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Epicardial Fat Thickness and Its Association with the Angiographic Severity of Coronary Artery Disease

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Abstract

Background: One of the risk factors for atherosclerotic cardiovascular disease (ASCVD) is obesity. Several methods can be used for the estimation of Epicardial Adipose Tissue (EAT). Even though Magnetic Resonance Imaging (MRI) and CT will give excellent results , Trans Thoracic Echocardiography is an easily available and cost effective method for the assessment of epicardial fat thickness.. EAT can be accurately measured by two-dimensional (2D) echocardiography. It is found to be higher in patients with acute coronary syndrome with definite angiographic evidence of coronary artery disease than in subjects without coronary artery disease (CAD). It is an index of high cardiovascular risk than anthropometric assessments. In our study, we evaluated the relationship of EAT to the presence and severity of CAD in clinical setting.

Methods: In this cross sectional, single-centre observational study conducted in the Department of Cardiology, Govt. Kilpauk Medical College, Chennai, India, consecutive patients with Acute Coronary Syndrome were enrolled. Sensitivity, specificity, and receiver operating characteristic (ROC) curve were estimated to find cut-off value of EAT thickness for diagnosing CAD using coronary angiographic findings as gold standard.

Results: Patients were diagnosed as CAD group (n = 127) and non-CAD group (n = 23) after assessing coronary angiograms. The EAT was measured at end-diastole from the PLAX views of three cardiac cycles on the free wall of the right ventricle. Lesion was significant if > 50% in left main and > 70% in other coronary arteries. The mean EAT thickness in CAD group was5.5+/-0.7mm and in non-CAD group was4.2+/-0.3 which was significant ($P < 0.001$). There was significant correlation demonstrated between EAT thickness and presence of CAD ($P < 0.001$). Higher EAT was associated with severe CAD and presence of multivessel disease. The high values of Epicardial fat thickness were associated with higher syntax score.

Conclusion: The noninvasive measurement of Epicardial Adipose Tissue thickness by trans thoracic echocardiography is giving a strong relation with the angiographically detected coronary artery disease in comparison to those with normal coronary arteries. As the severity of coronary artery diseases increases the EAT thickness also increases. It is thicker in multivessel disease with higher syntax scores in comparison to single vessel disease with low syntax scores

Keywords: Adipose , ACS, Syntax, Epicardial, Multivessel

Introduction

Different types of adipose tissue, particularly subcutaneous and visceral adipose depots, can be quantified.[1,2] Visceral adiposity is metabolically active and is deposited around internal organs[3]. It has diabetogenic and atherogenic features (e.g., increased triglycerides, decreased high density lipoproteins), prothrombotic factors (e.g., increased fibrinogen, Factor VII, plasminogen activator inhibitor-1) and proinflammatory cytokines (e.g., interleukin-6 [IL-6] and tumour necrosis factor-a [TNF- a])[4]. Epicardial adipose tissue (EAT) is considered as visceral fat deposited around the heart, particularly around epicardial coronary vessels. Epicardial fat may directly affect the coronary arteries and myocardium through paracrine actions of locally secreted adipocytokines and other bioactive molecules, contributing to the development of coronary artery disease (CAD)[5]. It is increasingly evident that visceral adipose tissue (VAT) is an important CAD risk factor[6,7]. Recently, it was reported that EAT measured by transthoracic echocardiography was well correlated with abdominal VAT assessed by MRI and computed tomography and that echocardiographic EA thickness could be used as a reliable imaging indicator of VAT [8,9]. Epicardial fat defined as an echo-free space between the outer wall of the myocardium and the visceral layer of pericardium [10].

The highest diameter of this fat is on right ventricular free wall. Transthoracic echocardiography provides a reliable measurement of epicardial fat thickness (EFT)[3]. The subcostal four chamber and parasternal long and short axis echocardiogram views show this finding in best way[11,12]. A normal upper-limit value for EFT has not been established yet [1]. Although epicardial fat is readily visualized on high-speed CT and MRI, widespread use of these methods for its assessment is not practical. In this context, Echocardiographic assessment of EAT could be a simple and practical tool for cardiovascular risk stratification in clinical practice and research. The general objective of this study was to identify the relationship between echocardiographic epicardial fat thickness and the extent of coronary artery disease. There were some specific objectives also, i.e., to measure epicardial fat thickness by transthoracic echocardiography; to measure the severity of coronary artery disease by CAG; to establish echocardiographic epicardial fat thickness measurement as a simple, non-invasive, time efficient and reliable imaging indicator for cardiovascular risk.

