Original Research Article

A STUDY OF RELATIONSHIP BETWEEN EPICARDIAL ADIPOSE TISSUE THICKNESSES BY COMPUTED TOMOGRAPHY WITH THE SEVERITY OF CORONARY ARTERY DISEASE

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Abstract

Background: The myocardial and visceral layer of the pericardium is encircled by visceral adipose tissue known as epicardial adipose tissue (EAT). In some conditions, EAT may produce inflammatory mediators via paracrine or endocrine pathways. This study is an attempt to describe the clinical and demographic profile of the subjects and assess the relation between epicardial fat thickness and with extent and severity of CAD by Syntax score.

Methods: Diagnosis of CAD was done according to the latest criteria with Clinical features, ECG changes, 2-ECHO, Cardiac biomarkers, and Coronary Angiography findings. Suggestive of ACS. Coronary angiography was performed in the catheterization laboratory (Siemens AXIOM-Artis, Munich, Germany), equipped with quantitative coronary analysis software. Coronary angiograms were interpreted visually and were analyzed in two orthogonal views and scored by a computer-assisted SYNTAX scoring algorithm.

Results: out of n=60 patients, n=17 patients had a Syntax score less than 22, n=18 patients had a Syntax score of 23 to 32, and n=25 patients had a Syntax score above 32. Epicardial adipose tissue thickness was 5.9 ±0.2mm in patients with a syntax score less than 23, 6.08±0.1mm in patients with a syntax score of 23-32, and 9.66 ±0.33mm in patients with a syntax score of 33 and above. Cut-off EAT value to predict significant CAD was identified as 6.25 mm (ROC analysis 0.046 p=0.00, 95% CI: 0.864- 1.000). The sensitivity and specificity of EAT cut-off 6.25mm to predict significant CAD were 100% and 70% respectively.

Conclusion: Epicardial adipose tissue thickness was significantly higher in patients with a syntax score of 33 and above when compared with patients having a syntax score of less than 33. EAT cut-off value to predict significant CAD was identified as 6.25 mm (ROC analysis 0.046 p=0.00, 95% CI: 0.864 - 1.000). The sensitivity and specificity of EAT cut-off 6.25mm to predict significant CAD were 100% and 70% respectively.

Keywords: Epicardial Adipose Tissue thickness, Coronary Artery Disease, SYNTAX score

Introduction

The rising prevalence of cardiovascular disease (CVD) worldwide has necessitated the development of simple yet effective tools that permit accurate risk stratification of individuals requiring primary prevention of CVD. The clinical manifestations of CAD include silent myocardial ischemia, angina pectoris, acute coronary syndromes (unstable angina pectoris, myocardial infarction), and sudden cardiac death. [1] The largest endocrine organ in the human body, adipose tissue is crucial for the production of energy. [2 - 4] The connection between adipose tissue and CAD has recently drawn more and more attention. New strategies for treating CAD may be offered by pertinent studies. Visceral adipose tissue called epicardial adipose tissue (EAT) surrounds the myocardial and visceral layer of the pericardium. EAT may release pro- and anti-inflammatory substances by paracrine or endocrine mechanisms under specific circumstances (e.g., TNF-, IL-6, adiponectin, and leptin). [5 - 7] Through modifying lipid metabolism and energy balance, research demonstrates that EAT is implicated in the regional control of myocardial and coronary function [8]. EAT contributes significantly to the prevention of CAD by enhancing the effectiveness of myocardial glucose utilization by controlling the release and absorption of free fatty acids (FFAs) [9, 10]. A variety of clinical and biochemical risk markers, risk algorithms, and imaging tests have been developed for this purpose, but with variable success. Visceral adiposity is one such marker that is associated with increased CVD risk. [11-14] Traditionally, visceral adiposity is measured either in the form of a waist-to-hip ratio or by quantifying hepatic fat using ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI). Unfortunately, while the waist-to-hip ratio provides only an indirect estimation of visceral adiposity, ultrasound, and CT are only qualitative and MRI is limited by expense and availability issues. Recently, epicardial fat has gained attention as a true visceral fat deposit that can be easily quantified non-invasively. Additionally, due to its proximity to coronary microvasculature, epicardial fat also has a stronger and more direct relationship with the risk of coronary artery disease (CAD). For these reasons, epicardial fat has emerged as a promising marker for CVD risk stratification. This study is an attempt to describe the clinical and demographic profile of the subjects and assess the relation between epicardial fat thickness and with extent and severity of CAD by Syntax score.

