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A Study of Epicardial Adipose Tissue Thickness by Echocardiography as A Risk Marker for Risk Stratification in Patients with Stable Angina Pectoris and Correlation with Lipid Profile, Waist Circumference and Lesion Severity by Coronary Angiography

Ramesh Kumar[1], Himanshu Mahla[2], Akshay Shekhawat[3], Laxmi[4], Anoop Jain[5], Deepak Maheshwari[6], V.V. Agrawal[7]

[1]Senior Resident, Department of Cardiology, SMS Medical College, Jaipur, India.
[2]Associate Professor, Department of Cardiology, SMS Medical College, Jaipur, India.
[3]Senior Resident, Department of Cardiology, SMS Medical College, Jaipur, India.
[4]Senior Resident, Department of Anesthesiology, SMS Medical College, Jaipur, India.
[5]Senior Professor, Department of Cardiology, SMS Medical College, Jaipur, India.
[6]Senior Professor, Department of Cardiology, SMS Medical College, Jaipur, India.
[7]Senior Professor & HOD, Department of Cardiology, SMS Medical College, Jaipur, India.

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Abstract

Background: Worldwide coronary artery disease is the leading cause of death and reduction in Disability Adjusted Life Years. Only a few studies of the association of epicardial adipose tissue (EAT) with the complexity of CAD have been there, therefore, this study was planned to calculate the anterior EAT thickness by 2D echocardiography, and to determine the severity of coronary lesion by syntax score (SS) on coronary angiogram. **Methodology:** This hospital-based observational study was carried out with total 100 patients with a diagnosis of CSAP got admitted in the department from August 2022 to July 2023 at a tertiary care facility. Patients of >18 years of age, who gave informed consent, diagnosed with CSAP undergoing coronary angiography were included in our study. The concentrations of triglycerides (TGs), total cholesterol, HDL, VLDL was measured, and LDL was lab tested, and the Syntax score was calculated. Data analysis was done using SPSS version 23.0. **Results:** In our study, the mean age of patients was 54.34±14.87 years, with male to female ratio was 3.5:1. Dyslipidemia was the most common risk factor. High syntax score was seen in 42 cases, followed by intermediate in 31 and low score in 27 cases. Mean EAT score was more in cases with higher syntax score and this score was statistically significant ($p<0.05$). Patients with abnormal waist circumference have significantly higher syntax score ($p<0.05$). Cutoff of EAT was 6.15 using ROC, and for this cutoff sensitivity and specificity was 87.5% and 100% respectively. **Conclusion:** When comparing patients with an SS of ≥33 to those with an SS of <33, the EAT thickness in the former group was considerably larger. The 6.15 mm EAT threshold value was found to be predictive of severe CAD. A noteworthy association was seen between EAT and both WC and lipid profile.

Keywords: **C**oronary artery disease (CAD), Dyslipidemia, Epicardial adipose tissue (EAT), Syntax score, Waist circumference.

Corresponding Author: Dr. Laxmi, Senior Resident, Department of Anesthesiology, SMS Medical College, Jaipur, India.
Email: laxmibishnoi129@gmail.com