Materials and Methods

This was a cross-sectional analytical study conducted in the Department of Cardiology, Govt. Kilpauk Medical College and Hospital over a period of 6 months (April, 2021to September 2021) on 150 randomly sampled patients with STEMI and NSTEMI who underwent echocardiography and CAG and who fulfilled the inclusion and exclusion criteria. To minimize the confounding effects, the following patients were excluded from the study, i.e., pericardial effusion, abnormal images on transthoracic echocardiography or poor echo window, history of coronary artery bypass graft surgery (CABG), history of percutaneous coronary intervention (PTCA), cardiomyopathy, severe comorbidities- like malignancy, chronic kidney disease, patients unwilling to given consent, moderate to severe degree of valvular heart disease, etc.

Prior to the commencement of this study, the research protocol was approved by the Research Review Committee of Department of Cardiology and the Ethical Committee of Govt. Kilpauk Medical College.

Detailed history, clinical examination and relevant investigation reports of all patients were recorded in pre-designed data collection sheet at the beginning of the study. Cardiac catheterizations and coronary angiography were performed using the Judkin's technique. All standard views were taken. In selected cases additional views were taken. CAG was analysed by visual estimation. 70% or more luminal stenosis was considered significant except in left main coronary artery lesion where 50% or more luminal stenosis was considered significant. The reporters of CAG had no prior knowledge of the echocardiographic findings. The report was defined as single vessel disease, double vessel disease and triple vessel disease as follows

1. Single-vessel disease: Presence of ≥70% diameter lumen narrowing in either the left anterior descending, left circumflex or right coronary artery or a major branch. ii) Double-vessel disease: Presence of ≥70% diameter lumen narrowing in two of the three major epicardial vessel systems. iii) Three-vessel disease: Presence of ≥70% diameter lumen narrowing in all three major epicardial vessel systems.
2. Each patient underwent transthoracic echocardiography (TTE) by AFFINITY 30(PHILIPS, USA) in the left lateral decubitus position the day of admission. EAT

thickness was measured on the free wall of right ventricle from the parasternal long-axis and short axis views. EAT was identified as the anterior echo-lucent space between the outer wall of the myocardium and the visceral layer of pericardium on the two-dimensional echocardiography and its thickness was measured in still images on the free wall of the right ventricle along the midline of the ultrasound beam with best effort to be perpendicular to the aortic annulus in parasternal long axis view, at end- diastole for 3 cardiac cycles

The average value from 3 cardiac cycles for each echocardiographic view was used for the statistical analysis. All the data were compiled duly in the data collection sheet for statistical analysis and interpretation.

Statistical Analysis

Data were entered in Microsoft Excel spread sheet. The records were explored by employing SPSS version 21.0 statistical software. Continuous parameters were expressed as mean ±SD and categorical parameters as frequency and percentage. Comparison between groups (continuous parameters) was done by unpaired t test. Categorical parameters were compared by chi- square test. Comparisons among groups (continuous parameters) was done by ANOVA test. Correlation analyses were done by Pearson corelation coefficient test. The significance of the results as determined in 95.0% confidence interval and a value of p<.05 was considered to be statistically significant.

Results

A total of 150 patients were recruited for the study of which127 had CAD on angiography and 23 had normal coronary angiogram. The baseline characteristics, CAD risk factors and Echocardiographic Epicardial Fat Thickness(EFT) were compared and presented in table and pictorial format below.

The mean age of presentation of CAD was 54.1±10.27 years and without CAD was 53.7±9.6(p value=0.829). Male patients were predominant in CAD group(74.0%) and in non CAD group females were more(65.2%).The mean epicardial fat thickness in patients with CAD was 5.5±.7 , which is thicker than the non CAD group(4.2±.3) and the p value is <.001which is significant statistically.

Dyslipidaemia, Diabetes mellitus and high body mass index (BMI) and smoking were the most common risk factors which were statistically significant in CAD group(p=.002).There were not significant difference noted in patients with hypertension(p=.320).