Material and Methods

The present study is a randomly selected observational study, with a total of n=60 patients who are admitted to the department of Cardiology, Osmania General Hospital, diagnosed with Acute coronary syndrome, who are willing to undergo Coronary Angiography. This study was approved by the institutional ethics committee. Written consent was obtained from all the participants of the study after explaining the nature of the study and possible outcomes in the vernacular language.

Inclusion Criteria

1. Consecutive patients diagnosed with acute coronary syndrome undergoing coronary angiography.
2. Males and females
3. Aged more than 20.
4. Willing to participate in the study voluntarily.

Exclusion criteria

1. Previous cardiac surgery
2. Previous chest irradiation
3. The subject is not willing to participate in the study.
4. Pericardial effusion.
5. Pregnancy.
6. Patients underwent percutaneous Transluminal coronary angioplasty (PTCA) for ST-

elevation myocardial infarction (STEMI).

Diagnosis of CAD: done according to the latest criteria with Clinical features, ECG changes, 2-ECHO, Cardiac biomarkers, and Coronary Angiography findings. Suggestive of ACS. The baseline evaluation included all participants being asked about Smoking habits (including ex- and current smokers) or tobacco in any other form, Alcohol habits, and Positive family history of CAD. Body mass index (BMI) was calculated with body weight (kg) divided by the square of height in meters. According to the current WHO classification, the normal range of BMI was considered between 18.5 to 24.9, and pre-obese or overweight was defined as BMI ≥25. Hypertension was defined as a systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mm Hg based on more than three measurements or the current use of antihypertensive drugs.

*Biochemical Assessment***:** Blood specimens were obtained after a 12- to 14-hour fast (8 pm–9.30 am) to reduce the influence of circadian variation. The concentrations of Triglycerides were measured using standard enzyme methods (Liquixx Triglycerides GPOTrinder Method). Total Cholesterol (CHOD-PAP) and High-density lipoprotein (HDL) cholesterol were assessed after very LDL with phosphotungstic acid precipitation, and LDL was calculated using the Friedewald formula. Fasting glucose levels were enzymatically examined by the hexokinase method. Type 2 diabetes mellitus (T2DM) was defined as a fasting blood glucose level was ≥126 mg/dL according to WHO and ADA criteria. Dyslipidemia was defined according to the recommendation of National Cholesterol Education Program (NCEP) guidelines.

Study Design: After selecting the cases a detailed questionnaire that includes a detailed history to assess symptoms, risk factor profile, current medical therapy, physical examination, and relevant investigations are done for each case. After confirming the diagnosis of ACS who are willing for CAG, measurement of EAT thickness is done by CT scan (TOSHIBA-Alexion, 4 Slice). All the patients were catheterized percutaneously via femoral or radial artery with standard Judkins or Tiger catheters respectively with modified Seldinger technique.

Coronary angiography was performed in the catheterization laboratory (Siemens AXIOM-Artis, Munich, Germany), equipped with quantitative coronary analysis software. Coronary angiograms were interpreted visually and were analyzed in two orthogonal views and scored by a computer-assisted SYNTAX scoring algorithm. [15, 16] Patients were divided into three groups based on

Syntax score namely.
1. Patients with Syntax Score up to 22.
2. Patients with Syntax Score 23-32.
3. Patients with Syntax Score 33 and above.

Statistical analysis:
All the data were collected, and Microsoft Word and Excel were used to generate tables and graphs. Data analysis was performed with IBM Statistical Package for Social Sciences (SPSS) for Windows version 20. SPSS Inc., Chicago, USA. The continuous variables were represented as mean and standard deviation and categorical variables were represented by p-values and the p-values of <0.05 was considered statistically significant.

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Results

Out of n=60 patients, n=17 patients had a Syntax score less than 22, n=18 patients had a Syntax score of 23 to 32, and n=25 patients had a Syntax score above 32. The patient's ages ranged from 28–85 years. The mean age of the patients was 56.45±11.39 years. The majority of the patients were in the 50-60 years age group as shown in figure 6 and table 1. Out of n=60 patients, n=48 (80%) were males and n=12 (20%) were females. Male to female ratio was 4:1. The mean age of males and females was 56.52 ± 11.59 years and 56.16 ± 11.05 years respectively.

