurement of intrathoracic fat, including the separation into epicardial and extrapericardial fat, is feasible and highly reproducible from multidetector computed tomography scans.

## INTRODUCTION

Cardiovascular disease (CVD) remains the number one cause of mortality among adult men and women in the USA despite recent decrease in the mortality rate (1). A major contributor to increased CVD events is central obesity, which has been implicated as a cardiovascular risk factor and a public health problem (2). Several studies have shown that increased abdominal visceral fat is a strong predictor of metabolic syndrome and CVD (3-5). Waist circumference and body mass index (BMI) are commonly used anthropometric measures for quantifying general and regional adiposity (3-8). However, both measures have been criticized for providing general measurements that do not directly correlate well with the underlying visceral fat component (6-8), such as abdominal and intrathoracic fat that are more highly correlated with cardiovascular risk compared with waist circumference and BMI alone (9, 10). An independent association between increased intrathoracic fat volume (ie, intrapericardial fat) and abdominal fat volume with atrial fibrillation and

coronary artery disease (CAD) was shown (11-13). However, most of these studies do not explicitly describe the methodology used to quantify thoracic fat or define intrathoracic fat compartments. Multidetector computed tomography (MDCT) scans are often used in research protocols for the measurement of visceral or intrathoracic adiposity (14), but these have been limited in the clinical setting owing to cost and radiation exposure. Some centers have developed and validated in-house semi- and full-automated software as part of research tools to calculate the epicardial fat volume from noncontrast-enhanced computed tomography (CT) (15). Although the epicardial fat may be an important measurement for identifying individuals at increased CVD risk (11, 12), the feasibility of intrathoracic fat compartment measurements obtained from clinically acquired contrast-enhanced chest MDCT scans using commercially available software has not been assessed. In this paper, we discuss the definitions of intrathoracic fat, its clinical significance, and the methodology of quantifying intrathoracic fat volume.

The primary goal of this study is to show the feasibility of intrathoracic fat volume measurements from prior clinically acquired contrast-enhanced cardiac MDCT examinations using commercially available postprocessing software. The second goal of the study is to show the reproducibility of the intrathoracic fat volume measurements by testing the inter-reader variability using the Bland–Altman interobserver variability test.

## MATERIALS AND METHODS

### Study Population

The study was approved by the Institutional Review Board with a waiver of informed consent. In total, 62 normal subjects free of any CVD formed the study population. The normal subjects were included after retrospectively reviewing the medical charts and coronary CT angiography (CCTA) reports of 675 adult subjects with atypical chest pain presenting either in the emergency department or at an outpatient clinic, who underwent CCTA between January 2006 and December 2011. The 62 subjects (34 females, 55%, and 28 males, 45%; mean age,  $49 \pm 11$  years; age range, 24–72 years) fulfilled the following inclusion criteria:

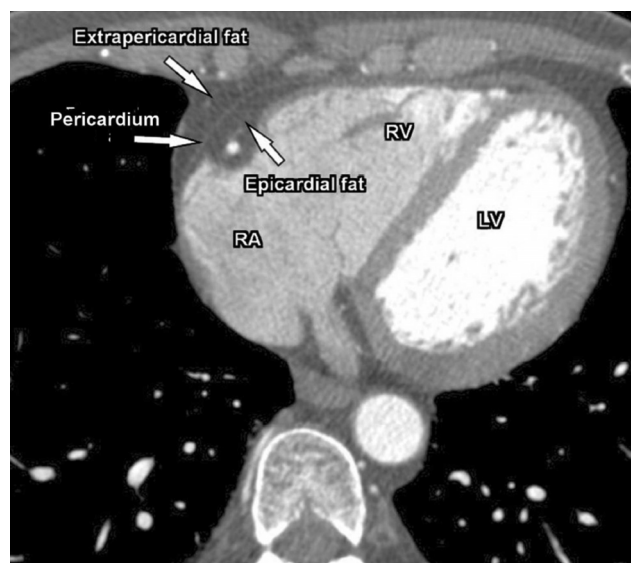
- (1) No evidence of CAD (normal electrocardiogram and normal retrospectively gated CCTA).
- (2) No CAD risk factors, such as hypertension, hypercholesterolemia, diabetes, or structural heart disease (normal medical history and physical examination).
- (3) Low pretest probability for CAD based on Framingham criteria (16).