VARIABLES	CAD (+) (N=127)	CAD (-) (N=23)	UNPAIRED T TEST P VALUE
AGE	54.1+/-9.9	53.7+/-9.6	0.829
BMI	22.9+/-2.3	21.2+/-2.0	0.001
TOTAL CHOLESTEROL	222.6+/-41.0	183.6+/-33.7	<0.001
NON HDL CHOLESTEROL	183.7+/-43.6	141.5+/-33.0	<0.001
EPICARDIAL FAT THICKNESS	5.5+/-0.7	4.2+/-0.3	<0.001
SYNTAX SCORE	10.9+/-8.9	0.0+/-0.0	<0.001
MALE	94 (74.0%)	8 (34.8%)	<0.001*
FEMALE	33 (26.0%)	15 (65.2%)	
SMOKING	60 (47.2)	5 (21.7%)	0.023*
DIABETES	84 (66.1%)	9 (39.1%)	0.014*

HYPERTENSION	64 (50.4%)	9 (39.1%)	0.320*
DYSLIPIDEMIA	92 (72.4%)	9 (39.1%)	0.002*

Table 1: Baseline characteristics of patients(n=150)

CAD(+) → coronary artery disease,

CAD(-) → normal coronary artery,

p value <.05 statistically significant,

BMI - body mass index*CHISQUARE TEST

It was noted that a significant difference in epicardial fat thickness in males and females of comparable age groups(p=.001). In male it was 5.5±.7 and females 5.±.9

VARIABLES	MALE (N=102)	FEMALE (-) (N=48)	UNPAIRED T TEST P VALUE
EPICARDIAL FAT THICKNESS	5.5+/-0.7	5.0+/-0.9	0.001

Table 2: Comparison of EFT between males and females

There was significant correlation between epicardial fat thickness with age (r=.239,p=.003), BMI (r=.484,p=.001), total cholesterol(r=.599, p<.001), non-HDL cholesterol (r=.600,p<.001) and Syntax score (r=.817, p<.001)

VARIABLES	PEARSON R VALUE	P VALUE
AGE	0.239	0.003
BMI	0.484	<0.001
TOTAL CHOLESTEROL	0.599	<0.001
NON HDL CHOLESTEROL	0.600	<0.001
SYNTAX SCORE	0.817	<0.001

Table 3: Correlation between epicardial fat thickness and clinical and lab parameters

The epicardial fat thickness varies according to the severity of CAD ,as it was 4.2±.3 in normal(n=23), 4.3±.2 in minimal CAD(n=19), , 5.4+/-0.3 in single vessel disease (n=60), 6.1+/-0.4 in

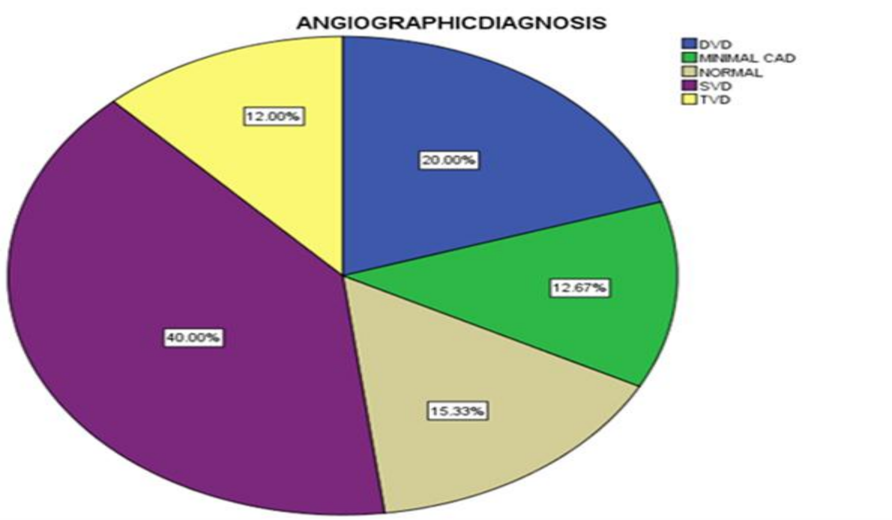

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Figure 1: diagram depicting CAD severity

