Correlation between Epicardial Adipose Tissue Volume and Coronary Artery Disease Incidence in A Group of Patients Complaining of Chest Pain

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Abstract

Background: Coronary artery disease is associated with many risk factors; one of them is the regional fat distribution that was found to play an important role in the development of atherosclerosis, vascular dysfunction as well as inflammatory promotion [1].

The current study analyses the long standing clinical impact of increased EAT volume evaluated by CT in a group of personnel without any previous documentation of having CAD [2].

Aim of Study: The aim of this study is to evaluate the relation between the volume of the epicardial adipose tissue versus incidence and severity of Coronary Artery Disease (CAD); thus depicting the association between their occurrence, if any.

Patients and Methods: Fifty patients presented by chest pain showing suspicious symptoms of CAD were investigated by coronary artery CTA on Toshiba 640 CT scan during nine months duration.

A pre-contrast study was performed for each patient followed by standard coronary artery CTA protocol.

Image processing and measurements were done on Toshiba 640 work station where measurements were performed at the mid-diastolic phase using retrospective cardiac gating about 75% of PR interval.

The data were analyzed independently by two consultant radiologists with experience of 10 to 20 years in cardiac imaging.

Results: The estimated epicardial adipose tissue volume ranged from 30 to 226 CM3 with mean of 93Cm 3 ± 50.7 SD and median of 92.5cm^3.

The least Agatstone CA scoring was 0, and the maximum one was 1400, while estimated mean was 253 ±383 SD.

Pearson correlation revealed significant correlation between EAT volume and each of calcium scoring and CAD severity.

Receiver operator characteristic curves were performed for the coronary artery disease as well as both EAT and CA scoring as etiological factors revealing statistically significant results.

Conclusion: Although the epicardial tissue fat has a protective, immuno-modulator buffering effect, the EATV was found to be proportional to the incidence of CAD and could be used as a bad prognostic factor for coronary artery disease.

Conflicts of Interest: None.

Key Words: *Coronary artery disease –Epicardial adipose tissue.*

Introduction

CORONARY artery disease is associated with many risk factors; one of them is the regional fat distribution that was found to play an important role in the development of atherosclerosis, vascular dysfunction as well as inflammatory promotion. EAT is associated with unhealthy lethal and un-lethal coronary consequences among general population in out of dependence of other well established cardiovascular morbidity risk factors [1].

The current study analyses the long standing clinical impact of increased EAT volume evaluated by CT in a group of personnel without any previous documentation of having CAD, and implying the evaluation of EATV as a prognostic factor obviating its relation with the severity and extent of CAD.

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Abbreviations:

CAD   : Coronary Artery Disease.
EAT   : Epicardial Adipose Tissue.
EATV : Epicardial Adipose Tissue Volume.
MPR   : Muti-Planar Reformation.
LAD   : Left Anterior Descending.
RCA   : RT Coronary Artery.
LCX : LT Circumflex Artery.

The fatty tissue of the heart is known to have a bi-layered distribution, including the visceral and pericardial layers separated by the parietal pericardium [2].

At embryonic life epicardial fat arise from brown adipose tissue. Epicardial fat and myocardium have a common blood supply, being perfused by the same coronary arterial territories, lacking muscular fascia thus allowing the epicardial fat and myocardium to share the same microcirculation intensifying the interactive metabolic relation between each other [3].

EAT has a forked dichromatic role, although having protective buffering, fatty acid absorbing and energy preserver role, it implicates hazardous effect, being associated with increased incidence of CAD, with subsequent myocardial affection [4].

EAT is the real visceral fatty tissue that is usually deposited within the atrio-ventricular and inter-ventricular grooves with local modulation and interference with the coronary arteries, where it alters insulin sensitivity in both paracrine and endocine routs, it also modifies the macrophage attraction, promoting the inflammatory cascades, with subsequent fatty tissue malfunction [5].

It has been assumed by multiple studies that the increased epicardial fatty tissue volume is highly associated with raising plaque instability, as well as arterial thrombosis chances, highlighting its potential effect as a pivot CAD development risk factor [6].

Aim of the work:

This is a prospective analytical cohort study. Its aim to assess the relation between the epicardial adipose tissue volume and the incidence as well as the degree of CAD, reflecting the prognostic association and evaluating the EATV as a predictor of CAD incidence.

At the present study, we evaluate the association between the volume of EAT (EATV) and incidence of atherosclerotic plaques as well as the CA++ scoring by Agatston score method as risk factors that would affect CAD incidence.

Patients and Methods

Our sample included 50 patients referred from the Cardiac and Intrenal Medicine Clinic, at International Medical Centre to the Radio-Diagnosis Department for coronary CT evaluation after approval of the ethical committee.

Their ages ranged from 36 to 73 years, with mean age of 53 years, including 33 (66%) males and 17 (34%) females.

Inclusion criteria included patients presented with chest pain having suspicious symptoms of CAD and no similar previous history.

