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Original article

Diagnostic Value of Multi Detector Computed Tomography in Assessment of Epicardial Adipose Tissue with Coronary Artery Disease

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Abstract:

Background: Current Multi Detector Computed Tomography (MDCT) systems allow the visualization of the entire heart volume during an entire heart cycle with high density resolution. MDCT imaging is thus opened to a wide spectrum of cardiac applications. This study aimed to evaluate the diagnostic value of multi detector computed tomographic in assessment of epicardial adipose tissue with coronary artery disease. **Methods:** This Prospective, non-controlled nonrandomized study was conducted on 75 patients who underwent CT angiogram due to acute coronary syndrome occurrence. For further assessment of CAD patients divided into two groups: non-CAD group: 25 subjects with normal coronary arteries and CAD group: 50 subjects with coronary artery lesion. **Results:** This study included 75 patients; their mean age was 61.85 years. 61% of the studied subjects were males and 38% were females. ROC curve of EFV was conducted for prediction of CAD disease activity. EFV showed 0.813 area under curve at cut off level 60.39 with good sensitivity and specificity. ROC curve of Ca score was conducted for prediction of CAD disease activity. Ca score showed 0.947 area under curve at cut off level 90 with high sensitivity and specificity. **Conclusion:** The EAT volume has good prognostic value for developing CAD and increased EAT is considered a risk factor for CAD. Ca score could have an appropriate prognostic value for the determination of coronary artery disease.

Keywords: Diagnostic value; Multi Detector Computed Tomography; Epicardial Adipose Tissue; Coronary Artery Disease.

Introduction

Fat surrounding the heart resides in two distinct depots separated by the pericardium: epicardial and paracardial adipose tissues [(1)]. Epicardial fat is defined as the adipose tissue located between the outer wall of the myocardium and the visceral layer of pericardium [(2)].

Epicardial adipose tissue (EAT) is true visceral fat deposit which is commonly found in the atrioventricular and interventricular grooves, interacting locally and modulating the coronary arteries through the paracrine or vasocrine secretion of proinflammatory adipokines[(3)] .

Epicardial fat is supplied by branches of the coronary arteries and no muscle fascia separates the fat depot and the myocardium. Hence, as the two tissues share the same microcirculation. This allows the hypothesis of a direct interaction between the epicardial fat and the myocardium [4].

EAT is a type of visceral adipose tissue that functions like an endocrine organ by secreting adipocytokine and certain other hormones that contribute to the atherosclerotic process. It is considered that the epicardial adipose tissue contributes to the pathogenesis of CAD due to its closeness to the adventitia of the coronary arteries [5]. Several studies have reported that epicardial fat volume (EFV) measured on multi-detector CT (MDCT) is related to CAD and cardiovascular risk [6]. EAT thickness not only predicts cardiovascular risk, but also correlates significantly with the extent and severity of CAD [7].

The increasing interest in the estimation of the amount of EAT has lead to development of different measurement strategies using the majority of non-invasive diagnostic imaging techniques [8]. Several imaging modalities can be used to quantify EF volume (EFV) such as echocardiography, computer tomography, and magnetic resonance imaging [9].

With respect to other imaging modalities, however, CT may provide a more accurate evaluation of fat tissue due to its higher spatial resolution compared to ultrasound and MRI. In addition, CT is widely used for evaluating coronary calcium score, which is an independent predictor of cardiovascular prognosis, and to obtain a non-invasive study of coronary morphology. Current Multi Detector Computed Tomography (MDCT) systems allow the visualization of the entire heart volume during an entire heart cycle with high density resolution. MDCT imaging is thus opened to a wide spectrum of cardiac applications. Different pieces of information about coronary morphology, myocardium structure and function may be simultaneously collected leading to a more complete assessment of the functional status of the heart. Quantitative evaluation of epicardial fat may add a prognostic value to cardiac CT examinations with a potential improvement of its cost-effectiveness [10].

The purpose of this study was to evaluate out the diagnostic value of multi detector computed tomographic in assessment of epicardial adipose tissue with coronary artery disease.