INVESTIGATION	NORMAL	SVD	DVD	TVD	MINIMAL CAD	ANOVA TEST P VALUE
EPICARDIAL FAT THICKNESS	4.2+/-0.3	5.4+-0.3	6.1+/-0.4	6.3+/-0.3	4.3+/-0.2	F=192.31 P<0.001

Table 4: Epicardial Fat Thickness (EFT) and severity of CAD(CAD = Coronary Artery Disease)

The epicardial fat thickness data were arranged in quartiles and the incidence was assessed which are showed in Table 5.The range was 1ST quartile (4.0-4.5) (n=38), 2nd quartile (4.6 - 5.4) (n=45), 3rd quartile (5.5 - 6.0) (n=31) and 4th quartile (6.1 - 7.0) (n=36).This table also demonstrated the percentage of significant coronary artery disease according to the quartiles of epicardial fat thickness.

CAD were found in 42.1% of patients in first quartile, 100.0% of patients in second quartile, 96.8% of patients in 3rd quartile and 100.0% in 4th quartile. The percentage of CAD was found to increase in higher quartiles (P value< .001)

EPICARDIAL FAT THICKNESS QUARTILES	CAD				Chi -square test P value
	PRESENT		ABSENT		
	N	%	N	%	
1ST quartile (4.0-4.5) (n=38)	16	42.1%	22	57.9%	<0.001
2nd quartile (4.6 - 5.4) (n=45)	45	100.0%	0	0.0%	
3rd quartile (5.5 - 6.0) (n=31)	30	96.8%	1	3.2%	
4th quartile (6.1 - 7.0) (n=36)	36	100.0%	0	0.0%	

Table 5: Incidence of coronary artery disease according to the quartiles of EFT(N=150)

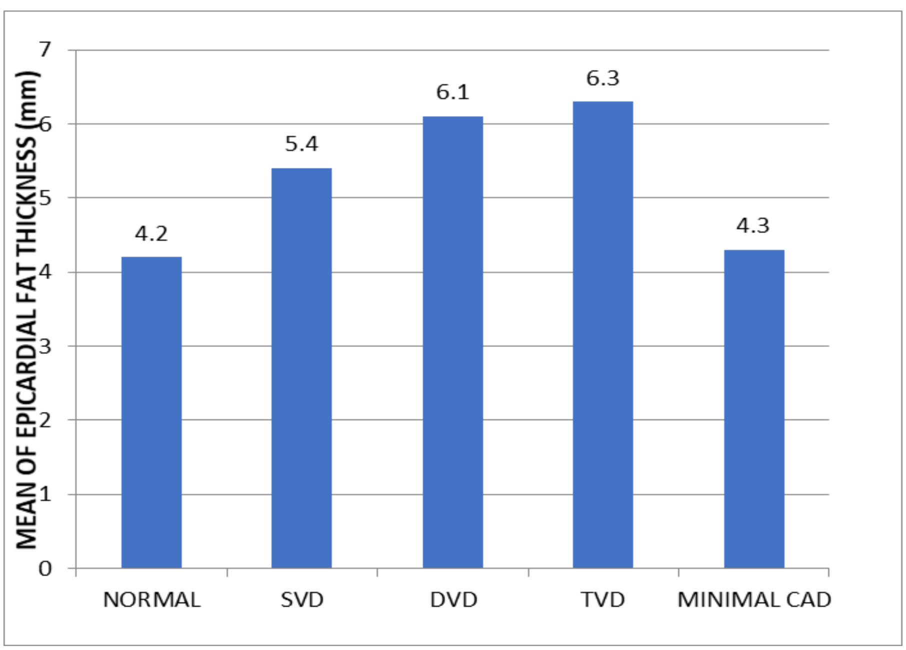

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Figure 2: Epicardial Fat Thickness (EFT) and severity of angiographic coronary artery disease(CAD)

