Original Article

Correlation between Echocardiographic Epicardial Fat Thickness and Angiographic Severity of Coronary Artery Disease

Shahid Mohammad Omar Faroque[1], Abdul Wadud Chowdhury[2], Mohsin Ahmed[3], Khandker Md. Nurus Sabah[4], Mohammad Khalilur Rahman Siddiqui[5], Chowdhury Md. Kudrat-E-Khuda[6], Pranob Karmaker[7]

Abstract:

Background: Epicardial adipose tissue (EAT) is a visceral adipose tissue surrounding the heart and the coronary arteries. Because of its endocrine and paracrine activity, secreting pro-inflammatory and anti-inflammatory cytokines and chemokines, it has been suggested to influence coronary atherosclerosis development. Objectives: To identify the relationship between echocardiographic epicardial fat thickness and the extent of coronary artery disease (CAD). Methods: Considering the inclusion and exclusion criteria, a total 87 patients with established or suspected coronary artery disease admitted for coronary angiogram were included in this study. After taking written consent, initial evaluation of the patients was done by history, clinical examination and relevant investigation. Variables, risk factors for CAD and investigation reports were recorded in data sheet. Echocardiography and coronary angiography were done. EAT thickness measurements by echocardiography were compared with coronary angiographic findings. Results: Echocardiographic EAT thickness was significantly higher in patients with CAD in comparison to those with normal coronary arteries 7.14±1.81 mm vs 4.08±1.06mm (p <0.001). Furthermore, EAT thickness increase with the severity of CAD. EAT is 4.08±1.06 mm in patients with normal/non-significant CAD (n=20), 5.75±0.96 mm in single vessel CAD (n=24), 6.54±1.09 mm in double vessel CAD (n=16) and 8.75±1.45 mm in patients with triple vessel CAD (n=27). Conclusions:EAT thickness was significantly higher in patients with angiographically detected CAD in comparison to those with normal coronary arteries. Furthermore, EAT thickness increased with the severity of CAD; i.e. it was thicker in multivessel coronary artery disease than in single vessel or non-significant coronary artery disease.

Key words: Coronary Artery Disease, Echocardiography, Adipose Tissue, Angiography.

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Introduction

Different types of adipose tissue, particularly subcutaneous and visceral adipose depots, are now recognized as having distinct quantitative characteristics.[1,2] Visceral adiposity is a fat deposition around internal organs. It is metabolically active.[3] It is strongly correlated with diabetogenic features (e.g., impaired insulin sensitivity, increased insulin levels),

1. Medical Officer, Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh.
2. Professor and Head, Department of Cardiology, Dhaka Medical College (DMC), Dhaka, Bangladesh.
3. Associate Professor, Department of Cardiology, Dhaka Medical College (DMC), Dhaka, Bangladesh.
4. Assistant Professor, Department of Cardiology, Dhaka Medical College (DMC), Dhaka, Bangladesh..
5. Junior Consultant, Cardiology, Comilla Medical College, Comilla.
6. Junior Consultant, Cardiology, Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh.
7. Junior Consultant, Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh.

Address of Correspondence: Dr. Shahid Mohammad Omar Faroque, Medical Officer, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh. Mobile: +8801712828552, E-mail: dromar.faroque@gmail.com

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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 tumor 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 EATmeasured by transthoracic echocardiography was well correlated with abdominal VAT assessed by MRI and computed tomography and that echocardiographic EAT thicknesscould 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.[13]

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 echocardiographicepicardial fat thicknessmeasurement as a simple, non-invasive, time efficient and reliable imaging indicator for cardiovascular risk

Methods:

This was a cross-sectional analytical study conducted in the Department of Cardiology, Dhaka Medical College&Hospital over a period of one year (July, 2015 to June 2016) on 87 purposively sampled patients with myocardial infarction, unstable angina and stable angina 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 DMCH, Dhaka. 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 was performed using the Judkin's technique. All standard views were taken. In selected cases additional views were taken. CAG was analyzed 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- i) 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. Each patient underwent transthoracic echocardiography (TTE) by Vivid 7 (GE, USA) in the left lateral decubitus position the next day after CAG. EAT thickness was measured on the free wall of right ventricle from the parasternal long-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. The offline measurement of EAT thickness was performed by two cardiologists, expert in echocardiography who would be unaware of the clinical and angiographic findings.All the data were compiled duly in the data collection sheet for statistical analysis and interpretation.