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Introduction

Worldwide coronary artery disease (CAD) is the leading cause of death and reduction in Disability Adjusted Life Years (DALYs).[1] According to the 2019 Global Disease Burden Study, India accounts for highest global burden of the disease after China, 27% of all fatalities worldwide and has 71.13 million cases of cardiovascular disease.[2] A crucial prerequisite for lowering CAD is to identifying people with subclinical disease who are at risk of having a coronary event and for whom early intervention can be beneficial. Therefore, the creation of straightforward yet efficient techniques is necessary for precise risk stratification of those in need of primary CAD prevention. There are so many established cardiovascular risk markers based on confirmed clinical outcomes related to biomolecules, its structure, and functions. Visceral adiposity is one such marker that is linked to higher CAD risk.[3] Body mass index (BMI), which is calculated by dividing weight by height squared, and Waist circumference (WC) can roughly predict level of visceral adiposity. Alternatively, one can use CT imaging to measure the cross-sectional area of visceral fat, which is a reliable and accurate substitute for measuring visceral fat volume. Ultrasound and CT are qualitative, and MRI is costly and has availability issues. The epicardial adipose tissue (EAT) is the visceral fat that deposits between the visceral pericardium and the myocardium and has direct contact with the myocardium and coronary artery.[4] Many proatherogenic and proinflammatory hormones and cytokines are secreted by EAT, and these substances may trigger the endocrine and paracrine processes that lead to the development and progression of coronary artery disease.[5] The assessment of EAT is mostly conducted using three non-invasive imaging modalities. To quantify the two-dimensional thickness of EAT, echocardiography is the first method utilised to evaluate EAT. This method is affordable, easily accessible, reasonably precise, and repeatable. Three-dimensional estimated energy expenditure (EAT) is possible with cardiac magnetic resonance imaging (CMR) and cardiac computed tomography (CCT).[6] On echocardiography, PLAX or PSAX view (mid-ventricular level) is the best view to visualize and quantify epicardial fat.[7] EAT is seen as an echo free space above the right ventricular free wall and measured the thickness from the anterior aspect of the right ventricular free wall through parasternal long and short axis windows.[8] The available evidence suggests that on echocardiography, EAT>7 mm indicates excess epicardial fat deposition.[9] Although the relationship between EAT and the severity and extent of CAD has been extensively investigated, only a few studies of the association of EAT with the complexity of CAD have been there. Therefore, this study was planned to calculate the anterior EAT thickness by 2D echocardiography, to determine the severity of coronary lesion by syntax score (SS) on coronary angiogram, and to correlate these findings.

Materials and Methods

This hospital-based observational study was carried out in a tertiary care facility at Jaipur under the Department of Cardiology. Total 100 patients with a diagnosis of CSAP got admitted in the department from August 2022 to July 2023 was enrolled in our study, after the approval from the Ethical Committee of the institute (Ref.No. 745 MC/EC/2023). Patients of >18 years of age, who gave informed consent, diagnosed with CSAP undergoing coronary angiography were included in our study. Patients with ACS, having history of prior coronary intervention-PCI or CABG, previous chest irradiation, having chest deformities, poor echo window, pericardial effusion, pregnant, and having CKD (eGFR<30 ml/min/1.73 m^2) were excluded from the study.

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Operational Definitions

Diagnosis of CSAP is done in patient with angina pectoris who does not have feature suggestive of unstable angina or acute MI (Angina that is prolonged, occurs at rest or occurs in accelerating pattern of increasing frequency and tempo).

Hypertension was considered having blood pressure ≥140/90 mmHg or current using antihypertensive drugs.

Type 2 diabetes mellitus was defined as fasting blood glucose level ≥126 mg/dL or HbA1C of ≥6.5 or the use of glucose-lowering drugs.

The WHO STEPS protocol was used for measuring WC.[10]

The concentrations of triglycerides (TGs), total cholesterol, HDL, VLDL was measured, and LDL was calculated using the Friedewald formula. And blood sample for the same was obtained after a 12- to 14-h fast to reduce the influence of circadian variation.

Some of the patients, when indicated, undergone exercise in the Treadmill according to the Bruce Protocol, using the graded multistage treadmill test. We continued exercise for three minutes at each treadmill stage. Metabolic equivalent (METS) was used to express the estimated workload. One METS is equivalent to 3.5ml O2 / Kg/min of body weight. Exercise testing was stopped if exertional hypotension, malignant ventricular arrhythmias, marked ST segment depression more than 3 mm, ST elevation more or equal to 1 mm in non-infarct leads without diagnostic Q waves (other than V1 or avR) and limiting chest pain develops. The positive exercise ECG was determined by ≥to 1 mm of horizontal or down sloping ST segment depression at 80 msec after the end of the QRS complex (from J point) in three consecutive beats. Exercise tests was interpreted as negative only if the patient achieve 85% of the predicted maximal heart rate at peak exercise (target heart rate) in the absence of significant ST changes. The tests was termed undetermined if any of the following occurred – (a) The patient failed to achieve target rate in the absence of significant ST segment change. (b) The patient has resting ECG abnormalities such as bundle branch block, precluding evaluation of ST segment at maximal stress. (c) Multiple premature beats or unstable base line activity at maximal heart rate obscured possible ST segment changes.