Table 1: Distribution of study population as per age group

Age Groups	*Frequency*	*Percent*
20 – 30	1	1.6 %
30 – 40	3	5.2 %
40 – 50	13	21.6 %
50 – 60	27	45.2 %
60 – 70	9	15 %
>70	7	11.66 %
Total	60	100.00 %

In the study population, the distribution of risk factors was 48.2% cases of hypertension, 32.2% were diabetics, 36.3% were smokers, 30% were having dyslipidemia and 5% were having a family history of premature CAD (figure 1). *Coronary Angiogram*: In the study population, out of n=60 patients, n=17 patients had a Syntax score less than 22, n=18 patients had a Syntax score of 23 to 32, and n=25 patients had a Syntax score above 32 depicted in table 2.

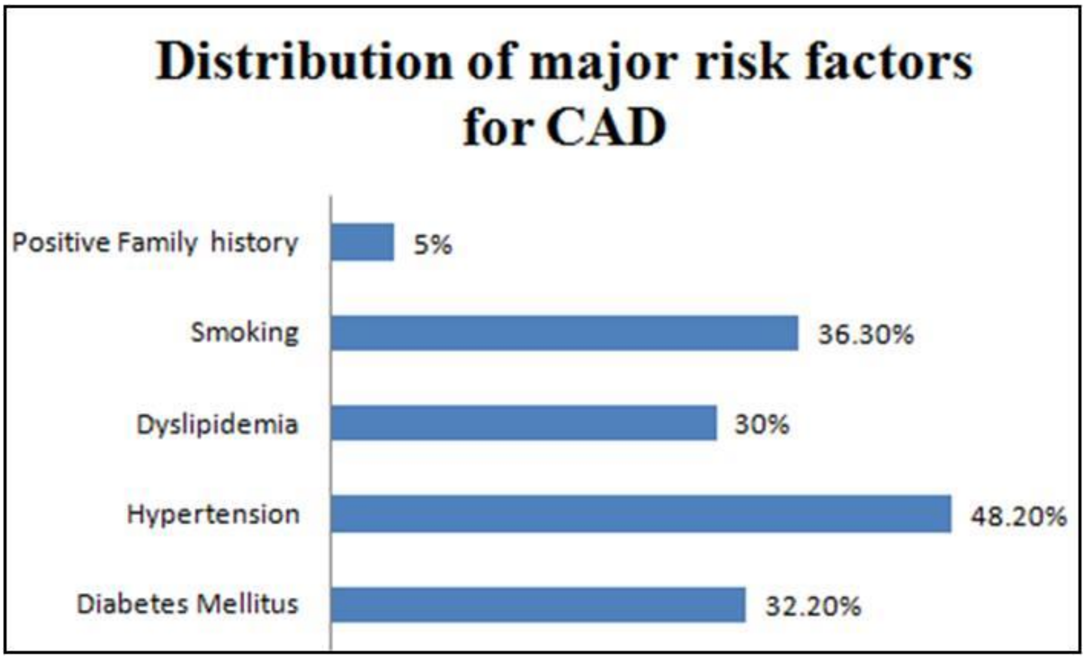


Figure 1: Showing the distribution of risk factors for CAD in the cases of the study.

Table 2: Distribution of cases based on the Syntax scores in the study.

CAG groups	*Frequency*	*Percentage*
Patients with Syntax Score up to 22	17	28.33%
Patients with Syntax Score 23-32	18	30%
Patients with Syntax Scores of 33 and above	25	41.66%

Epicardial adipose tissue thickness was 5.9 ±0.2mm in patients with a syntax score less than 23, 6.08±0.1mm in patients with a syntax score of 23-32, and 9.66 ±0.33mm in patients with a syntax score of 33 and above. Epicardial adipose tissue thickness was significantly higher in patients with a syntax score of 33 and above when compared with patients having a syntax score of less than 33.

Table 3: Distribution of mean EAT among study population groups.