Exclusion criteria included deteriorated renal function, clinical symptoms of heart failure, previous coronary artery by-pass surgeries and high clinical suspicious index of CAD with severe active symptoms warranting direct angiographic intervention.

The study was performed in nine months duration commencing at June 2018 till March 2019 at the International Medical Centre, Radiology Department, after obtaining a written consent from our study group patients after explaining the procedure to them with illustrated possible hazardous effects of the radiation exposure and IV contrast injection.

All scans were done on Toshiba 640 CT scan, where a pre-contrast study prior to contrast injection was performed for each patient, proceeded by ECG gated scanning, with standard coronary artery CTA protocol, patients should have a heart rate less than 75 BPM, otherwise a B-blocker may be used prior to the scanning in order to get an appropriate study (in case of lacking contraindication for the use of B-blockers).

Imaging acquisition was accomplished during inspiratory breath holding, in about 7 to 10 second duration with slice collimation of 64 X 0.625 and 420ms gantry rotation time.

Image processing and measurements were done on Toshiba 640 work station where measurements were performed at the mid-diastolic phase using retrospective cardiac gating about 75% of PR interval.

EAT three-D volumetric calculation was done considering the fatty attenuation values to lie between (–30 to –190) HU calculated at the pre-contrast study used for Agatston calcium scoring calcification.

The areas of epicardial visceral fatty pockets were traced during mid-diastolic phase extending from the lower margin of aortic root till about 7 mm inferior to the cardiac border, then the measured areas were summed and multiplied by the slice thickness 2mm to get the total volume of EAT.

The data were analyzed independently by three consultant radiologists with experience of 10 to 20 years in cardiac imaging. Numeric data were evaluated using mean and standard deviation, while percentage was used to express categorical data variables.

According to stenotic severity and extent we divided the candidates of the study into those with null (no plaques), mild (insignificant stenotic coronary segments less than 50% luminal stenosis of any coronary vessel other than LT main branch), moderate affection (50 to 75% luminal stenosis, in one or more vessel other than Lt main branch) and serve stenosis (more than 70%, or more than 50% of LT main branch).

Results

Our study included 50 patients. The range of patients' age in our study ranged from 36 to 73 years, with mean of 53.8±8.8 SD years.

The estimated epicardial adipose tissue volume ranged from 30 to 226CM^3 with mean of 93Cm 3±50.7SD and median of 92.5cm^3.

The least Agatstone CA scoring was 0, and the maximum one was 1400, while estimated mean was 253±383SD.

Pearson correlation was used to estimate the correlation coefficient, as well as to determine the correlation significance to prove, or disclose it.

Significant correlation was noted between EAT volume and each of calcium scoring and CAD severity.

The correlation coefficients were 0.450 and 0.627 respectively with statistically significant difference, where p-values were 0.001, and 0 respectively.

A positive correlation was noticed between CAD and CA scoring where there was a statistically significant results with 516 correlation coefficient

Receiver operator characteristic curves were performed for the coronary artery disease as well as both EAT and CA scoring as etiological factors, using the cutoff point between the normal (null) versus mild coronary artery disease, as a true positive status. The area under the curve for (EATV) was 713, with statistically significant result (the p-value=.028), while the area under the curve for Ca scoring was 0.818, showing p-value of 0.001, the estimated cut off value of EAT to predict the incidence of CAD is 102cm^3, while the cut off

value of CA scoring where beyond CAD is expected was estimated at 257.

The population pyramid count assigned between the EATV and CAD severity reflects that the efficacy of EATV as a bad prognostic factor is more evident at the moderate and severe CAD than at the mild CAD category, where the values of EATV is seen with rather proximity between the normal patients with normal CTA studies and those with mild degree of coronary artery diseases.

Table (1): Statistical parameters for age, EAT, and CA scoring.

	Age	EAT	CA
N:			
Valid	50	50	50
Missing	0	0	0
Mean	53.8400	93.0400	253.6600
Std. error of mean	1.25499	7.16642	54.18144
Median	54.5000	92.5000	85.0000
Std. deviation	8.87409	50.67421	383.12062
Variance	78.749	2567.876	146781.413
Range	37.00	196.00	1400.00
Minimum	36.00	30.00	.00
Maximum	73.00	226.00	1400.00

Table (2): Percentage of CAD severities among study population.

CADs:	
Mild	22.0%
Moderate	24.0%
Null	32.0%
Severe	22.0%

Table (3): Study population percentage according to their gender

Females	17	34.0%
Males	33	66.0%

Table (4): Correlation between EAT, Ca scoring, and CAD.