Coronary angiography was performed, and standard projections were taken.

The Syntax score was calculated in every patient and patients were divided into three groups based on SS, i.e. score up to 22 as low, between 23 and 32 as intermediate, and ≥33 as high SS.

Statistical Analysis

Data was entered into Microsoft excel spreadsheet. Discrete data was summarized in the form of proportions. And continuous data was presented in the form of mean and standard deviation, and difference in mean between two subgroups was analyzed using student’s t test and between three subgroups was analyzed using One Way ANOVA test. Receiver Operating Curve (ROC) curve was prepared to determine the cutoff for diagnostic value. Significance was kept at 95% level for all data analysis.

Results

In our study, the mean age of patients was 54.34±14.87 years, with male to female ratio was 3.5:1. [Table I] depicts that dyslipidemia was the most common risk factor, followed by hypertension and positive family history of CAD was seen in eight cases. High syntax score was seen in 42 cases, followed by intermediate in 31 and low score in 27 cases. [Table II] reported that with mean EAT score was more in cases with higher syntax score and this score was statistically significant ($p<0.05$). Patients with abnormal waist circumference have significantly higher syntax score ($p<0.05$). [Table IV] reported the difference in variable between cases lying in different categories as per their syntax score. There was significant

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difference in lipid profile of cases with different syntax score. [Table V] depicting that EAT has significant positive correlation with WC, TC, LDL, VLDL, and TG (p<0.05). and negative significant correlation with HDL (p<0.05). [Figure I] reported ROC curve for diagnostic value of EAT to diagnose significant CAD. Area under curve for the graph was 0.942 (95% Confidence Interval, 0.894-0.989), cutoff of EAT was 6.15, and for this cutoff sensitivity and specificity was 87.5% and 100% respectively.

Table I: Baseline characteristics of the population

Baseline descriptive variables	**Number (%)**
Male	78
Female	22
Age (Mean±SD)	54.34±14.87
Risk factors for CAD	
Hypertension	41
Smoking	38
Diabetes	38
Dyslipidaemia	62
Positive family history of CAD	8
Syntax score on CAG	
Low	27
Intermediate	31
High	42

Table II: Epicardial adipose tissue thickness among the groups categorized based on syntax score

Syntax Score	**n**	**EAT**	**p value**
Low	27	5.82±0.28	<0.001
Intermediate	31	6.12±0.18	
High	42	9.7±0.32	

Table III: Epicardial adipose tissue in patients with normal and abnormal waist circumference

WC	**n**	**EAT**	**p value**
Normal	66	6.32±1.12	<0.001
Abnormal	34	9.82±0.42	

Table IV: Lipid profile of the patients according to the syntax score

Variable	**Synatx Score**			**p Value**
	≤22 (n=27)	**23-32 (n=31)**	**≥33 (n=42)**	
Mean age (years)	54.48±6.78	55.88±9.58	57.43±8.57	0.364
Males	24	24	30	
Females	3	7	12	0.232
Epicardial fat thickness (mm)	5.84±0.24	5.98±1.32	10.21±0.32	<0.001
WC (cm)	78.68±5.34	82.78±7.23	89.65±6.75	<0.001
TC (mg/dl)	131.67±17.32	146.84±18.32	189.78±17.45	<0.001
LDL cholesterol (mg/dl)	92.32±10.83	97.98±16.12	116.86±11.72	<0.001
VLDL cholesterol (mg/dl)	16.4±4.7	22.98±7.56	27.42±13.23	<0.001
TGs (mg/dl)	93.32±9.9	98.86±17.09	138.32±18.09	<0.001
HDL cholesterol (mg/dl)	49.82±5.2	44.12±5.94	34.62±5.32	<0.001

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Table V: Correlation of epicardial adipose tissue with anthropometric and biochemical parameters