No major adverse cardiac events were noted at the subsequent 6-month chart review in any subject. Height, weight, BMI, age, and gender were recorded for all subjects.

### CT Acquisition Technique

All subjects underwent assessment of the vital signs (blood pressure and heart rate) at least 1 hour before the CCTA. Subjects with heart rate  $>65$  beats/min underwent oral premedication with 50 mg of metoprolol at least 45 minutes before CT acquisition. Heart rate of  $\leq 60$  beats/min was achieved in all patients during the scan. All subjects underwent premedication with 1 puff of sublingual nitroglycerin 1–5 minutes before the CT scan. All scans were acquired with the patient in the supine position and with arms elevated above and behind the head on a 64-row MDCT (Lightspeed VCT; GE Healthcare, Milwaukee, WI). Image acquisition was performed with electrocardiogram gating in the craniocaudal direction at end-inspiration within a single breath-hold. The scan z-axis coverage ranged from 2 cm above the most cephalad coronary artery to 2 cm below the cardiac apex. The scan parameters were as follows: section thickness = 0.625 mm, tube voltage = 100–120 kVp, gantry rotation time = 0.35 seconds, and the current unit (mA) was adjusted for patient size based on a BMI look-up table.

Iso-osmolar contrast material (Visipaque 370; GE Healthcare) was administered through an 18-g intravenous cannula placed in the right antecubital vein. A test bolus of 15 mL of contrast material was injected at 5 mL/s with the region of interest (ROI) placed in the aortic root at the level of the left main coronary artery. For each patient, a Hounsfield Unit (HU) time graph was obtained, from which the scan delay was calculated



**Figure 1.** Axial computed tomography (CT) image defining the intrathoracic fat compartments. The pericardium (white arrow) divides the intrathoracic fat into epicardial and extrapericardial fat (arrows).

as peak enhancement plus 6 seconds. The dedicated CCTA acquisition was then acquired using a triphasic contrast bolus with a total of 80 mL of contrast material. The first 50 mL of contrast material was followed by 30 mL of contrast material diluted with 30 mL of normal saline. A 50 mL of normal saline push comprised the final phase of the bolus injection. The entire volume was delivered at a rate of 5 mL/s. All examinations were performed using retrospective gating with tube current modulation (100% peak tube current during mid- to end-diastole and up to 80% reduction at end-systole) to reduce radiation exposure.

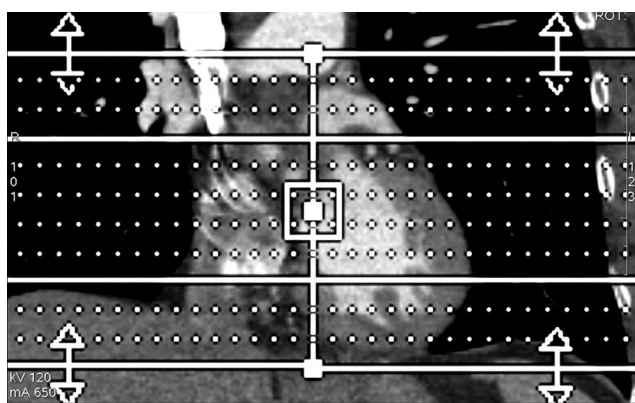
### Definition of Thoracic Fat Compartments

The intrathoracic adipose tissue is defined as the adipose tissue surrounding the heart, enclosed by the inner aspect of the sternum, spine, and lungs, extending from the bifurcation of the pulmonary artery through the cardiac apex over the diaphragm. It includes both the extrapericardial and epicardial fat.