	Age	EAT	CA	CADs
Age:				
Pearson correlation	1	.022	.147	.109
Sig. (2-tailed)		.878	.308	.451
N	50	50	50	50
EAT:				
Pearson correlation	.022	1	.450**	.627**
Sig. (2-tailed)	.878		.001	.000
N	50	50	50	50
CA:				
Pearson correlation	.147	.450**	1	.516**
Sig. (2-tailed)	.308	.001		.000
N	50	50	50	50
CADs:				
Pearson correlation	.109	.627**	.516**	1
Sig. (2-tailed)	.451	.000	.000	
N	50	50	50	50

**: Correlation is significant at the 0.01 level (2-tailed).
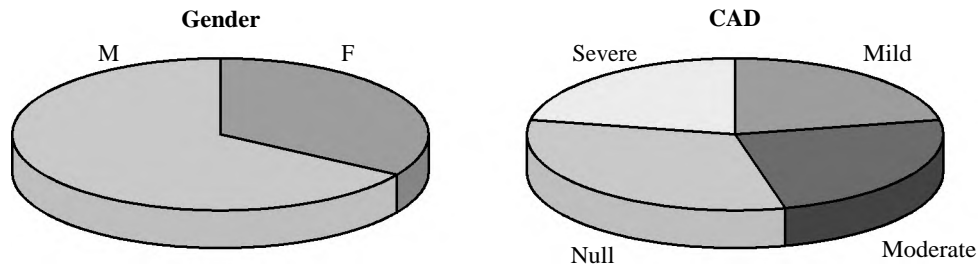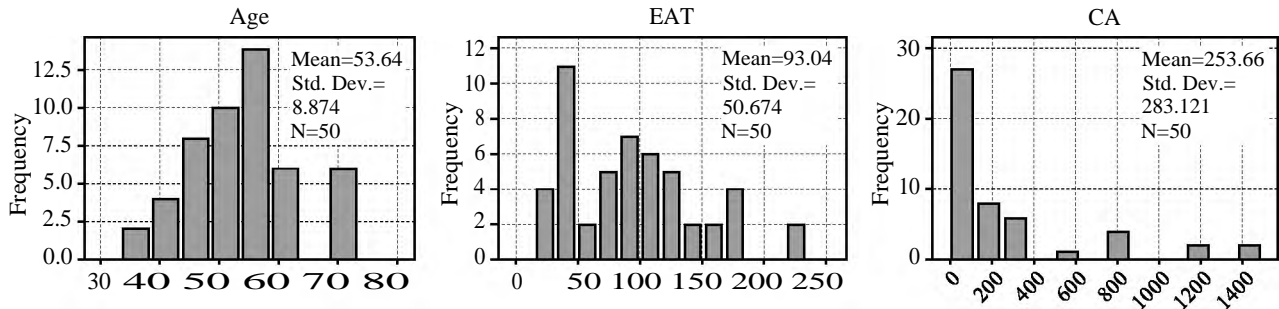
Gender

CAD

Fig. (1): Pie charts for gender, and CAD severity.

Fig. (2): Representative bars, for the frequency of age, EAT volume and CA scoring among study group personnel.
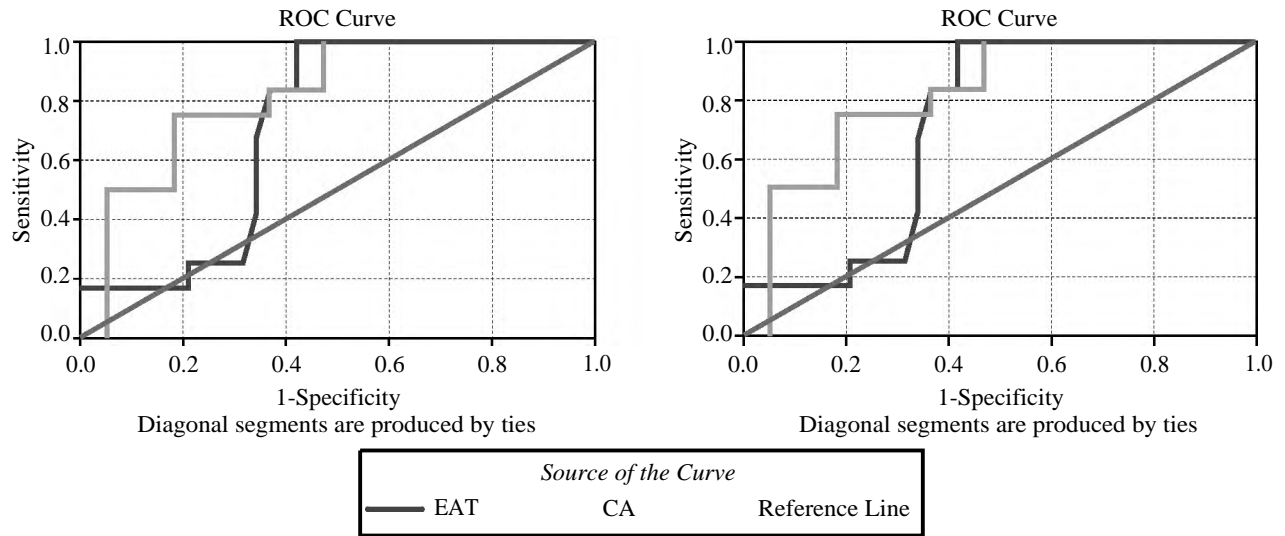
Source of the Curve

EAT   CA   Reference Line

Fig. (3): The area under the curve for EAT (blue), and CA scoring (red) as aetiological l factors of coronary artery disease.