Patients and methods

This prospective, non-controlled, non-randomized study was conducted at the Radiology Department of an international medical center. A total of 75 patients were included in the study between January 2018 and December 2019. Informed written consent was obtained from all patients, and a secret code numbering system was used to ensure confidentiality.

An informed written consent was obtained from the patients. Every patient received an explanation of the purpose of the study and had a secret code number. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University.

Inclusion criteria were patients under 80 years old who underwent CT angiography due to acute coronary syndrome, ST segment elevation myocardial infarction, or symptoms highly suggestive of CAD.

Exclusion criteria were patients with severe valvular heart disease, cardiomyopathies, pericardial effusion and patients with contrast contraindication or poor image quality.

The study population was divided into two groups: CAD group: 50 patients with coronary artery lesions. Non-CAD group: 25 subjects with normal coronary arteries.

All patients underwent the following procedures:

Full medical history: Relevant information was collected, including symptoms, risk factors, allergies, and relevant medical conditions. Revision of previous laboratory and cardiac investigations: Kidney functions, lipid profile, echocardiography, stress test, and electrocardiogram were reviewed. Patient preparation.

Scanning protocol and parameters:

Scanogram: Planar X-ray images were used to select the region of interest for subsequent imaging.

Calcium score: A non-contrast scan was performed to determine the coronary artery calcium score.

CT coronary angiography: Contrast material was injected, and a series of images were acquired to visualize the coronary arteries.

Image analysis: Axial images were transferred to a dedicated workstation for analysis, including quantification of coronary artery calcium. Multi-planar reconstructions and maximum intensity projections were used for further evaluation of the coronary arteries.

Measurement of epicardial fat: Epicardial fat thickness was measured at three sites in the horizontal long-axis plane: right atrio-ventricular groove, left atrio-ventricular groove, and anterior interventricular groove.

Evaluation of coronary artery lesions: A systematic analysis of the MDCT images was performed to assess the anatomical distribution, presence of lesions, composition, morphology, and degree of stenosis in the coronary arteries. Lesions were classified based on the number of vessels involved, location, extension, and degree of obstruction.

The study utilized MDCT to evaluate epicardial adipose tissue in patients with suspected CAD. Patients underwent various imaging procedures, including CT angiography, and the acquired images were analyzed using dedicated workstations. Epicardial fat thickness and coronary artery lesions were assessed, and a classification system was used to characterize the severity and components of the lesions.

Approval code: MD.14.8.2016

Statistical analysis

The collected data was revised, coded, and tabulated using the Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. Shapiro-Wilk test was done to test the normality of data distribution. Mean, Standard deviation (± SD) for normally distributed numerical data. Median and range for not normally distributed numerical data. Student T Test was used to assess the statistical significance of the difference between two study group means. Mann Whitney Test (U test) was used to assess the statistical significance of the difference of a non-parametric variable between two study groups. The Kruskal-Wallis test is was used to assess the statistical significance of the difference between more than two study group non parametric variables. Chi-Square test was used to examine the relationship between two qualitative variables. Correlation analysis: To assess the strength of association between two quantitative variables. The ROC Curve (receiver operating characteristic) was performed. Logistic regression analyses was used for prediction of risk factors when dependent variable is categorical, using generalized linear models. An odds ratio (OR) is a measure of association between an exposure and an outcome. The OR represents the odds that an outcome was occurred. A two tailed P value < 0.05 was considered statistically significant.

Results

This study included 75 patients; their mean age was 61.85 years. 61% of the studied subjects were males and 38% were females. According to risk factors, 61% were diabetic, 37% were hypertensive and 54% had hyperlipidemia. Patients had positive family history of CAD were 61%. When it comes to special habits, 54% were

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nonsmokers, 26% Ex-smokers and 18% were smokers. For further assessment of CAD patients divided into two groups: non-CAD group included 25 subjects with normal coronary arteries and CAD group with coronary artery lesion, Table (1).

Demographic data of the studied groups showed that mean age for non-CAD group was 61.08 years and 62.24 years for CAD group. Male were 44% of the non-CAD group and 70% in CAD group. Significant p value (0.029) showed toward male gender in CAD group.