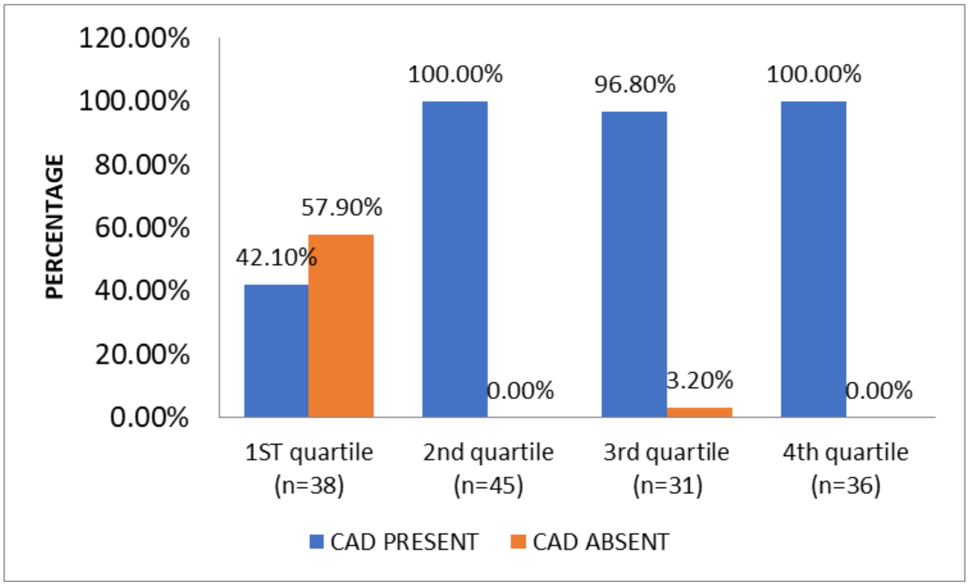

Figure 3: Bar diagram showing the incidence of coronary artery disease(CAD) according to the quartiles of echocardiographic Epicardial Fat Thickness(EFT)

Nonparametric Tests

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of AGE is the same across categories of CAD	Independent samples Mann Whitney U test	0.946	Reject the null hypothesis
2	The distribution of BMI is the same across categories of CAD	Independent samples Mann Whitney U test	0.000	Reject the null hypothesis
3	The distribution of Total Cholesterol is the same across categories of CAD	Independent samples Mann Whitney U test	0.000	Reject the null hypothesis
4	The distribution of Non-HDL Cholesterol is the same across categories of CAD	Independent samples Mann Whitney U test	0.000	Reject the null hypothesis
5	The distribution of Epicardial Thickness is the same across categories of CAD	Independent samples Mann Whitney U test	0.000	Reject the null hypothesis
6	The distribution of Syntax Scores is the same across categories of CAD	Independent samples Mann Whitney U test	0.000	Reject the null hypothesis

Table 6: Asymptomatic Significances as displayed. The significance level is 0.05

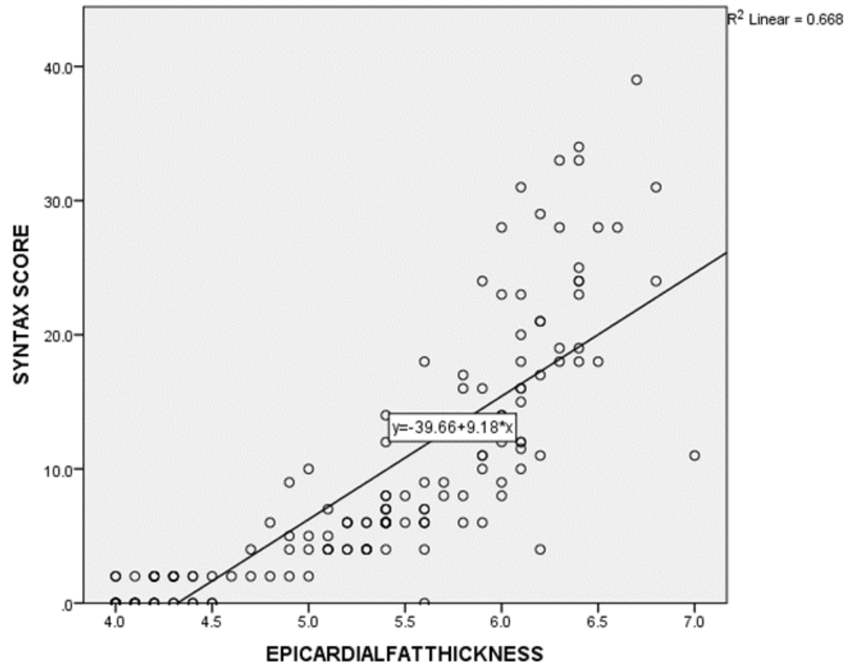

Figure 4 The positive association between the epicardial fat thickness and coronary artery severity by Syntax score is depicted in the scatter plot.