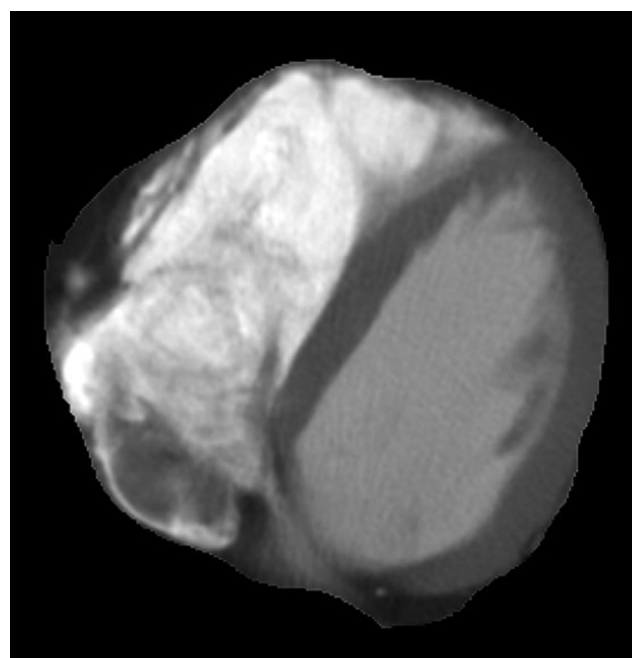
The epicardial adipose tissue is defined as the adipose tissue enclosed by the visceral pericardium and is concentrated in the atrioventricular and interventricular grooves, along the major branches of the coronary arteries, around the atria, over the free wall of the right ventricle, and over the apex of the left ventricle (17) (Figure 1). The extrapericardial fat is defined as the adipose tissue situated on the external surface of the parietal pericardium within the mediastinum, alternatively termed the mediastinal fat (17).

### CT Image Reconstruction, Fat Measurement Technique, and Postprocessing

All reconstructed images were postprocessed on a GE Advantage Workstation (AW) (version 4.5, GE Healthcare) using the Refor-



**Figure 2.** Coronal CT image of the chest showing batch horizontal lines covering the heart from the left atrial appendage to the diaphragm.



**Figure 3.** Axial CT image of an epicardial region of interest (ROI) after tracing the pericardium, leaving the epicardial fat concentrated in the atrioventricular grooves, interventricular grooves, along the major branches of coronary arteries, around the atria, over the free wall of the right ventricle, and over the apex of the left ventricle.

mat software tool (GE Healthcare). Further 10–14, 10-mm-thick contiguous axial sections were obtained using the Reformat tool and batch lines off the previously obtained CCTA axial images, with coverage extending from the bifurcation of the pulmonary artery through the cardiac apex over the diaphragm (Figure 2). The fat volume of each thoracic compartment was obtained by tracing the mediastinal and epicardial areas in a systematic fashion as detailed below, and data were processed using a histogram-based statistical program based on the method described by Borkan et al. (18). The field of view encompassed all soft tissues of the chest at that level. All CT reformats were performed on the same AW workstation to reduce measurement error. Reformats were loaded into the Reformat software on the AW workstation to measure the thoracic fat compartments using semiautomatic segmentation.

The total fat represented the adipose tissue covering from the bifurcation of the pulmonary artery through the cardiac apex over the diaphragm (Figures 1 and 2). The resulting histogram displayed the computer-generated volume of all 10–14 10-mm-thick sections. The fat volume was then calculated in cubic centimeters by designating an attenuation threshold that would isolate and quantify fat. The threshold range was set from –250 to –50 HU to allow for the lower density of fat by bone artifact (18). Another ROI was manually traced at the interface between the mediastinal fat and lungs and adjacent vertebral bodies and paraspinal musculature on all sections. This tracing was placed at the inner edge of the interface to completely exclude the subcutaneous fat, osseous structures, and lungs. The area outside this tracing was deleted, leaving an internal area designated as “intrathoracic”. The intrathoracic volume comprised the extrapericardial and epicardial volumes (Figure 1). The intrathoracic and fat volumes were calculated as explained above. The last ROI was traced along the pericardium on all sections to completely include the epicardial volume/fat. The region outside this tracing was deleted, leaving an internal area designated as “epicardial” (Figure 3). Similar to the other regions, the epicardial volume and epicardial fat volume were calculated. Subtracting these volumes from the intrathoracic

volume and fat volume resulted in the “extrapericardial” and fat volumes, respectively. This methodology of obtaining the fat volume measurements in the thorax is in agreement with the defined anatomy of the epicardium, pericardium (pericardial sac), and mediastinum (15, 17).