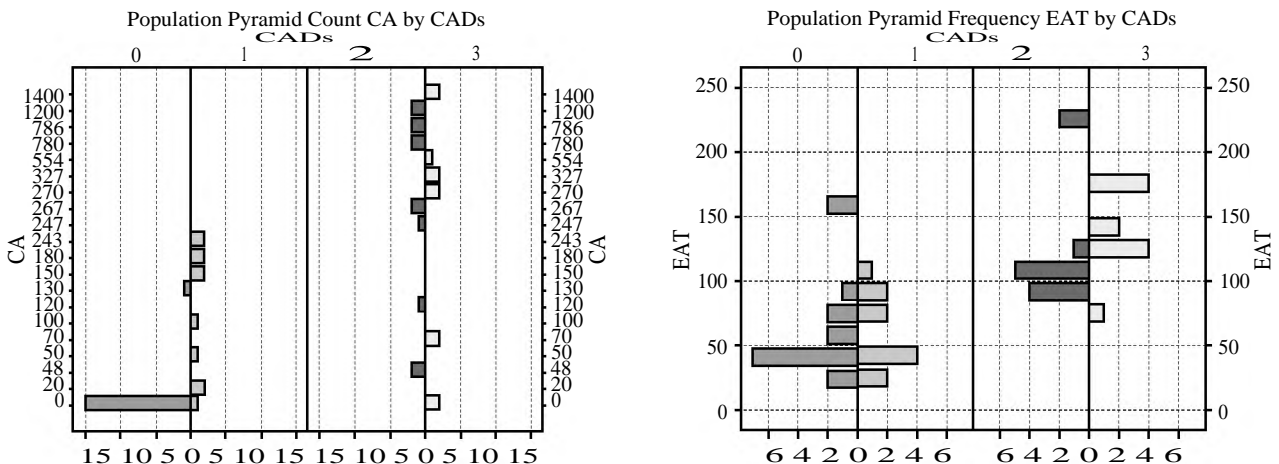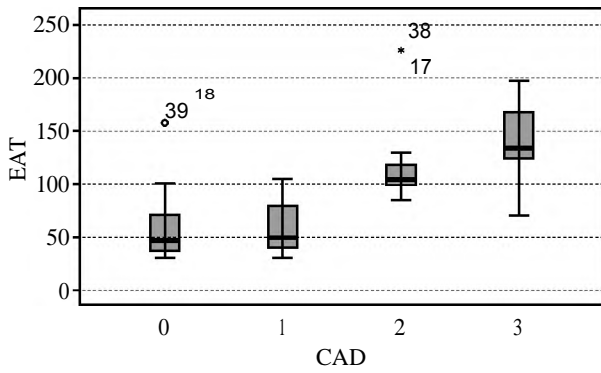Fig. (4): EAT Stem-and-Leaf Plot for CAD, 0=Null , I=Mild , 2=Moderate, while 3=Severe coronary artery disease.

Fig. (5):

Table (5): Area under the curve for EAT, and CA scoring.

Test result variable (s)	Area	Std. Errora	Asymptotic Sig.b	Asymptotic 95% confidence interval	
				Lower Bound	Upper Bound
EAT	.713	.073	.028	.570	.856
CA	.818	.063	.001	.694	.942

The test result variable(s): EAT has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.
a: Under the nonparametric assumption
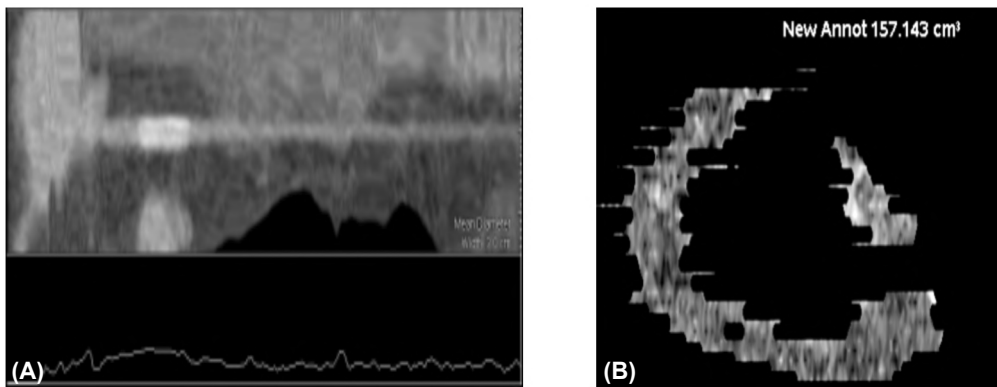b: Null hypothesis: True area=0.5.