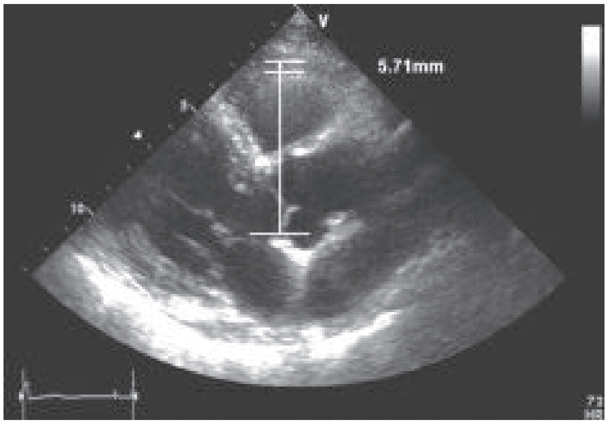

Fig-1: Example of measurement of epicardial fat thickness (EAT). Epicardial fat was identified as an echo-free space in the pericardial layers on the 2-dimensional echocardiography and its thickness was measured perpendicularly on the free wall of the right ventricle at end-diastole.

Statistical analysis was conducted using SPSS 22software on Windows 7. 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-squared test. Comparisons among groups (continuous parameters) was done by ANOVA test.Correlation analyses were done by Pearson correlation coefficient test. The significance of the results as determined in 95.0% confidence interval and a value of $p < 0.05$ was consider to be statistically significant.

Results:

A total 87 patients were selected for the study of which 67 had CAD and 20 had normal coronary angiogram. Baseline characteristics, risk factors for CAD and echocardiographic EAT thickness were compared and presented in different tables and figures below.

Table-I shows that patients with CAD were older. Mean age was 53.25±10.27 years in patients with CAD and 46.80±8.25 years in patients without CAD (p=0.012). Male (77.6%) was predominant in patients with coronary artery disease, but in patients without coronary artery disease, female (65.0%) was found as predominant gender. The mean EAT thickness of the patients was 6.44±2.11 mm (range 2.20-11.0 mm). It was significantly thicker in patients with CAD (7.14±1.81mm) than those without CAD (4.08±1.06mm) (p=<0.001).

Diabetes mellitus anddyslipidemia were more common in patients with significant coronary artery disease ($p<0.05$). There was no significant inter group difference on smoking, hypertension and BMI ($p>0.05$). Waist circumference were statistically significant in patients with CAD (p =0.009).

Table II shows the distribution of EAT between male and female patients, mean EAT was 6.81±1.94 in male and

Table-I

Baseline characteristics of patients (n=87)

Characteristics	CAD (-) (n=20)		CAD (+) (n=67)		P value
Age (years)	46.80±8.25		53.25±10.27		^{a}0.012^{s}
Body mass index (kg/m^{2})	23.68±1.95		24.74±3.23		^{a}0.170^{ns}
Waist circumference (cm)	85.25±7.41		90.75±8.29		^{a}0.009^{s}
Epicardial adipose tissue (mm)	4.08±1.06		7.14±1.81		^{a}<0.001^{s}
Sex	n	%	N	%	
Male	9	45.0	52	77.6	^{b}0.005^{s}
Female	11	65.0	15	22.4	
Smoking	6	30.0	35	52.2	^{b}0.080^{ns}
Hypertension	7	35.0	37	55.2	^{b}0.112^{ns}
Diabetes mellitus	4	20.0	31	46.3	^{b}0.036^{s}
Dyslipidaemia	10	50.0	57	85.1	^{b}0.001^{s}

CAD (-)= normal coronary artery. CAD (+) = coronary artery disease, s = significant, ns=not significant, ^{a} = p value reached from unpaired 't' test. ^{b}= p value reached from chi-square test

Table-II

Comparison of EAT between male and female patients (n=87)

Gender	Male (n=61) Mean±SD	Female (n=26) Mean±SD	P value
EAT	6.81±1.94	5.58±2.27	0.012^{s}

EAT = epicardial adipose tissue,p value reached from unpaired t-test, s= significant

5.58±2.27 in female patients. There is statistical significant difference between male and female patients (p=0.012).

Table III shows a significant positive correlation between epicardial adipose tissue (EAT) thickness and Age (r=0.373, p<0.001), BMI (r=0.275, p=0.01), waist circumference (r=0.471, p<0.001), TC (r=0.272, p=0.011), TG (r=0.305, p=0.004) and LDL (r=0.271, p=0.011) and negative correlation with HDL (r=-0.298, p=0.005).

The data of echocardiographic EAT thickness were arranged in quartiles and the incidence of CAD was assessed which are showed in Table-IV. The range of thickness was 2.20-5.00mm (n=20) in 1st quartile, 5.01-6.00mm (n=23) in 2nd quartile, 6.01-8.00mm (n=23) in 3rd quartile and 8.01-11.0mm (n=21) in 4th quartile. Table IV shows the percentage of significant coronary artery disease according to the quartiles of echocardiographicEAT thickness. CAD were found in 12(60.0%) patients in 1st quartile, 16(69.6%) patients in 2nd quartile, 19(82.6%) patients in 3rd quartile and 20(95.2%) patients in 4th quartile. The increasing percentage of CAD in the quartiles was significant (p <0.05).