### Reproducibility

All thoracic fat and volume measurements were performed by a single CT-certified technologist with >5 years of experience in advanced image processing. To test for inter-reader variability of the contouring, all 62 examinations were independently analyzed 6 months later by a second reader (a cardiothoracic fellowship-trained radiologist with >7 years of experience) using the same methodology used by the first reader, and blinded to the patient information and results from the first reading.

### Statistical Analysis

Continuous data were presented as mean  $\pm$  standard deviation or median (25th–75th interquartile range), as appropriate. Categorical data were presented as numbers and percentages. The univariate association between the tested variables was assessed with the Student *t* test for continuous variables with normal distribution, Wilcoxon test for continuous variables without normal distribution, and  $\chi^2$  test or Fisher test for categorical variables, as appropriate. A general linear model was used to evaluate the associations between the thoracic fat volumes and

**Table 1.** Study Sample Characteristics

	All subjects (N = 62)	Women (N = 34/62)	Men (N = 28/62)	P-Value <sup>a</sup>
Age (years)	48 ± 11	49 ± 11	47 ± 11	.51
BMI (kg/m <sup>2</sup> )	27, 24–30	27, 24–30	27, 25–30	.73
Weight (kg)	79, 72–91	78, 70–88	81, 74–95	.25
Height (cm)	173, 160–180	170, 160–178	178, 170–183	.13
Intrathoracic fat (cm <sup>3</sup> )	141 ± 72	125 ± 62	162 ± 79	.04 <sup>b</sup>
Epicardial fat (cm <sup>3</sup> )	58 ± 27	56 ± 28	59 ± 26	.62
Extrapericardial fat (cm <sup>3</sup> )	84 ± 50	69 ± 38	103 ± 57	.02 <sup>b</sup>

The sample characteristics are presented as median, interquartile range (IQR) or mean ± standard deviation (SD), where appropriate, in all subjects and stratified by gender.

<sup>a</sup>P is the statistical significance between the thoracic fat compartment measurements and gender using the Student *t* test.

<sup>b</sup>Significant at level <.05 using Wilcoxon test for continuous variables without normal distribution and Student *t* test for continuous variables with normal distribution.

gender. The Pearson correlation coefficient of the means was used to quantify the relationships between the measurements from the 2 readers. However, as the Pearson correlation coefficient does not assess variability, that is, linear error between the 2 readers, the Bland–Altman test (19) was used to evaluate the inter-reader agreement. The statistical significance of the difference of the measurements' means from the 2 readers was assessed with correlation procedure. A *P*-value of <.05 was considered statistically significant. All computations were performed using the SAS/STAT software (Version 9.2, SAS Institute Inc, Cary, NC).

**RESULTS**

**Baseline Characteristics**

The mean systolic and diastolic blood pressures were 122 ± 9 and 73 ± 10 Hg, respectively. The median BMI was 27 kg/m<sup>2</sup>, and the 25th–75th interquartile range (IQR) was 24–30 kg/m<sup>2</sup>. The study sample characteristics for all subjects, stratified by gender, are presented in Table 1.

**Thoracic CT Fat Compartments**

Thoracic MDCT fat volume measurements in cubic centimeters in all patients and stratified by gender are presented in Table 1. The intrathoracic fat volume consisted of 59% extrapericardial fat volume (83 cm<sup>3</sup> out of the total of 140 cm<sup>3</sup>) and 41% epicardial fat volume (57 cm<sup>3</sup> out of the total of 140 cm<sup>3</sup>). Women had 36 ± 12 cm<sup>3</sup> less extrapericardial fat than men (103 ±

57 cm<sup>3</sup>; *P* = .004). Women also had less intrathoracic fat (difference of 40 ± 18 cm<sup>3</sup> from the men's volume of 162 ± 79 cm<sup>3</sup>; *P* = .03).

