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Epicardial Adipose Tissue Thickness and Its Association with the Severity of Coronary Artery Disease

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I. Introduction

Adipose tissue that surrounds the Heart and its vessels functions as a complex organ being composed of adipocytes, stromal cells, macrophages, and a neuronal network, all these being nourished through a rich micro-circulation. Adipose tissue around the heart can further be subdivided into intrapericardial and extra pericardial fat. Their thicknesses and volumes can be quantified by echocardiography as well as computed tomography or magnetic resonance imaging.

The term extra-pericardial fat consists of thoracic adipose tissue external to the parietal pericardium. Its origin is from the primitive thoracic mesenchyme and thus its blood supply is derived from noncoronary sources. Intrapericardial fat can further be subcategorised into epicardial and pericardial fat. Hence, anatomically, epicardial and pericardial adipose tissues have clear cut differences.

Epicardial fat is localised between the myocardium (it's outer wall) and the visceral layer of pericardium. Pericardial fat is anterior to the epicardial fat and therefore located between the visceral and the parietal pericardium.

The epicardial fat is right at the forefront of research and all the attention it gets is due to its anatomical closeness to the myocardium and due to the fact that these two tissues share the same microcirculation. The epicardial fat layer originates from mesothelial cells and hence obtains its vascular supply from the coronary arteries. It has been shown that epicardial fat is metabolically active and a source of several adipokines and inflammatory cytokines, and there seems to be potential interactions through paracrine or vasocrine mechanisms between epicardial fat and myocardium.

Obesity is considered an important and more so, a modifiable risk factor for atherosclerotic cardiovascular disease (ASCVD). Estimation of visceral adipose tissue is gaining importance and several methods are being evaluated for the same. Correlation of epicardial adipose tissue (EAT) with the amount of visceral adipose tissue through magnetic resonance imaging (MRI) and/or CT (computed tomography) is excellent, the disadvantage being both are either costly and/or cumbersome.

EAT can be quite accurately measured using two-dimensional (2D) echocardiography. Some studies have found EAT to be thicker in patients with acute coronary syndrome than in subjects with stable angina. EAT being a direct measure of visceral fat rather than anthropometric measurements, carries the advantage of predicting high cardiometabolic risk

The present study evaluated the relationship of Epicardial Adipose Tissue Thickness and the severity of Coronary Artery Disease.

AIM OF THE STUDY

To assess the association between epicardial adipose tissue thickness, measured using transthoracic echocardiography (TTE), and the severity of coronary artery disease, measured using coronary angiography.

II. Materials And Methods

STUDY POPULATION:

The study was conducted on 100 consecutive patients admitted to the Department of Cardiology, Government Rajaji Hospital & Madurai Medical College during the study period who underwent coronary angiography for suspected coronary artery disease.

INCLUSION CRITERIA:

Patients who underwent coronary angiogram for suspected coronary artery disease without meeting the exclusion criteria

EXCLUSION CRITERIA:
- Prior history of documented acute coronary syndrome
- Trans Thorasic Echo imaging was inadequate for the measurement of epicardial fat thickness (poor echo window)
- Previously history of coronary artery bypass graft surgery (CABG)
- Previous history of percutaneous coronary intervention (PTCA)
- Chronic kidney disease
- Chest deformities
- Chronic lung disease
- Pericardial and/or pleural effusion on transthoracic echocardiography
- forms of CAD other than angina pectoris or acute myocardial infarction (MI), including coronary vasospasm, coronary ectasia, or turbulent or slow flow

ANTICIPATED OUTCOME:
- Significant correlation between epicardial fat thickness, measured using transthoracic echocardiography (TTE), and the severity of coronary artery stenosis, measured using coronary angiography.