Risk factors for CAD showed statistical significance in the number of hypertensive and diabetic patients. Hypertension represents 56% in no CAD group and 72% in CAD group. Diabetes was shown in 28% of non-CAD group and 78% in CAD group. 64% of non-CAD group had hyperlipidemia and 50% of non-CAD group. Special habits in non-CAD group (28% were Ex-smokers and 12% smokers) and in CAD group (26% were ex-smokers and 22% smokers). Previous family history of CAD was 28% in non-CAD group and 44% of the CAD group, Table (2).

Estimated epicardial fat volume (EFV) mean level was 60.08±26.25 in non-CAD group and 94.67±17.74 in the CAD group. It measured significantly higher in CAD group, Figure 1 A).

The mean Calcium score in non-CAD group was 31.28±64.77 and 208.57±89.40 for the CAD group. It was significantly higher in CAD group, Figure 1 B).

Table 1: Assessment of CAD and grading of the studied subjects.

	Total subjects n=75
Assessment of CAD	
EFV, M±SD	83.14±26.48
Ca score, M±SD	149.47±117.18
Risk score for CAD, n (%)	
Low risk	7(9)
Mild risk	14(18)
Moderate risk	13(17)
High risk	41(54)
CAD grading, n (%)	
No CAD	25(33)
Eccentric lesion	9(12)
Mild lesion	16(21)
Borderline lesion	10(13)
Significant lesion	11(14)
Occlusive lesion	4(5)

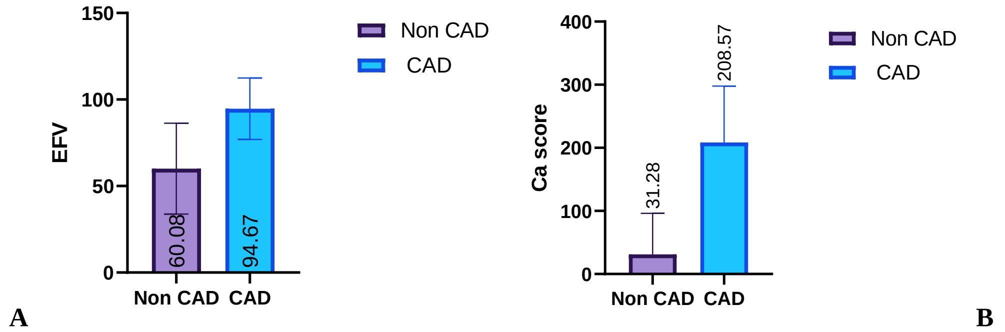

Figure 1: A) EFV in the studied groups and B) Ca score in the studied groups

Table 2: Risk factors in the studied groups.

	Non-CAD group n=25	CAD group n=50	Test Chi-Square	p
Hypertension, n (%)				
Hypertension	14(56)	36(72)	5.585	0.018*
Non hypertension	11(44)	14(28)		
Diabetes, n (%)				
Diabetic	7(28)	39(78)	17.569	<0.001*
Non-Diabetic	18(72)	11(22)		
Lipid profile, n (%)				
Hyperlipidemia	16(64)	25(50)	1.318	0.251
Non hyperlipidemia	9(36)	25(50)		
Smoking, n (%)				
Nonsmoker	15(60)	26(52)	1.113	0.573
Ex-Smoker	7(28)	13(26)		
Smoker	3(12)	11(22)		
Family history of CAD, n (%)				
Positive family history	18(72)	28(56)	1.799	0.180
Negative family history	7(28)	22(44)		

Subjects were further classified according to risk of CAD by Ca score. Non-CAD group show low risk 40%, mild risk 52% and 8% moderate risk. On the other hand, CAD group showed 2% mild risk, 20% moderate risk and 78% high risk. Significant p value in high-risk Ca score showed toward CAD group. CAD group further classified according to lesion type into five subgroups, eccentric lesion (18%), Milid lesion (32%), Borderline lesion (20%), Significant lesion (22%) and Occlusive lesion (8%).

Mean level of EFV was measured in different grades of CAD lesion. A significant increase in mean level of EFV according to severity of CAD, Figure (2 A).

Similar to EFV, CA score mean level was measured in different CAD lesion grades. A statistically significance ($p<0.001$) showed a strong relation with level of Ca score with severity and grading of CAD, Figure (2 B).