Cases:

Fig. (1): 60 years old male presented with severe typical chest pain. (A) Luminal MPR shows a luminal stent, with adequate distal run off, (B) Shows epicardial adipoase tissue volumetry, estimated volume was 157cm^3.
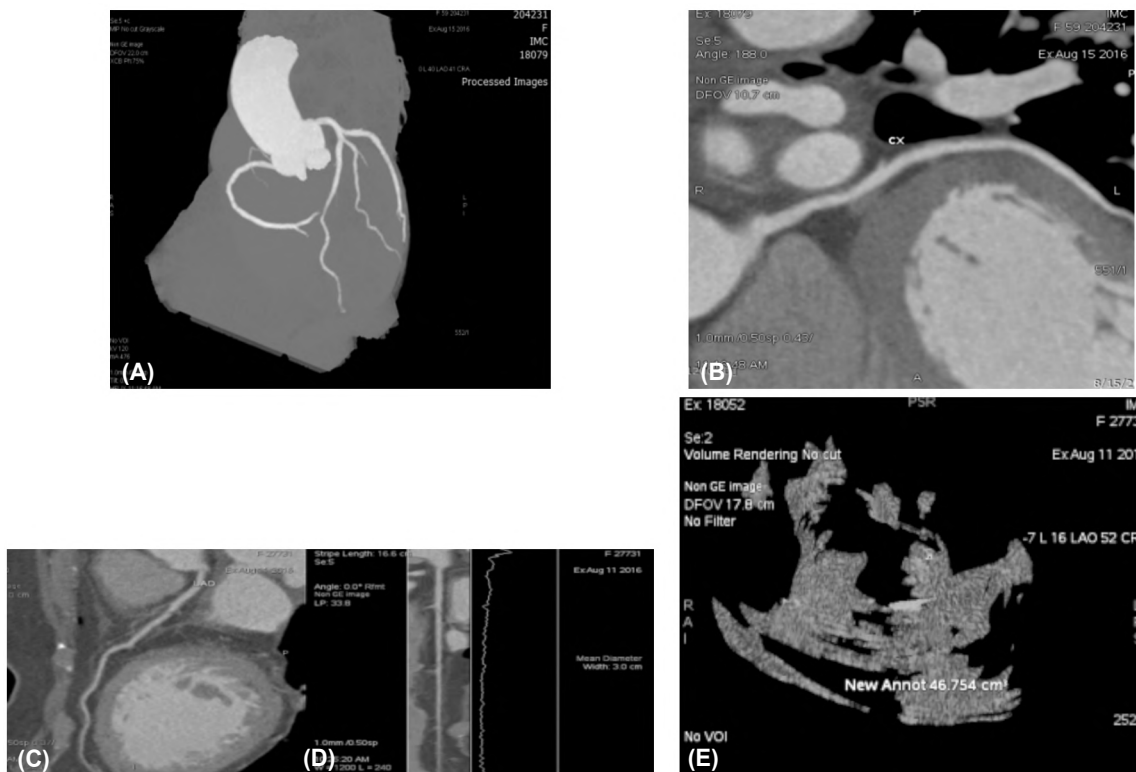

Fig. (2): 55 years old female presented with atypical chest pain. (A) Angiographic view (B,C) Curved planar reformation, (D) Luminal MPR showing normal scanned well opacified scanned coronary arteries, no luminal stenosis, (E) Estimated EATV was about 67.7cm^3, CA score was 0.
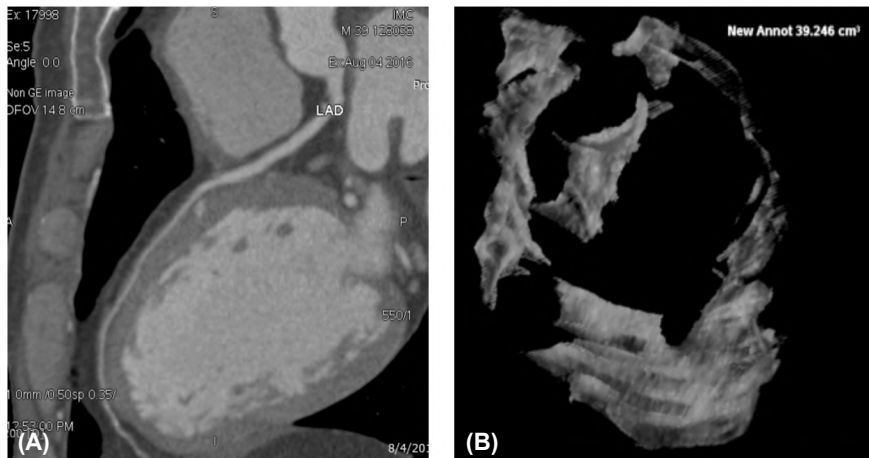
Fig. (3): 55 years old male presented by typical chest pain and dysnea. (A) Shows CPR of the LAD, no stenotic segments nor definite plaques seen, superficial myometrial bridging was noted although the body mass index in this patient was 25.5 (over-weight) the estimated EATV was 39.4cm^3 (as illustrated in B). CA score was 0.