DATA COLLECTION

Enrolled patients underwent complete evaluation including detailed clinical examination and investigations including ECG, 2D echocardiography and coronary angiogram as a part of their diagnostic procedure to identify the involved coronary artery. The 12-lead ECG was recorded for all patients at a speed of 25 mm/s and voltage of 10 mm/mV

Echocardiography

All echocardiographic measurements were performed by the same cardiologist, who was blinded to the patients' clinical information. Parasternal and apical views were obtained. The EAT thickness was measured from the standard parasternal long-axis view on the free wall of the right ventricle, perpendicular to the aortic annulus at end-systole as it was compressed during diastole. The EAT was identified as the echo-free space between the outermost border of the myocardium and the visceral layer of the pericardium. The thickest point of the EAT was measured in each of 3 cycles, and the average value was calculated.

Coronary angiography

With the help of the Judkins' technique, Coronary angiography was performed with either the femoral artery or radial artery approach. The severity of coronary atherosclerotic lesions was evaluated from at least 3 projections and patients were appropriately classified into single, double or triple vessel according to the number of vessels involved. Hemodynamically, significant stenosis was defined as a diameter stenosis of ≥ 50% in left main coronary artery (LMCA) and ≥ 70% in vessels other than LMCA.

INVESTIGATIONS

a) Complete blood count with ESR
b) Renal function test [blood urea and serum Creatinine]
c) Fasting and post prandial blood glucose
d) Fasting lipid profile [Triglycerides, LDL, HDL]
e) Serum electrolytes [Serum Sodium, Potassium]
f) Electrocardiogram
g) Echocardiography
h) Coronary Angiography

DESIGN OF STUDY:
Prospective study.

III. Results and Interpretation

TABLE 1. AGE DISTRIBUTION OF STUDY POPULATION (n=100)

Age in years	No. of cases
< 40	9
41 - 50	28
51 - 60	46
> 60	17
Total	100

COMMENTS
1. >50 % of cases were between 40-60 years of age, the most common age group with significant CAD
2. Less than 10 % of study population below 40 years of age.
3. 17% of study population were above 60 years of age.

TABLE 2. GENDER DISTRIBUTION OF STUDY POPULATION (n=100)

Sex	No. of cases
Male	79
Female	21
Total	100

Comments
1. Majority of study population were males (80 %)
2. while the remaining (20%) were females.

Table 3. DISTRIBUTION OF DURATION OF DIABETESAMONG STUDY POPULATION (n=100)

Diabetes	No. of cases
Yes	74
No	26
Total	100

COMMENTS
Among the study population 74% of cases were diabetic.

Table 3. DISTRIBUTION OF DURATION OF HYPERTENSION AMONG STUDY POPULATION (n=100)

Hypertension	No. of cases
Yes	62
No	38
Total	100

Comments
Out of our study population 62% were Hypertensive.

Table 5. DISTRIBUTION OF LDL & SEVEREITY OF CAD AMONG STUDYPOPULATION (n=100)

LDL Distribution	No. of cases
< 150	44
151 - 200	42
> 200	14
Total	100

CAG	No. of cases
SVD	41
DVD	34
TVD	25
Total	100

COMMENTS
In our study population 41% patients had single vessel disease, 34% had Double vessel disease, 25 % had triple vessel disease.

TABLE 6. DISTRIBUTION OF EFT AMONG STUDY POPULATION (n=100)

EFT level	No. of cases
< 6	9
6.1 - 10	67
> 10	24
Total	100

COMMENTS
1.Among study population just 9% had Epicardial Adipose Thickness [EFT] less than 6mm.
2. 67% of had EFT in the range of 6.1-10 mm.
3. Rest 24% had EFT more than 10mm.

DISTRIBUTION OF **EPICARDIAL FAT THICKNESS VS CAD SEVERITY**AMONG STUDY POPULATION (n=100)

CAG vs EFT	Mean EFT	
SVD (41)	6.56	
DVD (34)	8.42	
TVD (25)	11.06	
p value	< 0.001	Significant

COMMENTS
In our study population the mean EFT for patients with Single Vessel Disease was 6.56 mm, for those with Double Vessel Disease was 8.42 mm and for those with Triple Vessel Disease was 11.06 mm. **Significant P value of <0.001** shows that EFT correlates well with the complexity/severity of CAD and shows linear increase in association.