Variable	Correlation coefficient	p value
WC	0.813	<0.001
TC	0.894	<0.001
LDL	0.816	<0.001
VLDL	0.783	<0.001
TG	0.908	<0.001
HDL	-0.732	<0.001

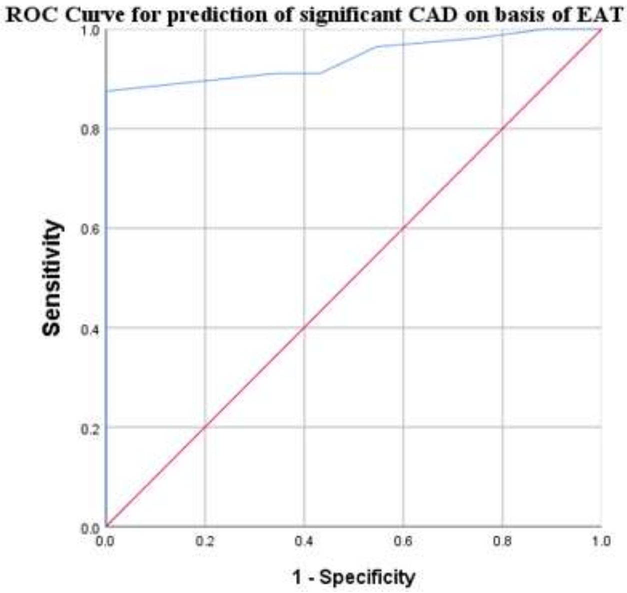

Figure I: Receiver Operating Curve for EAT

Discussion

This study was done to calculate the anterior EAT thickness by 2D echocardiography, to determine association with syntax score (SS) on coronary angiogram.

We observed significant difference in mean EAT among strata of waist circumference, this establishes strong association between both of them, which was also established by various studies.[11,12] Framingham heart study supported that pericardial adiposity increased the risk of coronary artery disease. In our study, patients who have high syntax score had higher EAT thickness compared to patients with low and intermediate syntax score and this association was significant. Similar findings were reported by Tao Wang *et al.*[13], they reported an association of echocardiographically determined EAT thickness with Syntax score in patients. The high-scoring group (Syntax score, ≥33) had a mean EAT thickness that was higher than that of their lower-score group (Syntax score, <33): P <0.01). The correlation between EFT and the complexity of CAD may be explained by the atherogenic impact of several mediators released by the adipose tissue surrounding the heart. Atherosclerosis, inflammatory mediators derived from epicardial fat tissue, and changes in the content and evolution of atherosclerotic plaques are all possible outcomes.[14] In individuals without diabetes, Gökdeniz *et al.*[14] found a correlation between the complexity of CAD and EAT thickness. They found a strong correlation between SS and EAT thickness. In contrast, we found a correlation between EAT thickness and CAD complexity in a group that included both diabetics and non-diabetics. However, their study only included non-diabetic patients.

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We compared the correlation of EAT with all lipid molecules, which showed a significant correlation with all, which was contrary to many articles. Pierdomenico *et al.* showed a significant correlation with HDL and TG but not with LDL.[15] This indicated that patients with higher EAT have higher proportion of deranged lipid profile. In our study, patients with higher syntax score have higher mean value of lipids except HDL which was lower in patients with higher syntax score. This association of mean lipid value with syntax score was significant. This result was similar to results of previous studies.[16,17]
A EAT value of >6.15 mm on ROC curve analysis with a sensitivity of 87.5% and a specificity of 100% predicted significant CAD. This indicates that EAT is a sensitive and very specific predictor of CAD and can be used for screening and early detection, and being less costly it will be very useful. The most important limitation of this study is the relatively small sample size. Moreover, the distribution of epicardial fat tissue is three-dimensional and might not accurately represent the distribution of epicardial fat. Computed tomography and cardiac magnetic resonance imaging could offer more details.