Fig. (4): 65 years old female presented with dysnea on exertion and typical chest pain. (A): (Luminal MPR), (B) (Curved MPR) revealed a mid course RCA stenosing soft plaque (moderate stenosis), with positive remodeling, the estimated EATV was about 168.9CM^3.
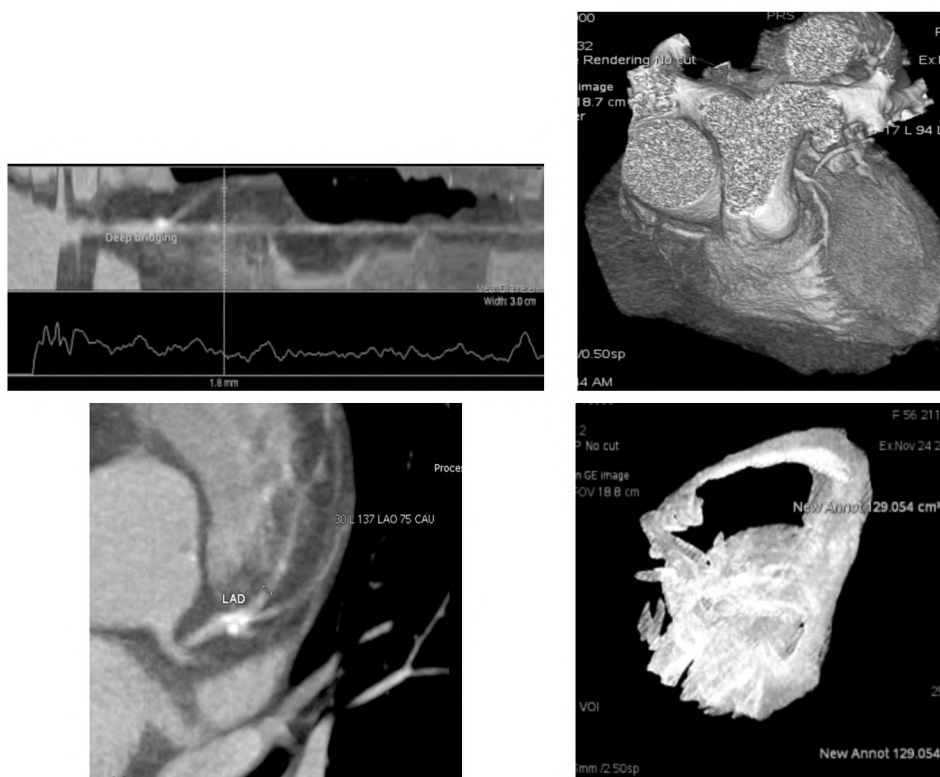