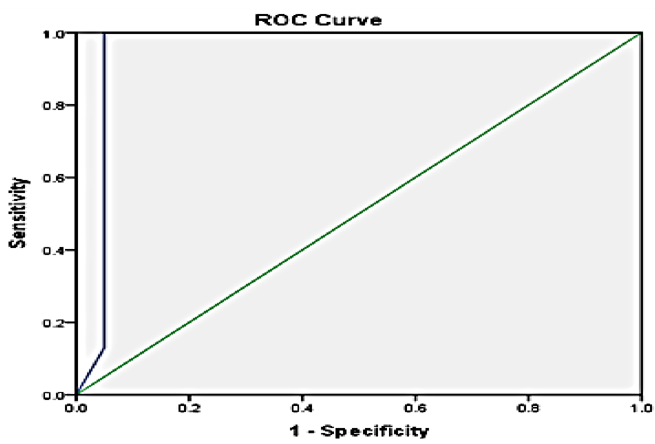
CAG groups	*N*	*Mean EAT ±SD (mm)*	*p-value*
Patients with Syntax Score up to 22	17	5.9 ±0.24	0.0001
Patients with Syntax Score 23-32	18	6.08 ±0.10	
Patients with Syntax Scores of 33 and above	25	9.66 ±0.33	

The mean EAT differences between different age groups were compared and the p values were found to be 0.62 hence, there was no significant EAT difference between different age groups in the study. Similarly, the mean EAT between males and females was compared and there was no significant EAT difference between males and females in the study.

Table 4: Distribution of various characteristics among the study population groups

Variable	*Patients with Syntax Score up to 22*	*Patients with Syntax Score 23 - 32*	*Patients with Syntax Score 33 and above*
Number of cases	17	18	25
Mean age	60.35	55.9	54.16
Males	16	13	19
Females	1	5	6
Mean EAT (mm)	5.93 ± 0.24	6.08 ± 0.1	9.66 ± 0.32

Cut-off EAT value to predict significant CAD was identified as 6.25 mm (ROC analysis 0.046 p=0.00, 95% CI: 0.864- 1.000). The sensitivity and specificity of EAT cut-off 6.25mm to predict significant CAD were 100% and 70% respectively.



Diagonal segments are produced by ties.

Table 5: Area under the ROC curve

Area	*Std Error*	*Asymptotic Sig*	*Asymptotic 95% Confidence Interval*	
			Lower bound	Upper Bound
0.953	0.046	0.000	0.846	1.000

Discussion

Epicardial adipose tissue (EAT), found between the visceral pericardium and myocardium, is a specialized visceral adipose tissue in which the coronary arteries are embedded. The lack of an anatomic barrier between EAT and the myocardium enables them to share microcirculation. Epicardial adipose tissue produces numerous proinflammatory and proatherogenic mediators that might promote the initiation and progression of coronary atherosclerosis, including subclinical atherosclerosis. High EAT Thickness has been shown to increase the prognostic value of coronary artery calcium score in predicting future cardiac events. The thickness and volume of EAT are related to the severity and extent of atherosclerotic coronary artery disease (CAD). [17 – 21] However, some investigators have found no significant association between EAT volume or thickness and CAD presence or severity. Although the relationship between EAT and the severity and extent of CAD has been extensively investigated, comparatively few studies about the association of EAT with CAD complexity. [22 – 25] The complexity of CAD, an important factor in clinical decision-making, is typically evaluated utilizing the Syntax score. Another important factor in choosing treatment approaches is the presence of critical lesions, which potentially qualify the patient for interventional treatment.