**Influence of BMI on Thoracic Fat Compartments**

Our study population group is represented by 12/63 (19%) normal, 33/63 (52%) overweight, and 18/63 (28%) obese subjects (mean, 28.5 ± 4.7 kg/m<sup>2</sup>; median, 28 kg/m<sup>2</sup>; range, 16.6–43 kg/m<sup>2</sup>). The mean BMI in women was 28.5 ± 5.3 kg/m<sup>2</sup> and ranged between 16.6 and 43 kg/m<sup>2</sup> (median, 27.7 kg/m<sup>2</sup>), and in men, the BMI was 28.6 ± 4 kg/m<sup>2</sup>, ranging between 24 and 42 kg/m<sup>2</sup> (median, 28.1 kg/m<sup>2</sup>). There was no statistically significant difference in the BMI distribution according to gender (*P*-value of .65). The mean BMI distribution by the 3 groups was as follows:

- group 1 (n = 12): 23 ± 2 kg/m<sup>2</sup>, range: between 16.6 and 24.8 kg/m<sup>2</sup> (median, 23.8 kg/m<sup>2</sup>);
- group 2 (n = 33): 27.4 ± 1 kg/m<sup>2</sup>, range: between 25 and 29.6 kg/m<sup>2</sup> (median, 27.7 kg/m<sup>2</sup>); and
- group 3 (n = 18): 34.3 ± 4.1 kg/m<sup>2</sup>, range: between 31 and 42.9 kg/m<sup>2</sup> (median, 32.5 kg/m<sup>2</sup>).

There was statistically significant difference in the BMI distribution according to obese groups (*P*-value of .0001). There were 6/12 (50%) women in the normal group, 17/33 (49%) women in the overweight group, and 10/18 (60%) women in the obese group. No statistically significant difference was observed

**Table 2.** Thoracic Fat in Cubic Centimeters Stratified by Obesity

	Normal (N = 18)	Overweight (N = 33)	Obese (N = 18)	P-Value
Total fat, cm <sup>3</sup>	736 ± 300	700 ± 235	783 ± 284	.50
Mediastinal fat, cm <sup>3</sup>	134 ± 88	133 ± 53	146 ± 64	.72
Pericardial fat, cm <sup>3</sup>	57 ± 37	55 ± 22	56 ± 21	.87
Epicardial fat, cm <sup>3</sup>	76 ± 54	78 ± 37	91 ± 48	.59

Data are presented as mean ± SD.

**Table 3.** Interrater Variability Between 2 Readers for Intrathoracic CT Fat and Volume Measurements

	Pearson Correlation of the Means of the 2 Raters (N = 62)				Method Comparison Test Using Bland-Altman Procedure (N = 62)			
	Mean Rater1/ Rater2	SD Rater1/ Rater2	Pearson Correlation Coefficient of the Mean (r)	P-Value <sup>a</sup>	Mean Difference of 2 Raters	SD of the Mean Difference of 2 Raters	Pearson Correlation Coefficient of the Mean Difference (r)	P-Value <sup>a</sup>
Intrathoracic fat (cm <sup>3</sup> )	140/133	72/71	0.98	<.001 <sup>b</sup>	3.7	6.2	0.08	.50
Intrathoracic volume (cm <sup>3</sup> )	1084/1103	245/249	0.94	<.001 <sup>b</sup>	-9.07	43.2	-0.03	.83
Epicardial fat (cm <sup>3</sup> )	57/55	27/28	0.96	<.001 <sup>b</sup>	0.81	3.76	-0.12	.33
Epicardial volume (cm <sup>3</sup> )	863/867	186/187	0.98	<.001 <sup>b</sup>	-1.93	17.87	-0.02	.89

<sup>a</sup>P is the statistical significance using Pearson correlation or Bland-Altman test, where appropriate.

<sup>b</sup>Significant at level <.05 using Bland-Altman test.

with respect to gender and obesity groups (*P*-value of .94). Table 2 presents thoracic fat in cubic centimeters stratified by the 3 obesity groups. No statistically significant difference was seen between total, mediastinal, pericardial, and epicardial fat and BMI as a continuous variable. In addition, no statistically significant difference was found between the obese and overweight groups compared with the normal group. The statistically significant difference was not reached even with gender stratification.