Fig. (5): A 45 years old male presented with atypical chest pain and epigastric pain. (A): Luminal MPR, (B) Curved MPR shows a calcified atherosclerotic plaque at the proximal segment of LAD exerting severe luminal stenosis (more than 75%). (C) VR, revealing preserved distal run off. (D) Illustrates the EATV that was about 129CM^3, CA score was 265.
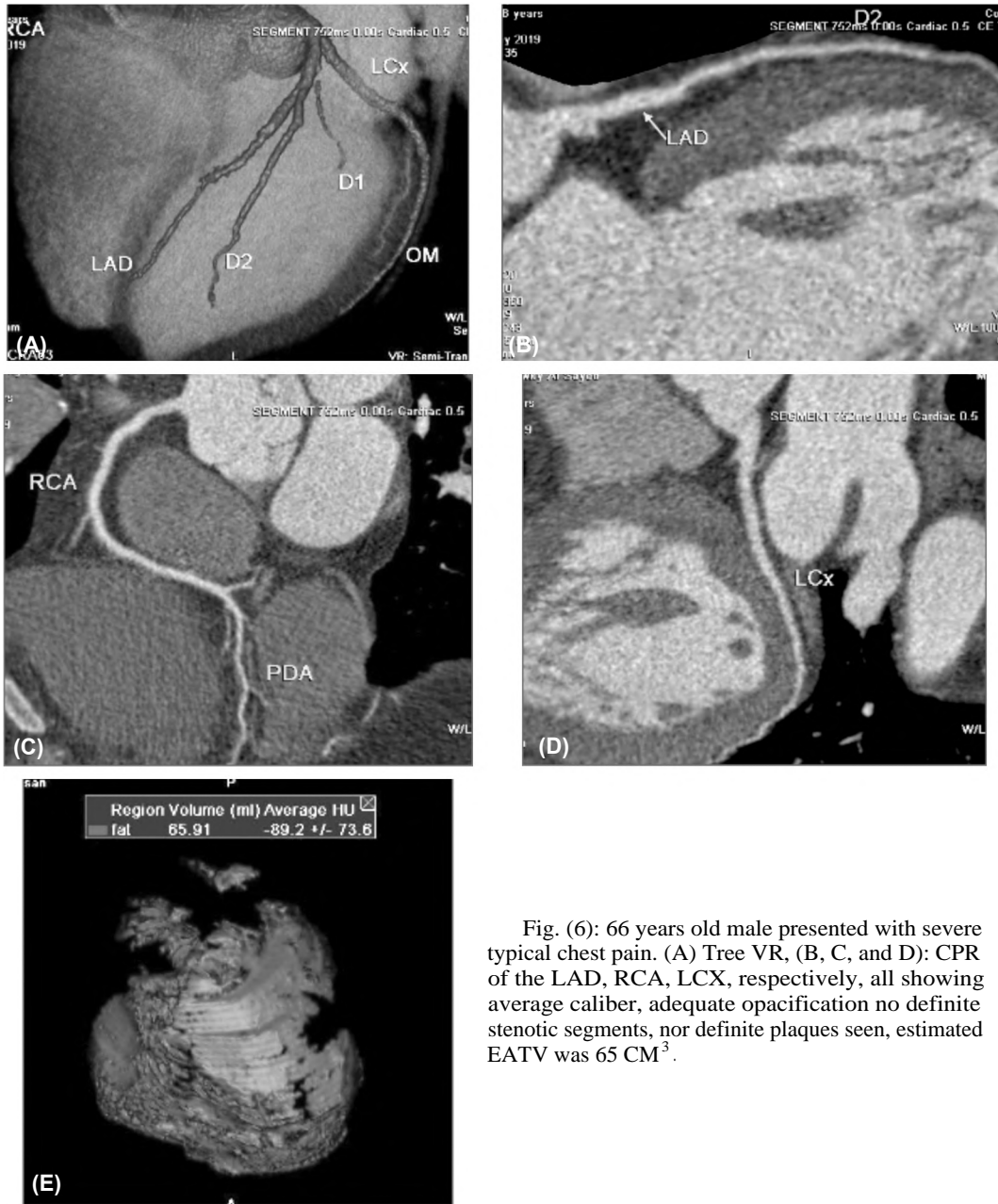
Fig. (6): 66 years old male presented with severe typical chest pain. (A) Tree VR, (B, C, and D): CPR of the LAD, RCA, LCX, respectively, all showing average caliber, adequate opacification no definite stenotic segments, nor definite plaques seen, estimated EATV was 65 CM^3.

Discussion

It is well known that the EAT is composed of adipocytes that alters the cellular function of both paracrine and endocrine bases via modification of insulin resistance, thus exacerbate macrophage activities, promoting an inflammatory cascade [7]. EAT is directly proportional to the inflammatory activities, with subsequent vascular stiffness, plaque instability, arterial thrombosis and degree of athero-sclerosis [8].

At the present study, the estimated cut off value for pericardial tissue volume to predict association with CAD incidence was 102cm^3, this value was approximate to that reported by Sarin et al., [9] where the EFTV was measured, and coronary computed tomographic angiography was performed using a standard protocol, at their studies, they found that EFV ranged from 25 to 274ml (mean 121 ± 47), and correlated with age, coronary calcium score, it was significantly higher in patients with EFV >100ml (67 ± 155 vs. 216 ± 639; $p=0.03$), and a higher percentage of patients with increased EFV had CAD (46% vs. 31%; $p<0.05$). At their study, they concluded that quantification of EFV was feasible using MSCT. And assumed that measurement of EFV may provide another useful noninvasive indicator of heightened risk of CAD in addition to calcium score and coronary angiography.

In a study for Kunita, et al., [3], they reported that coronary attacks were associated with increased CAC score categories. These were significantly higher in those with higher EAT volume group (> median; 107.2mL, 0.7% vs., 2.1%, adjusted hazard ratio; 2.65, p=0.0090), that result is approximate to ours where a positive correlation were found between both calcium scoring, and EATV, and the coronary artery disease incidence, with a rather close cut off value of about 107cm^3 compared to 102 at ours.

Their analytical study demonstrated that a combination of CAC score ≥100 and high EAT volume had a significantly higher event rate than CAC score <100, while our result assumed a value of 257 CA scoring as a cut off value for CAD incidence.

Rishabh et al., [11], performed a study among Indian populations, concerning the correlation of epicardial fat quantification and severity of coronary artery disease, and they reported that a higher quantity of epicardial fat is found in patients with increasing severity of coronary artery stenosis. EATV correlated with age, weight, and Body Mass Index (BMI). Multivariate analysis revealed EFV to be an independent risk factor for the presence of CAD.

They estimated EATV cutoff for the presence of CAD and obstructive CAD are 49.75 and 67.69ml. This difference from our results may be due to an ethnic variation between the Indian and Egyptian people.