Discussion

The cross sectional, analytical study was conducted on 150 patients with acute coronary syndrome who were admitted to Govt. Kilpauk Medical College Chennai and underwent coronary angiogram. After matching the inclusion criteria 150 patients were recruited for evaluation. Trans-thoracic Echocardiographic measurement of epicardial fat thickness was done accordingly after admission. Based on coronary angiogram- patients had coronary artery disease and -patients had normal coronary angiogram.

In our study, mean epicardial fat thickness was found to be 5.6mm. Epicardial thickness may differ from race to race. As per the study by Lacobellis et. al. in USA, median values of epicardial fat thickness was 9.5 mm in men and 7.5 mm in women. Mean epicardial fat thickness was found 6.1 mm in a study by Sadea et. al. on European population. Another study by Jeong et. Al. found mean epicardial fat thickness of 6.3 mm. In our study the EFT in CAD group was significantly higher than normal group (5.6mm+/-.5mm vs4.1+/-.2 mm, p=.0001).it is in consensus with the study conducted by Shimirani et. al. who found significantly higher the EFT in CAD group than in normal group (5.4+/-1.9mm vs 4.4+/-1.8 mm, p=.0001).

EAT thickness had some definite relationship with some clinical and biochemical parameters. Our study showed a correlation between EFT and age (P=.04), Body Mass Index(P=.01), non-HDL cholesterol (P =.036). Other studies like Ahn et. al. showed the same findings. Shemirani et. al. found that EFT had a positive correlation with LDL, BMI(P=.001), serum triglyceride(p=.04) which correlate with our study. Jeong et. al. showed a significant correlation between EAT and age (r=.332, p<0.001), BMI(r=0.142, p=.044).

In our study, significant CAD was found in25.33% patients in first quartile (EFT=4-4.5 mm),30%patients in 2nd quartile (EFT=4.6-5.4mm), 20.67%patients in 3rd quartile (EFT=5.5-6mm) and 24%patinets in 4th quartile of EAT thickness (EFT=6.1-7mm). The increasing percentage of CAD in higher quartile was significant(p=.036) .The above findings were consistent with those of some previous studies, which also showed that EAT was significantly thicker in subjects with CAD than those without CAD.

EAT thickness revealed significant variation among patients with normal/minimal CAD, single vessel disease, double vessel disease and triple vessel disease. The thickness was 4-4.5mm in normal or minimal CAD (28% patients),4.6-5.4mm in single vessel disease (40% patients). 5.5-6mm in double vessel CAD (20% patients) and 6.-7mm in patients with triple vessel (12% patients). The increasing thickness of EAT is also correlating with the Syntax score also. As the increased thickness was associated with higher syntax scores.

Our study strongly supports that there is association between EAT thickness and the presence and severity of angiographically detected CAD. The pathophysiological mechanisms associated with this relationship is Epicardial Adipose Tissue is a component of visceral adiposity and is linked to cardiovascular risk factors.2.EAT has endocrine and paracrine functions. It secretes so many bioactive molecules(adipokines)such as adiponectin, resisitin and inflammatory cytokines, like interleukin 1b(IL 1b), IL6, Tumour Necrosis Factor alpha etc. The genesis of atherogenesis is related with the above mentioned paracrine and vasocrine signaling effects as pointed out by Sacks et al.

Conclusion

The noninvasive measurement of Epicardial Adipose Tissue thickness by trans thoracic echocardiography is giving a strong relation with the angiographically detected coronary artery disease in comparison to those with normal coronary arteries. As the severity of coronary artery diseases increases the EAT thickness also increases. It is thicker in multivessel disease with higher syntax scores in comparison to single vessel disease with low syntax scores.

Limitations of the Study: The study included only those patients preselected to undergo coronary angiogram i.e. patients with Acute Coronary Syndrome. Epicardial Adipose Tissue has a three-dimensional distribution so the two-dimensional echocardiography may not assess the total volume of epicardial adiposity completely. It can be measured as a mean of values from parasternal long axis and short axis views. In our study, the average values from both parasternal long and short axis views were used. A large, prospective cohort study might be required to elucidate the clinical significance of Epicardial Adipose Tissue (EAT) thickness in general population.

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