ROC curve of EFV was conducted for prediction of CAD disease activity. EFV showed 0.813 area under curve at cut off level 60.39 with good sensitivity and specificity, Figure (3 A).

ROC curve of Ca score was conducted for prediction of CAD disease activity. Ca score showed 0.947 area under curve at cut off level 90 with high sensitivity and specificity, Figure (3 B).

Correlation analysis of CAD grading and other markers in this study showed a strong positive relation with both EFV and Ca score in CAD group. While no significant relation with age of the patients, Table (3).

Logistic regression analysis was conducted for the prediction of CAD activity using DM, hypertension, EFV, Ca score and CAD risk score. DM, hypertension, EFV, Ca score and moderate CAD risk were associated with risk of CAD in univariate analysis. Only EFV was associated with risk of CAD in univariate and multivariate analysis, Table (4).

Table 3: Correlation between grade of CAD with other studied parameters among CAD patients.

	Grade of CAD	
	r	**p**
Age	0.097	0.408
EFV	0.973	<0.001*
Ca score	0.913	<0.001*

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Table 4: Logistic regression analysis for prediction of CAD among the studied subjects.

	Univariable			Multivariable		
	p	**OR**	**95% CI**	**p**	**OR**	**95% CI**
DM	<0.001*	0.110	0.037-0.330			
Hypertension	0.02*	3.273	1.201-8.917			
EFV	<0.001*	0.942	0.919-0.965	0.04*	3.125	1.135-9.351
Ca score	<0.001*	0.977	0.967-0.987			
CAD risk (Moderate risk)	<0.001*	25.35	21.204-303.06			

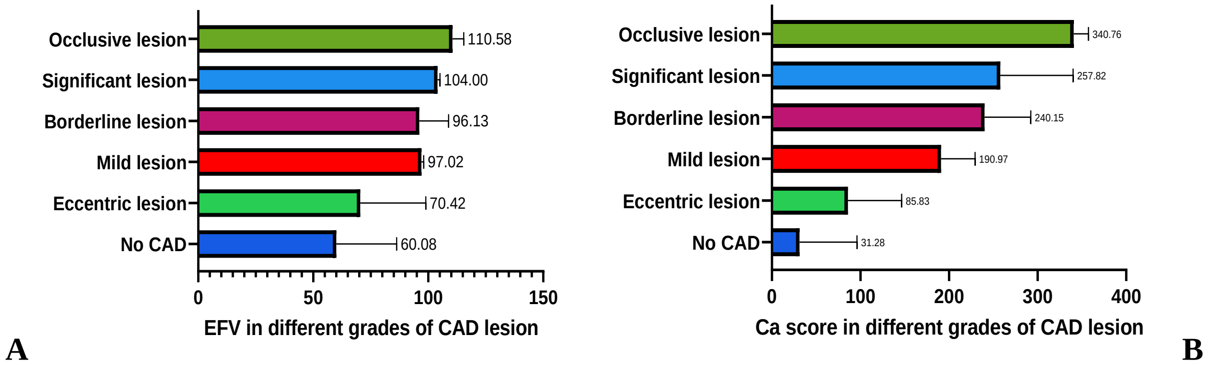

Figure 2: A) EFV level in different grades of CAD lesion and B) Ca score level in different grades of CAD lesion