Table-V shows that EAT thickness is 4.08±1.06 mm in patients with normal/non-significant CAD (n=20), 5.75±0.96 mm in single vessel CAD (n=24), 6.54±1.09 mm in double vessel CAD (n=16) and 8.75±1.45 mm in patients with triple vessel CAD (n=27). The increasing thickness of EAT in more severe form of coronary artery disease was significant (p<0.001).

Table – III

Correlation between epicardial adipose tissue (EAT) thickness and clinical and laboratory parameters

	r	p-value
Age	0.373	<0.001^s
BMI	0.275	0.010^s
Waist circumference	0.471	<0.001^s
TC	0.272	0.011^s
Triglyceride	0.305	0.004^s
HDL-C	-0.298	0.005^s
LDL-C	0.271	0.011^s

r =Pearson‘s correlation co-efficient, s= significant (p< 0.05).

Table –IV

Incidence of coronary artery disease according to the quartiles of epicardial adipose tissue (EAT) thickness (n=87)

Quartiles	CAD (+) (n=67)		CAD (-) (n=20)		P-value
	n	%	n	%	^{a}0.039^s
1st quartile (2.20-5.00) (n=20)	12	60.0	8	40.0	
2nd quartile (5.01-6.00) (n=23)	16	69.6	7	30.4	
3rd quartile (6.01-8.00) (n=23)	19	82.6	4	17.4	
4th quartile (8.01-11.0) (n=21)	20	95.2	1	4.8	

s=significant (p<0.05), a=p-value reached from chi-square test, 1st quartile=Below Q_1, 2nd quartile=Q_1 to below Q_2, 3rd quartile=Q_2 to below Q_3, 4th quartile = Q_3 and above, CAD (-) =normal coronary artery, CAD (+) =coronary artery disease

Table-V

Epicardial adipose tissue (EAT) thickness and severity of coronary artery disease (CAD)

Investigation	Normal/non-significant CAD (n=20) Mean±SD	Single vessel CAD (n=24) Mean±SD	Double vessel CAD (n=16) Mean±SD	Triple vessel CAD (n=27) Mean±SD	p-value
EAT thickness (mm)	4.08±1.06	5.75±0.96	6.54±1.09	8.75±1.45	^{a}<0.001^s

EAT= epicardial adipose tissue, CAD=coronary artery disease, a= p value reached from ‘one way ANOVA’ (F=64.04), s= significant (p<0.05)

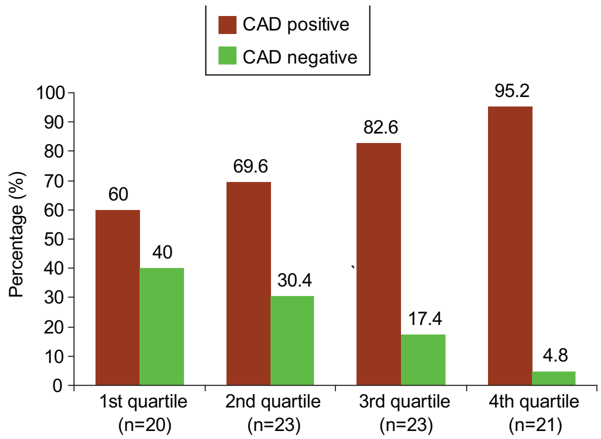

Fig-2: *Bar diagram showing the Incidence of coronary artery disease (CAD) according to the quartiles of echocardiographic epicardial adipose tissue thickness (EAT). (Q= Quartile)*

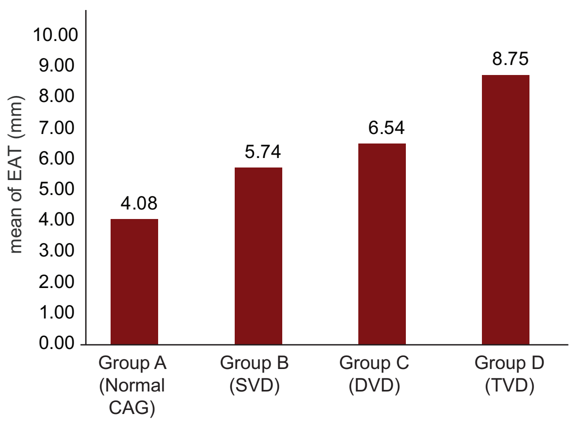

Fig-3: *Epicardial adipose tissue (EAT) thickness and severity of angiographic coronary artery disease (CAD).*

Discussion:

This cross sectional, analytical study was conducted on 87 patients with established or suspected coronary artery disease who were admitted to Department of Cardiology of Dhaka Medical College &Hospital, Dhaka and underwent coronary angiogram. After exclusion, a total 87 patients were included. Echocardiographic measurement of epicardial adipose tissue (EAT) thickness was done accordingly after admission. Based on coronary angiogram, 67 patients had coronary artery disease (CAD) and 20 patients had normal coronary angiogram.