Conclusion

When comparing patients with an SS of ≥33 to those with an SS of <33, the EAT thickness in the former group was considerably larger. The 6.15 mm EAT threshold value was found to be predictive of severe CAD. A noteworthy association was seen between EAT and both WC and lipid profile. Therefore, echocardiography is a widely accessible, fairly priced method of measuring EAT thickness and may be useful in the early detection of those with complex or significant CAD.

References

1. Ralapanawa U, Sivakanesan R. Epidemiology and the Magnitude of Coronary Artery Disease and Acute Coronary Syndrome: A Narrative Review. J Epidemiol Glob Health. 2021 Jun;11(2):169-177.
2. Kodali NK, Bhat LD, Philip NE, Koya SF. Prevalence and associated factors of cardiovascular diseases among men and women aged 45 years and above: Analysis of the longitudinal ageing study in India, 2017–2019. Indian Heart Journal. 2023; 75(1):31-35.
3. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999;341:1097-105.
4. Li C, Liu X, Adhikari BK, Chen L, Liu W, Wang Y, Zhang H. The role of epicardial adipose tissue dysfunction in cardiovascular diseases: an overview of pathophysiology, evaluation, and management. Frontiers in Endocrinology.2023 May;14:1167952.
5. Tanındı A, Kocaman SA, Erkan AF, Uğurlu M, Alhan A, Töre HF. Epicardial adipose tissue thickness is associated with myocardial infarction and impaired coronary perfusion. Anatol J Cardiol. 2015 Mar;15(3):224-31.
6. Eroğlu S. How do we measure epicardial adipose tissue thickness by transthoracic echocardiography? Anatol J Cardiol. 2015 May;15(5):416-9.
7. Iacobellis G, Willens HJ. Echocardiographic epicardial fat: A review of research and clinical applications. J Am Soc Echocardiogr. 2009;22:1311-9
8. Iacobellis G, Assael F, Ribaudo MC, Zappaterreno A, Alessi G, Di Mario U, *et al.* Epicardial fat from echocardiography:a new method for visceral adipose tissue prediction. Obes Res. 2003;11:304e310.
9. Jeong JW, Jeong MH, Yun KH, Oh SK, Park EM, Kim YK, *et al.* Echocardiographic epicardial fat thickness and coronary artery disease. Circ J 2007;71:536-9.
10. World Health Organisation. Noncommunicable Disease Surveillance, Monitoring and Reporting. Available at https://www.who.int/teams/noncommunicable-diseases/surveillance/systems-tools/steps/instrument

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 12, 2023

11. Iacobellis G, Ribaudo MC, Assael F, Vecci E, Tiberti C, Zappaterreno A *et al*. Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters of metabolic syndrome: a new indicator of cardiovascular risk. J Clin Endocrinol Metab. 2003;88(11):5163–8.
12. Iacobellis G, Assael F, Ribaudo MC, *et al*. Epicardial fat from echocardiography: a new method for visceral adipose tissue prediction. Obes Res. 2003;11(2):304–10
13. Wang T, Liu Q, Liu C, Sun L, Li D, Liu A, Jia R. Correlation of echocardiographic epicardial fat thickness with severity of coronary artery disease in patients with acute myocardial infarction. Echocardiography. 2014 Nov;31(10):1177-81
14. Gökdeniz T, Turan T, Aykan AÇ, Gül I, Boyacı F, Hatem E, Bektaş H, Celik S. Relation of epicardial fat thickness and cardio-ankle vascular index to complexity of coronary artery disease in nondiabetic patients. Cardiology. 2013;124(1):41-8.
15. Pierdomenico SD, Pierdomenico AM, Neri M, Cuccurullo F. Epicardial adipose tissue and metabolic syndrome in hypertensive patients with normal body weight and waist circumference. Am J Hypertens 2011;24:1245-9.
16. Mazur A, Ostański M, Telega G, Malecka‑ Tendera E. Is epicardial fat tissue a marker of metabolic syndrome in obese children? Atherosclerosis 2010;211:596-600.
17. Rajkumar M. Epicardial adipose tissue thickness and its association with the severity of coronary artery disease. IOSR J Dent Med Sci 2019;18:65-71.