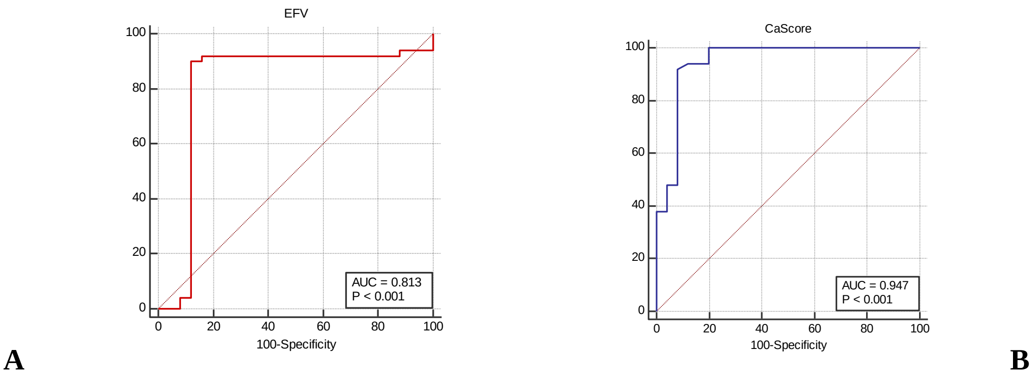

Figure 3: A) ROC curve analysis of validity of EFV for prediction of CAD severity and B) ROC curve analysis of validity of Ca score for prediction of CAD severity.

Cases:

Case (1): Male patient 49 years old, hypertensive and non-diabetic. He had chest pain on exertion. He is not a smoker with a negative family history of ischemic heart disease. He was referred to perform multi-slice CT coronary angiography. Epicardial fat volume equals 93.23 ml (Figures D1, D2, D3&D4). Calcium score is 49, matching with mild coronary artery disease risk.

MDCT coronary findings: LMT: normal caliber, LM is dividing into LAD and LCX, LM shows no hemodynamically significant stenosis or occlusion. LAD: Mildly atherosclerotic LAD, demonstrating proximal calcific plaque (2030 %) causing mild non-significant stenosis, Mid LAD show focal segment of incomplete myocardial bridging. It gives origin to early rising mildly atherosclerotic D1 branch (Figures 4 A1, A2, C4 & C5). LCX: LCx is seen arising from LM, remains free from significant stenosis. LCx gives origin to patent obtuse marginal artery (OM) (Figures 4 B1, B2, C4 & C5). RCA: Dominant RCA average caliber, no stenosis, RCA is giving off patent PDA and PLB branches (Figures: 4 C1, C4 & C5).

Case (8): 47 years old female patient complained of attacks of chest tightness related to exertion and sometimes dyspnea. He is not a smoker, hypertensive with negative family history of ischemic heart disease. He was referred to perform multislice CT coronary angiography. Epicardial fat volume equals 47.53 ml (Figures D1, D2, D3 & D4) Calcium score is 412; matching with high risk of coronary artery disease risk.

MDCT coronary findings: LMT: patent LM is bifurcating into LAD and LCX that remaining patent free from significant lesion. LAD: It show few proximal and mid non-significant eccentric calcific lesions causing +/- 10 % stenosis, rest of vessel is patent free from significant lesion. Diagonal branches are patented with mild atherosclerotic changes. (Figures A1, A2, C5 & C6). LCX: LCX is seen arising from LM, remains free from significant stenosis. LCX gives origin to patent obtuse marginal artery (OM). (Figures B, C5 & C6). RCA: Dominant RCA showing normal course, it remains free from stenotic segments. Gives origin to patent PDA and PLB branches (Figures 5 C1, C5 & C6).