**Inter-Reader Agreement**

There was no statistically significant difference in the intrathoracic or epicardial fat volumes between the readers by either Pearson correlation coefficient or Bland-Altman analysis (*P*-value = .50 for intrathoracic fat volume and 0.33 for epicardial fat volume) (Table 3). Figure 4 shows the Bland-Altman plots showing the inter-reader differences for the intrathoracic (A) and epicardial (B) fat volume measurements.

**DISCUSSION**

In this cross-sectional retrospective cohort study, we showed the feasibility and inter-reader reproducibility of intrathoracic fat volume measurements on prior clinically acquired contrast-enhanced cardiac MDCT examinations using commercially available postprocessing software.

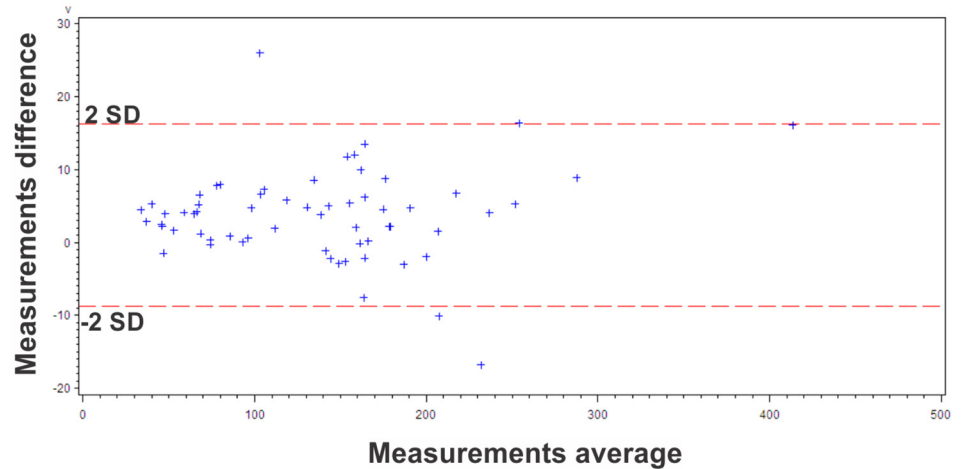
The layers surrounding the heart are composed of intra- and extrapericardial fat (17). We used the pericardium as a landmark to divide the intrathoracic fat into intra- (epicardial) and extrapericardial fat compartments, as they have different embryological origins, blood supply, and functional properties such as the secretion of adipokines. The extrapericardial fat, also known as paracardial fat, is defined as the fat tissue external to the parietal pericardium. It originates from the primitive thoracic mesenchyme that also forms the outer thoracic wall and is supplied by a pericardiophrenic artery, which is a branch of the internal mammary artery (17).

In contrast, the epicardial fat, also known as intrapericardial fat, is defined as the fat tissue enclosed by the visceral pericardium that is composed of mesothelial cells and is supplied by the coronary arteries that also supply the myocardium (17, 20). The epicardial fat is in direct contact with the surface of the myo-