TABLE 10. DISTRIBUTION OF EFT VS LDL LEVELS AMONG STUDY POPULATION (n=100)

LDL Distribution	Mean EFT	
< 150 (44)	6.73	
151 - 200 (42)	9.22	
> 200 (14)	10.59	
p value	< 0.001	Significant

COMMENTS
In our study population the mean EFT for patients with Low LDL [<70] was for those with LDL in the range of 71-189 mg/dl the EFT mean was and for those with LDL >190 mg/dl the mean EFT
Significant P value of <0.001 shows that EFT correlates well with the LDL levels and shows a linear increase with increase in LDL levels.

LIMITATIONS OF THE STUDY
1. Sample size is relatively small.
2. The study population involved patients seeking medical care in our hospital which is a tertiary care centre and hence they may not represent the general population.
3. Serum levels of interleukins, cytokines, and adipokines, which could hint at the underlying mechanisms, were not evaluated.
4. We measured EAT thickness by means of echocardiography, rather than the comparatively more precise computed tomography.
5. Echocardiography was a relatively simple and inexpensive method, but the accuracy and reproducibility should be further tested.
6. In addition, as epicardial adipose tissue has a 3-dimensional distribution, 2- dimensional echocardiography may not completely assess the total amount of epicardial adiposity
7. Although patients admitted with acute coronary syndromes have reportedly had higher EAT values than do patients with stable angina, we did not categorize patients with respect to clinical presentation.

IV. Discussion

The study was conducted in the patients who attended cardiology clinic and were admitted for Coronary Angiogram to assess the severity of CAD, at Govt Rajaji hospital, Madurai.

Enrolled patients underwent complete evaluation including detailed clinical examination and investigations including ECG, 2D echocardiography and coronary angiogram as a part of their diagnostic procedure to identify the involved coronary artery and to document the extent of CAD.

All echocardiographic measurements were performed by the same cardiologist, who was blinded to the patients' clinical information

Parasternal and apical views were obtained. The EAT thickness was measured from the standard parasternal long-axis view on the free wall of the right ventricle, perpendicular to the aortic annulus at end-systole as it was compressed during diastole

The EAT was identified as the echo-free space between the outermost border of the myocardium and the visceral layer of the pericardium. The thickest point of the EAT was measured in each of 3 cycles, and the average value was calculated

Out of 100 patients 79 patients were male and 21 patients were female (~1.5:1). It is consistent with previous studies because nature of disease is more common in male as compared to female.

Out of these 100 patients 74 had diabetes, 62 had hypertension, and more than had LDL in the range of and 41 had SVD, 34 had DVD, 25 had TVD.

In these 100 patients EAT correlated very well with the severity of CAD with mean of 6.56 for SVD, 8.42 for DVD and 11.06 for TVD patients.

AK. Agarwal et al., have done similar study with 77 patients. But they divided those patients having non-CAD group and CAD group. Among them 28% (22 patients) having silent ischemia in CAD group which is founded by TMT. But in our study among 100 study population purely non-CAD group (i.e., asymptomatic), 40 patients (40%) having silent ischemia that is detected by TMT alone, though ECG and ECHO showing normal results.

In our country, Meenakshi K et.al performed a similar study in Madras Medical College Where One hundred and ten patients (70 males and 40 females with mean age of 51.5 and 52.6 respectively) were studied. It was demonstrated that burden of coronary arterial lesions denoted by Gensini score shows linear association with epicardial fat thickness and the severity of the coronary disease.

Another study by An Erkan AF et.al where 221 consecutive patients who had no histories of myocardial revascularization and who had undergone coronary angiography because of clinical diagnoses of CAD were studied. It demonstrated a significant and positive correlation between EAT thickness and the extent and complexity of CAD, as evidenced by the Gensini score and SYNTAX scores.

Gökdeniz and associates12 studied the relationship of EAT thickness to the complexity of CAD in nondiabetic subjects. They also determined a cut off value of 5-mm EAT thickness for the prediction of an intermediate-to high Syntax score. However, those investigators studied nondiabetic patients only, whereas our study has a predominant Diabetic [74%] population.