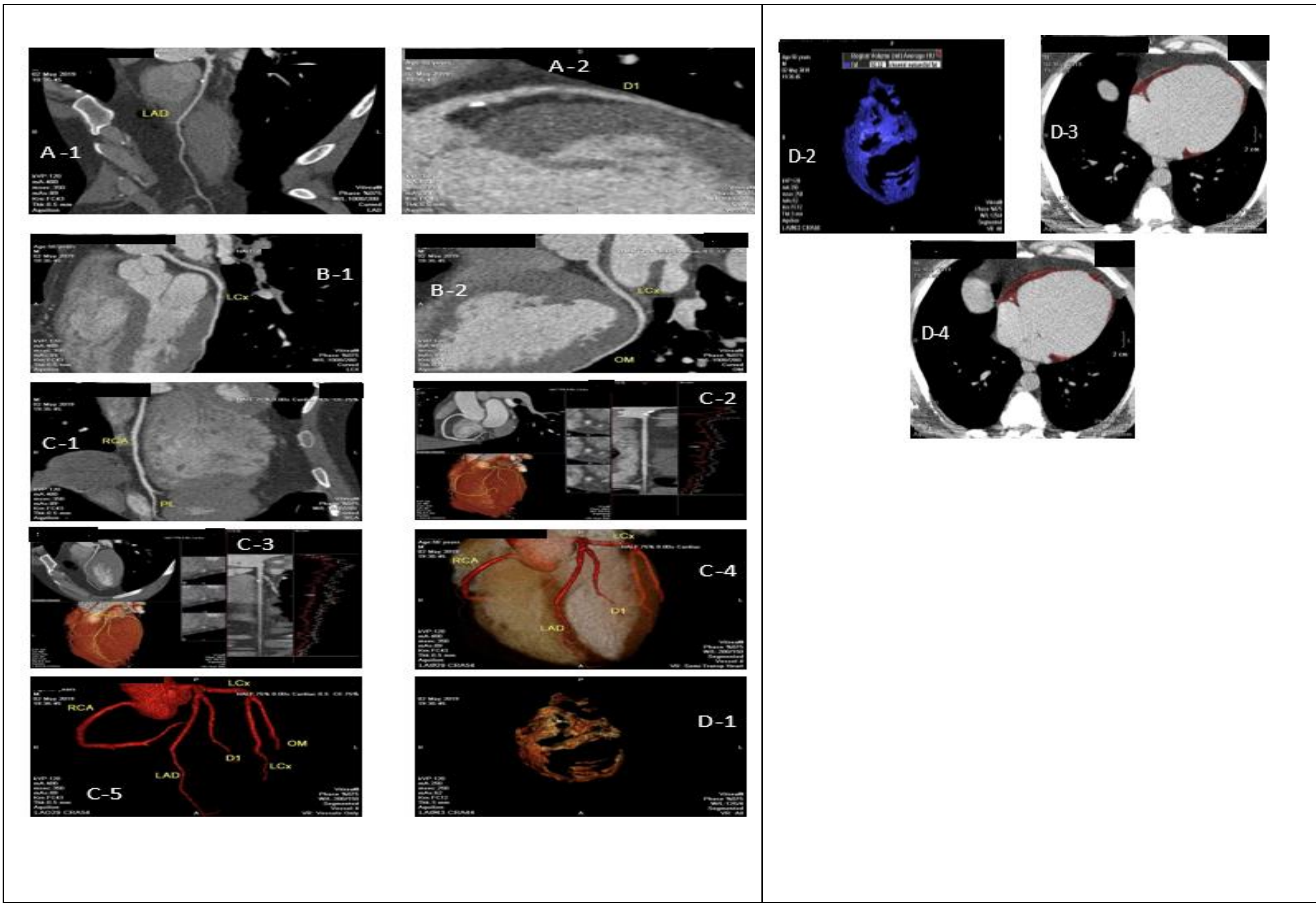

Figure 4: 49 years old hypertensive male patient; Ca score matching with mild risk of CAD. Mild increased epicardial Fat thickness. CAD-RAD 2 (mild lesion).