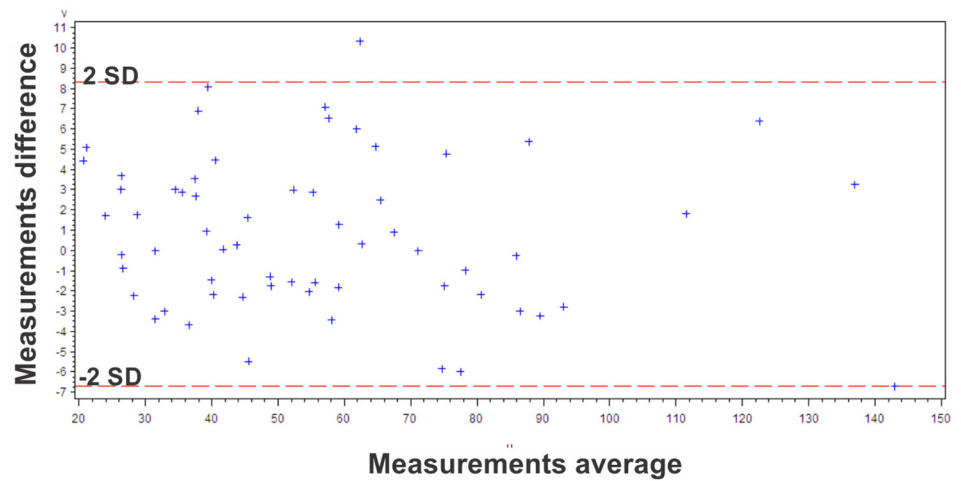
cardium and coronary arteries with no separation by a physical fascia, and it is virtually impossible to accurately dissect the epicardial fat from the myocardium *ex vivo* (21). Thus, molecules secreted by the epicardial fat may diffuse between the fat and these adjacent structures. The epicardial fat, for example, the omental and mesenteric fat, shares a common origin as arising from the splanchnopleuric mesoderm associated with the gut (17). A dichotomous role, both protective and detrimental, has been attributed to the epicardial fat. Under normal physiological conditions, the epicardial fat may serve as a buffer, absorbing fatty acids and protecting the heart against high fatty acids levels, and may release factors such as adiponectin that blunt the toxic effects of high fatty acid levels on the myocardium (22). Nevertheless, with fat accumulation in the epicardial fat depot, recognized as one of the ectopic sites in increased abdominal visceral adiposity, the epicardial fat may promote atherosclerotic changes in the coronary arteries and myocardium by triggering a cellular and molecular inflammatory cascade that leads to increased lipolysis, decreased adiponectin, and increased leptin levels (17). Adiponectin is known for its anti-inflammatory and antiatherogenic properties; thus, reductions in adiponectin may reduce its potential vasoprotective effects and play an important role in metabolic syndrome and CVD (17, 22-24). Excessive epicardial fat, but not extrapericardial fat, has been shown to be associated with CAD and decreased cardiac function (23, 24) and it is an emerging imaging biomarker for identifying patients at risk for CVD.

The term pericardial fat is variably used to describe the adipose tissue in the space either between the visceral and parietal pericardium, that is, pericardial sac, between the pericardium and the myocardium, just external to the pericardium, or in the intrathoracic space (11, 12, 21). All studied subjects had normal pericardium thickness, and the studied ROI was placed on the pericardium itself, which we used as a landmark to discern the intra- from extrapericardial fat compartments; therefore, the space between the visceral and parietal pericardium was included in the epicardial fat volume measurements. In reality, the layers of the pericardium are closely opposed in normal subjects and separated by a small amount of physiological fluid. In addition, the heart and coronary arteries are in-

**A Bland-Altman plot for mean differences of two readers for Intra-thoracic Fat**



**B Bland-Altman plot for mean differences of two readers for Epicardial Fat**



**Figure 4.** Inter-reader agreement (Bland–Altman plots) for intrathoracic and epicardial fat volumes. Dotted lines represent 95% limits of agreement. Mean difference and 95% confidence interval for intrathoracic fat volume after applying the threshold of minimum of  $-250$  Hounsfield Unit (HU) and maximum of  $-50$  HU (A). Mean difference and 95% confidence interval for epicardial fat volume after applying the threshold of minimum of  $-250$  HU and maximum of  $-50$  HU (B).

cluded in the epicardial fat volume measurement, primarily because there is mutual vascular supply and no separate physical fascia between the 2; therefore, any attempt to exclude the heart would increase the postprocessing time and may lead to measurement errors. Because the arteries and the heart are primarily made of soft tissue and possess fluid attenuation characteristics, which are enhanced by the contrast agent in this study, there is very little fat within the heart itself that would be included. Lipomatous hypertrophy of the atrial septum is conceivable as a fair amount of fat in the interatrial septum, which would be included when present, and in abnormal subjects, small amounts of fatty myocardial replacement from old infarcts would be included.