Jeong et al showed the relationship between echocardiographic EAT and CAD in 203 patients who underwent echocardiography and coronary angiography. Coronary angiograms were analysed for the extent and severity of CAD using Gensini score. The patients with a higher epicardial fat thickness were associated with a high Gensini score.

The present study is a clinical study indicating that echocardiographic epicardial fat thickness is associated with the severity of coronary artery stenosis in patients with known coronary artery disease.

Obesity is an important risk factor for atherosclerotic cardiovascular disease. Regional body adipose tissue distribution, rather than total body adiposity, has increasingly gained attention as a marker for cardiovascular disease. Hence, the detection of visceral adipose tissue, the fat deposited around the internal organs, might be important for the risk stratification of cardiovascular disease and metabolic syndrome.

Epicardial adipose tissue is a true visceral fat tissue, deposited around the heart on the free wall of the right ventricle, left ventricular apex and atrium. Previous reports indicated that epicardial adipose tissue is strongly correlated with abdominal fat deposits. This finding was explained through the common embryogenesis pathway; that is, epicardial fat and intra-abdominal fat seem to be originally brown adipose tissue in infancy. The biochemical properties of epicardial fat tissue suggest its possible role as a cardiovascular risk factor.

Studies using epicardial fat obtained during coronary artery bypass surgery revealed that a significantly higher expression of interleukin-1, interleukin-6, tumour necrosis factor-alpha and mRNA was shown in epicardial fat than those in leg subcutaneous adipose tissue. Other studies revealed epicardial and omental fat exhibit a comparable pathogenic inflammatory mRNA profile. Therefore, epicardial fat plays a role as a local inflammatory burden and store in patients with coronary artery disease.

Until now, magnetic resonance imaging (MRI) has been accepted as a gold standard for measuring epicardial fat thickness. In 2003, Iacobellis et al first reported the development of the echocardiographic measurement of epicardial fat. It showed that echocardiographic epicardial fat thickness has good correlation with MRI abdominal fat and epicardial fat measurements, and anthropometric and metabolic parameters.

Chaowalit et al performed the first clinical study to confirm this association in 139 patients; however, they failed to demonstrate the association with the severity of coronary artery disease.

EAT assessment by echocardiography does not require much time and can be easily applied during a routine examination for evaluating other functional cardiac parameters in those with obesity, diabetes, and hypertension. Echocardiography though a relatively simple as well as an inexpensive method, it’s accuracy and reproducibility should be submitted for further testing. As non-invasive tools for the diagnosis of coronary artery disease, However Echocardiography will have an important role to play in early identification of patients with CAD as shown in our study.

V. Summary

This prospective observational study was conducted to study EPICARDIAL ADIPOSE TISSUE THICKNESS AND ITS ASSOCIATION WITH SEVERITY OF CORONARY ARTERY DISEASE.

With 100 patients were selected carefully and were evaluated on clinical and laboratory aspects after an institutional ethical clearance with an informed consent. The data were entered in Microsoft Excel spread sheet and analysed statistically.

Out of 100 patients 79 were Male, 74 were Diabetic, 62 were hypertensive. The prevalence of SVD, DVD, TVD was 41%, 34%, 25% respectively. The mean EAT for SVD was 6.56 mm, for DVD was 9.22 mm, TVD was 11.06mm. Epicardial fat thickness measured using transthoracic echocardiography significantly correlated with the severity of coronary artery stenosis in patients with known coronary artery disease.

VI. Conclusion

Echocardiographic epicardial fat is an inexpensive, reproducible, and direct measure of visceral fat. It may have an important role in predicting and stratifying cardiovascular risk in both clinical care and the research setting.

Epicardial fat has multiple functions to support a healthy heart. An increased amount of epicardial fat is associated with both obesity and coronary artery disease

Quantification of EAT thickness by means of echocardiography—a relatively inexpensive, readily available method—might be beneficial in the early identification of patients who have complex or critical CAD.

This knowledge could enable earlier referral of these patients for diagnostic coronary angiography and timely interventions as its assessment is sensitive, easy, non-invasive and cost-effective for prediction and severity of CAD patients

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