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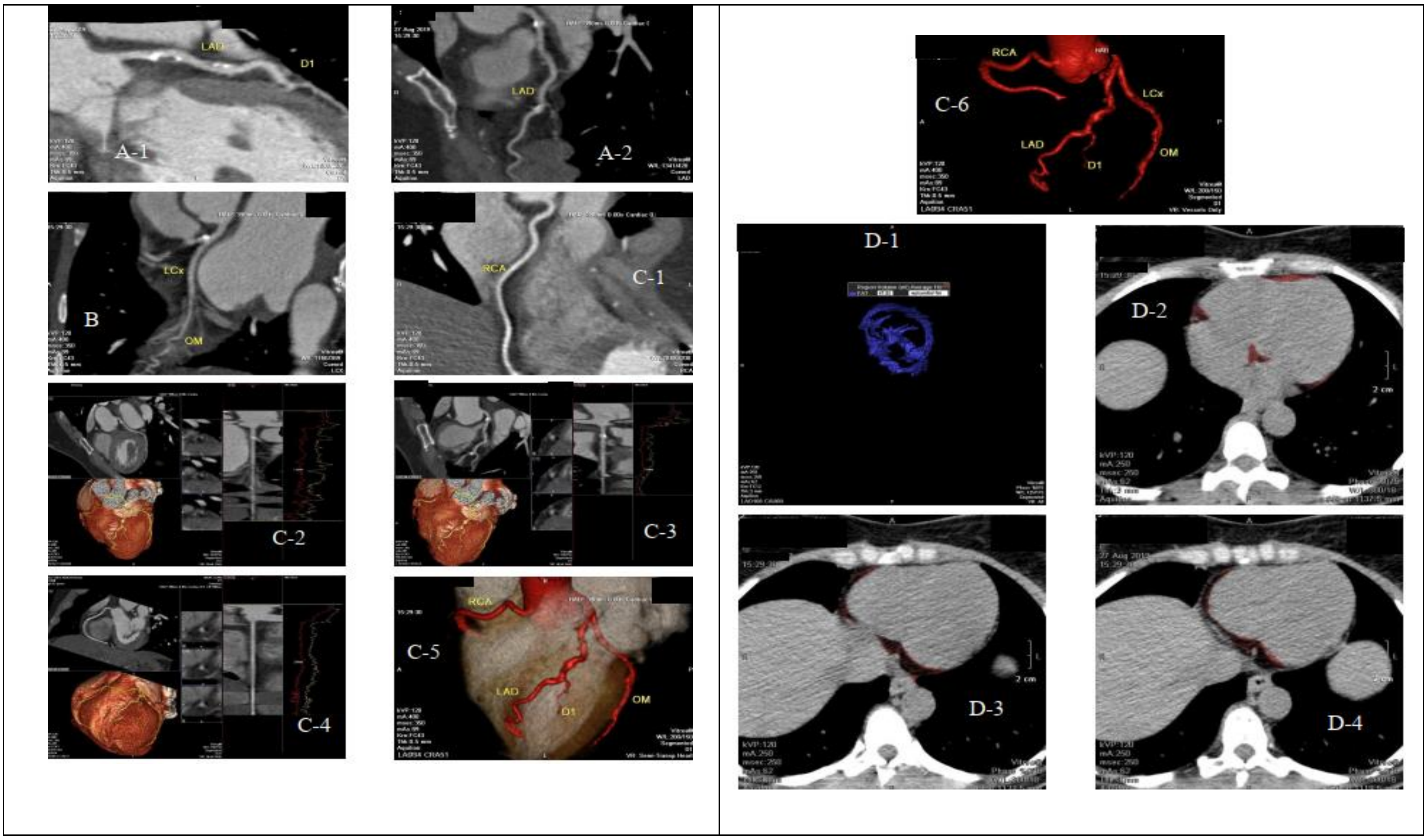

Figure 5: (47 years old) female patient, not smoker, hypertensive with negative family history of CAD; Ca score matching with high risk of CAD, however epicardial fat volume is normal. (CAD-RAD 1).

Discussion

In our study, the mean age was insignificantly different between the two groups. Male were 44% of the non-CAD group and 70% in CAD group. Significant p value (0.029) showed toward male gender in CAD group.

However, a study consisted of 90 consecutive subjects (age: 63 ± 12 years; men: 47, women: 43) who underwent 256-slice MDCT coronary angiography. EATV was measured as the sum of cross-sectional epicardial fat area on CT images, from the lower surface of the left pulmonary artery origin to the apex. Subjects were segregated into the CAD group (coronary luminal narrowing > 50%) and non-CAD group. They reported that age was higher in the CAD group than in the non-CAD group (P=0.003) [11]. This may be contributed to different ethnic group or geographical factors or different lifestyle.

In the current study, risk factors for CAD showed statistical significance in the number of hypertensive and diabetic patients.

This was disagreed with a study that found no differences between the hypertensive and normotensive patients concerning significant CAD (35.9% and 24%) [12].

According to EFV in our study, came in line with our study, a study reported that patients with CAD had significantly greater epicardial fat volumes (mean = 86.785 cm3) than those with normal (non-CAD group) (mean = 40.135 cm3) (P value < 0.0001) [13].

Also**,** a study on 120 patients, 22 patients were negative for CAD, while 98 patients had positive CAD. They found that there was significant difference between negative CTA patients and positive CTA patients as regard epicardial fat volume ($p < 0.001$) [14].