This study compared epicardial adipose tissue (EAT) thickness measured by Computed Tomography with Coronary artery disease burden assessed through SYNTAX score. In a pilot study Willens HJ et al., [11] used two-dimensional Transthoracic Echocardiography to measure pericardial and maximum and minimum epicardial fat thickness anterior to the right ventricle in 50 African American and 106 non-Hispanic White men, aged 40–75 years, consecutively referred for echocardiography for standard clinical indications. Results showed that maximum epicardial fat along the distal right ventricular wall was 19% greater in non-Hispanic Whites, but this difference was not statistically significant (4.3±2.6 mm vs. 3.6±2.0 mm, P=0.133). In a study by Hirata Y et al., [3] the systolic and diastolic EAT thickness was significantly greater in the CAD group than the non-CAD group (systole: 7.6±2.8 vs. 5.6±2.3 mm, p<0.001, diastole: 5.8±2.2 vs. 4.3±2.2 mm, p<0.001). In The Heinz Nixdorf Recall Study, from the overall 4,093 participants, 130 subjects developed a fatal or nonfatal coronary event. Incidence of coronary events increased by quartile of EAT (0.9% vs. 4.7% for 1st and 4th quartile, respectively, p≤ 0.001). Doubling of EAT was associated with a 1.5-fold risk of coronary events when adjusting for cardiovascular risk, which remained unaltered after further adjustment for CAC score (HR [95% CI]: 1.50 [1.07 to 2.11]). [26] In a study EAT volume was also associated with the Agatston calcium score, volume calcium score, Gensini score, and Framingham Risk Score. An EAT volume > 200 cm^3 was the strongest independent risk factor for CAC. [27] In a study by Erkan A.F et al., [28] Mean EAT was 4.3±0.9, 5.2±1.5, and 7.5±1.9 mm in the patients with normal coronary arteries, minimal CAD, and significant CAD groups respectively (p<0.001). Multivariate analysis and ROC analysis revealed that EAT can be used as an independent predictor of significant CAD. Cut-off EAT value to predict significant CAD was identified as 5.8 mm (ROC analysis 0.875 p<0.001, 95% CI: 0.825- 0.926). The sensitivity and specificity of EAT cut-off 5.8 to predict significant CAD was 77% and 83% respectively. In the present study EAT cut-off value to predict significant CAD was identified as 6.25 mm (ROC analysis 0.046 p=0.00, 95% CI:

0.864- 1.000). The sensitivity and specificity of EAT cut-off 6.25mm to predict significant CAD were 100% and 70% respectively. Gökdeniz and associates studied the relationship of EAT thickness to the complexity of CAD in non-diabetic subjects. They found EAT thickness to be significantly correlated to Syntax score (r =0.629 P <0.001). [29] However, those investigators studied nondiabetic patients only whereas we identified the relationship of EAT thickness with CAD complexity in a diabetic and non-diabetic population. In a recent study done by Meenakshi K and associates involving 110 Indian subjects undergoing coronary angiography, the burden of CAD assessed by the Gensini score showed a linear association with echocardiographically measured epicardial fat thickness. [30] In 2014, Yanez-Rivera et al., [31] and colleagues found no significant relationship between Echocardiography EAT thickness and the angiographic severity of CAD. This discrepancy might have resulted from the method used to evaluate CAD severity. Whereas those investigators [31] used the number of stenotic major coronary arteries as the surrogate of CAD severity, we used the Syntax Score—a more quantitative method to assess the severity of coronary artery disease. In the present study, Epicardial adipose tissue thickness was measured by Non-contrast Cardiac Computed Tomography. Coronary angiography was performed, and the Syntax score was calculated. Patients were divided into three groups based on Syntax score namely.

1. Patients with Syntax Score up to 22.
2. Patients with Syntax Score 23-32.
3. Patients with Syntax Score 33 and above.

Out of n=60 patients, n=17 patients had a Syntax score less than 22, n=18 patients had a Syntax score of 23 to 32, and n=25 patients had a Syntax score above 32. Epicardial adipose tissue thickness was 5.9 ±0.2mm in patients with a syntax score less than 23, 6.08 ± 0.1mm in patients with a syntax score of 23-32 and 9.66 ± 0.33mm in patients with a syntax score of 33 and above. Epicardial adipose tissue thickness was significantly higher in patients with a syntax score of 33 and above when compared with patients having a syntax score of less than 33. There was no significant EAT difference between different age groups in the study. There was no significant EAT difference between males and females in the study.

Conclusion

Within the limitations of the current study, the following conclusion were established.

1. Epicardial adipose tissue thickness was significantly higher in patients with a syntax score of 33 and above when compared with patients having a syntax score of less than 33.
2. EAT cut-off value to predict significant CAD was identified as 6.25 mm (ROC analysis 0.046 p=0.00, 95% CI: 0.864 - 1.000). The sensitivity and specificity of EAT cut-off 6.25mm to predict significant CAD were 100% and 70% respectively.
3. There was no significant EAT difference between different age groups in the study.
4. There was no significant EAT difference between males and females in the study.

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