The results of this study showed excellent inter-reader reproducibility for quantifying intrathoracic fat volumes from contrast-enhanced CT scans using commercially available software for which we used thoracic fat tissue voxels with HU between  $-250$  and  $-50$ , as previously described (18). In the literature, various window widths, ranging from  $-250$  to  $-30$  HU (15, 23–26), have been described. Nevertheless, it should be noted that the original studies defining the CT fat range were performed using single-section CT scanners and different sec-

tion thicknesses (18, 27). Whether the fat window width will change using the newer-generation CT scanners and whether there is any significant difference in the fat volume measurements between the 2 different fat tissue CT window widths ( $-250$  to  $-50$  HU and  $-190$  to  $-30$  HU, with the latter being most recently used) are open questions for future research using a larger sample size. Typically, voxel-based fat measurements are significantly different when different CT window widths are used. They also vary with section thickness used. Our reconstructed images had 10 mm of section thickness, which follows Borkan study where fat is identified with HU between  $-250$  and  $-50$ . The section thickness described in the study where they used HU between  $-190$  and  $-30$  was 5 mm. If the CT fat window widths do not use the recommended section thicknesses, the quantitative data may be inaccurate, and their future application questionable. We correlated the 2 different fat tissue CT window widths that were assessed using the Bland–Altman analysis. Epicardial fat volume (EFV) using a CT window width of  $-190$  and  $-30$  HU was significantly greater than that using a CT window width of  $-250$  and  $-50$  HU (mean  $\pm$  STD of  $69 \pm 34$  cm<sup>3</sup> versus  $58 \pm 27$  cm<sup>3</sup>,  $P$ -value of  $<.0001$ ). There was statistically significant difference in the EFV measurements between different

fat tissue CT window width, with a mean difference of  $-6.3 \pm 4$  and correlation coefficient of  $-0.93$  ( $P$  value of  $<.0001$ ).

The results from this study have important implications in our understanding of the intrathoracic fat compartments measured using MDCT. Here, we illustrated the feasibility of quantifying the intrathoracic fat volume from MDCT scans performed as part of a chest pain workup in otherwise healthy subjects free of CVD, using commercially available software for fat volume quantification. This methodology can be used as a reference guide in future clinical and research studies for intrathoracic fat volume quantification from already obtained thoracic MDCT scans as part of standard patient care, which may enable the incorporation of these measurements into thoracic and cardiac MDCT examination reports in the future, particularly with additional technical work to make these quantifications more automated.

We failed to show any significant difference between the 3 obesity groups defined by their BMIs and any compartment of intrathoracic adiposity. Even though BMI is used as one of the anthropometric surrogate markers to predict metabolic syndrome (12), it represents general adiposity more than regional adiposity. Regional adiposity, such as epicardial, mesenteric, and omental fat distribution, shares a common origin from splanchnopleuric mesoderm associated with the gut. There is a functional difference between the subcutaneous and intrathoracic fat, as the latter shows twice as many macrophages secreting more vasoactive products, tumor necrosis factor- $\alpha$ , interleukin, vascular endothelial growth factor, adiponectin, and leptin (13). Taking into account the intrathoracic fat functional properties, it serves as a better predictor of metabolic syndrome.

Our small sample size is a limitation, as well as the postprocessing time of 15 minutes every case, thus, limiting

the methodology's applicability among the general practicing radiologists or cardiovascular imagers and its use as a screening modality in the clinical setting. Therefore, the development of completely automated software for fat volume quantification may justify its use in the clinical setting. It should be noted that in this study, we used commercially available software that comes as a package with purchasing scanners. This software is widely available for their users. Automated software is not commercially available. They are still used for in-house usage purpose. If the tool addresses clinical significance questions, vendors may invest in developing automated segmentation tool that could be commercially available for their end-users. However, multiple future questions should be addressed to assess the clinical utility. The correlation between automated intrathoracic fat volume measurements from imaging that is already ordered for another reason and easily incorporated into the report and potentially added value to the patient's management is one future question. The correlation between fat volume measurements and adipocytokines, blood lipids, or parameters of glucose homeostasis, which are useful for further assessment of the association between regional and global adiposity, is another question. Epicardial fat biology and response to cardiometabolic disease and obesity are other future questions.

In conclusion, this study stresses the importance and shows the feasibility and reproducibility of intrathoracic fat volume quantification from previously performed chest MDCT as part of standard patient care among relatively healthy individuals free of CVD, using commercially available software. The feasibility and inter-reader reproducibility reported in this study will help in future quantification of epicardial fat volume, an emerging surrogate marker for cardiometabolic risks.

Disclosures: No disclosures to report.

Conflict of Interest: None reported.

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