In this study, mean EAT thickness was found 6.44±2.11 mm. EAT thickness may be different according to the race. In a study in USA, conducted by Iacobellis et al.[13] median values of EAT thickness was 9.5 mm in men and 7.5 mm in women. Mean EAT thickness was found 6.1 mm in a study conducted by Sadeaet al.[14] on European population. Mean EAT thickness was found 6.3 mm in a study conducted by jeong et al [15]. In this study the EFT in CAD group was significantly higher than in normal group (7.14±1.81 mm vs 4.08±1.06 mm, p<0.001). These findingsare consistent with study of Shimiraniet al[3] who found significantly higher the EFT in CAD group than in normal group (5.4±1.9 mm vs 4.4±1.8mm, p=0.0001).We found EATto be thicker in men than in women (6.81±1.94 mm vs 5.58±2.27 mm; p =0.012), which was consistent with the study of Sadea et al.[14]whereEAT was also found significantly thicker in men than in women (6.5± 1.6mm vs 5.5± 1.8mm; P<0.001). But, Ahn et al[16]. did not find any difference of EAT thickness between men and women.

EAT thickness showed definite relationship with some clinical and biochemical parameters. In this study, shows a significant positive correlation between EAT thickness and age (r=0.373, p<0.001), BMI (r=0.275, p=0.01), waist circumference (r=0.471, p<0.001), TC (r=0.272, p=0.011), TG (r=0.305, p=0.004) and LDL (r=0.271, p=0.011) and inversely correlated with HDL-C (r=-0.298, p=0.005). Ahnet al[16]. revealed similar findings in their study.Shemiraniet al.[3]found that EFT had a positive correlation with LDL, BMI (p=0.001), serum triglyceride (p=0.04) and WC (p=0.04), which correlate with this study.Jeonget al[15]. stated a significant correlation was revealed between EAT and age (r=0.332, p<0.001), body mass index (r=0.142, p=0.044) and waist circumference (r=0.229, p=0.001).

In this study, significant CAD was found in 60% patients in 1st quartile, 69.6% patients in 2nd quartile, 82.6% patients in 3rd quartile and 95.2% patients in 4th quartile of EAT thickness. The increasing percentage of CAD in higher quartiles was significant (p<0.039). This finding was consistent with those of some previous studies, which also showed that EAT was significantly thicker in subjects with CAD than those without CAD.[14,15]

EAT thickness showed significant variation among patients with normal/non-significant CAD, single vessel CAD, double and triple vessel CAD. The thickness was 4.08±1.06 mm in patients with normal/non-significant CAD (n=20), 5.75±0.96 mm in single vessel CAD (n=24), 6.54±1.09 mm in double vessel CAD (n=16) and 8.75±1.45 mm in patients with triple vessel CAD (n=27) in this study. This increasing thickness of EAT in more severe form of coronary artery disease was statistically significant (p <0.001). This finding of correlation between EAT thickness and the severity of CAD was compatible with that of previous two studies.[14,15]

Data of this study strongly support that there is association between EAT thickness and the presence and severity of angiographically detected CAD. Two potential mechanisms for this association have been proposed: First, EAT is a component of visceral adiposity and is related to cardiovascular risk factors[13] ; secondly, EAT has paracrine and endocrine functions. It can secrete numerous bioactive molecules (adipokines) such as adiponectin, resistin and inflammatory cytokines, like- interleukin (IL) - 1b, IL-6, tumor necrosis factor- alpha etc[17]. Sacks et al. pointed out the paracrine and vasocrine signaling effects of epicardial adipokines for the development of atherogenesis. It is evident that EAT thickness is part of active adipose tissue that mediates coronary circulation via secretion of inflammatory mediators and adipokines.[18]

Conclusion:

Epicardial adipose tissue (EAT) thickness, which can easily be and non-invasively evaluated by transthoracic echocardiography, is significantly higher in patients with angiographically detected coronary artery disease in comparison to those with normal coronary arteries. Furthermore, EAT thickness increases with the severity of coronary artery disease; i.e it is thicker in multivessel coronary artery disease than in single vessel or non-significant coronary artery disease.

Study limitations

There may be selection bias because this study included only those patients pre-selected to undergo coronary angiography.As epicardial adipose tissue has a three-dimensional (3D) distribution, two dimensional (2D) echocardiography may not assess the total amount of epicardial adiposity completely. Epicardial adipose tissue thickness can be measured as a mean of values from parasternal long axis and short axis views.In this study, the value measured from the parasternal long axis view was used. A large, prospective, cohort study might be necessary to elucidate the clinical significance of epicardial adipose tissue (EAT) thickness in the general population.

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