The mean Calcium score in non-CAD group was 31.28±64.77 and 208.57±89.40 for the CAD group. It was significantly higher in CAD group.

This was agreed by a study which found that median CAC score was 5 Agatston units (IQR, 0–107; range, 0–5073). Median EAT volume was significantly higher in patients who had baseline coronary calcification compared to those with a CAC score of zero on the baseline scan (85.8 cm3 vs. 69.3 cm3, respectively, $p < 0.001$) [13]**.**

Also, a study measured Ca in 6814 participants during 5.8 years of follow-up; among patients with coronary calcifications; 5878 CHD events occurred, of which 122 were myocardial infarction death from CHD, or resuscitated cardiac arrest with statistically significant difference from the remaining patients without coronary calcification included in the study [15].

In the present work, mean level of EFV was measured in different grades of CAD lesion. A significant increase in mean level of EFV according to severity of CAD. Similar to EFV, CA score mean level was measured in different CAD lesion grades. A statistically significance ($p<0.001$) showed a strong relation with level of Ca score with severity and grading of CAD.

A study found that here was significant difference between both groups as regard epicardial fat volume ($p < 0.001$), and good relation was found between the amount of epicardial fat volume and coronary calcium score, number of affected vessel, plaque burden and degree of stenosis ($p < 0.001$) [14].

ROC curve of EFV was conducted for prediction of CAD disease activity. EFV showed 0.813 area under curve at cut off level 60.39 with good sensitivity and specificity.

In a study and by using the ROC curve, epicardial fat volume > 124 cm3 was identified as optimal cut off value (sensitivity 78.57%, Specificity 72.73%) to detect positive CTA patients (AUC = 0.833, $p < 0.001$) [14].

In the current study, ROC curve of Ca score was conducted for prediction of CAD disease activity. Ca score showed 0.947 area under curve at cut off level 90 with high sensitivity and specificity. A study on 2527 patients found that using calcium score cutoff point of 100, has a high specificity (87%), sensitivity (79%) for diagnosing significant stenosis [16].

Also a study involved132 consecutive patients. Coronary computed tomography (CCT) angiography was performed in a multi-detector computed tomography scanner. They showed that based on the ROC curve, CAC score of 9.8 (≈ 10) presented as an optimal cut-off point for discriminating obstructive CAD (sensitivity: 0.79, specificity: 0.75). Yet, when the cut-off was upgraded to 100, the sensitivity and specificity were 0.48 and 0.92, respectively [17].

In our work, correlation analysis of CAD grading and other markers in this study showed a strong positive relation with both EFV and Ca score in CAD group. While no significant relation with age of the patients.

In line with our study, in another cross-sectional study, 748 consecutive patients with suspected CAD, referred for coronary computed tomography angiography (CCTA), were enrolled. The mean CACS was compared between patients with different severities of coronary artery stenosis. Their study reported a significant positive association between the severity of CAD and Ca score (P value<0.001, r=0.781) [18].

Additionally, a study enrolled one hundred and fifty-one patients undergoing MSCT for suspected CAD. Non-enhanced images were acquired to assess calcium score.

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Contrast enhanced images were used to quantify EFV, PFV and severity of luminal stenosis. There was a significant linear correlation between coronary artery stenosis severity and EFV [(19)].

Our study showed that logistic regression analysis was conducted for the prediction of CAD activity using DM, hypertension, EFV, Ca score and CAD risk score. DM, hypertension, EFV, Ca score and moderate CAD risk were associated with risk of CAD in univariate analysis. Only EFV was associated with risk of CAD in univariate and multivariate analysis.

EFV and regional epicardial thickness are correlated with severity of CAD and could be used as a reliable marker in predicting CAD severity [(19)].

The prevalence of coronary artery calcium, significant stenosis, and high-risk plaque increased sharply in patients with high EFV, which was associated with higher rate of cardiac death and myocardial infarction [(20)].

Conclusion

The EAT volume has good prognostic value for developing CAD and increased EAT is considered a risk factor for CAD. Ca score could have an appropriate prognostic value for the determination of coronary artery disease.

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Author contribution

Authors contributed equally in the study**.**

Conflicts of interest

No conflicts of interest

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