One of the studies that evaluated the CA score and correlated it with CAD incidence is that of Kaczmarska and his colleagues [12], where 1132 patients were included in analysis (58.7±10.9 years, 46.7% males). Coronary Computed Tomography (CCT) angiography was performed in a multidetector computed tomography scanner. Coronary artery calcium score was calculated by the Agatston score. Obstructive CAD was assumed as the presence of coronary artery stenosis ≥50% on CCT angiography. In the Receiver Operating Characteristics (ROC) curve analysis a CAC score of 10 was used as an optimal cut-off point for discriminating obstructive CAD (sensitivity: 0.79, specificity: 0.75, p<0.0001), and concluded that the cutoff point of 10 for CAC score determined patients with CAD with the best sensitivity and specificity. This result varies with ours, where the estimated cut off for coronary disease incidence was 257 CA score.

This broad variation between the cut of value of Ca scoring as a CAD predictor among studies may be supported by the results of Almoudi M and Sun Z study [10]; that documented that there are many limitations of applying CA scoring as a screening tool to broad populations, and this has been systematically reviewed, by the authers who remarked that CA score should be judiciously used by physicians in patients with different risk factors of developing cardiovascular events. And recommended further screening wide based population studies.

Another study for Zhou et al., [13], where results were derived from 5743 patients used an internal cohort study type. They estimated area under the receiver operating characteristic curves, the authors supposed that EATV improved prediction above conventional risk factors and coronary calcium score (area under the receiver operating characteristic curve increased from 0.856 to 0.874. Our study showed that AUC for EATV, and CA score were about 0.713, and 0.818 respectivly, with statistically significant results values.

Conclusively, our study shares the same fact that epicardial adipose tissue volume could be used as a bad prognostic indicator for coronary artery disease incidence.

Limitation of the study:

This study determines only the association between the EATV, and the coronary artery diseases incidence, thus did not evaluate the amount of inflammatory mediators that likely to be implicated in the pathogenesis of atherosclerosis and CAD incidence.

Lack of body mass index measurement was another limitation at the current study. We suggest future research work up to assess those.

Conclusion:

The results of our study suggests the association between the amount of EATV and the incidence of CAD, reflecting the association between their incidence, despite the well known protective effect of epicardial adipose tissue for the coronaries via preventing the direct traumatizing effects, yet it has a harmful effect in large amount, where it acts as a source of inflammatory mediator thus contribute to the atherosclerotic pathogenesis.

In summary, although the epicardial tissue fat has a protective, immuno-modulator buffering effect, the EATV was found to be proportional to the incidence of CAD and could be used as a bad prognostic factor for the latter occurrence.

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العلاقة بين آحجام الدهون النخابية المحيطة بالقلب
وإمكانية حدوث آمراض الشرايين التاجية
فى مجموعة من المرضى يعانون من آلام صدرية

الدهون المحيطة بالقلب تكمن فى إثنين من مستودعات مميزة مفصولة بالتامور، وهى الآنسجة الدهنية النخابية ومجاور التامور. وتعرف الدهون النخابية مثل الآنسجة الدهنية الواقعة بين الجدار الخارجى للعضلة القلب وطبقة عميقة من التامور.

يتم تزويد الدهون النخابية من فروع الشرايين التاجية ولا يوجد رباط عضلى يفصل بين مستودع الدهون وعضلة القلب. ومن هنا، وحيث آن الإثنين يشتركان فى نفس الآوعية الدموية الدقيقة المغذية فهذا يسمح بفرضية وجود تفاعل مباشر بين الدهون النخابية وعضلة القلب.

الآنسجة الدهنية النخابية تفرز بعض الهرمونات التى تساعد فى عملية تصلب الشرايين. وبذلك تساهم فى التسبب فى آمراض الشرايين التاجية نظراً لقربها كما يمكن قياس حجم الدهون النخابية بإستخدام الآشعة المقطعية متعددة الكواشف وتهدف هذه الدراسة لتقييم العلاقة بين آحجام الدهون المحيطة بالقلب وإمكانية حدوث آمراض الشريان التاجى.

وبالإضافة إلى ذلك، يتم إستخدام الآشعة المقطعية متعددة الكواشف على نطاق واسع لتقييم درجة الكالسيوم التاجى، وهو مؤشراً مستقلاً لتشخيص آمراض القلب والآوعية الدموية، والحصول على دراسة غير الغازية لتقييم الشرايين التاجية.

حيث وجد آن النظم الحالية الآشعة المقطعية متعددة الكواشف تسمح بتصوير حجم القلب بآكمله خلال دورة القلب كامل وهكذا فتحت التصوير إلى مجموعة واسعة من التطبيقات القلب. وقد وصلت الدراسة إلى آن هناك علاقة وإرتباط بين كل من كمية الدهون النخابية حول القلب ودرجة الكالسيوم التاجى، من جهة وإمكانية حدوث آمراض الشرايين التاجية من جهة آخرى ومن ثم معرفة التدخل المناسب لحماية المريض والوقاية المبكرة للذين يعانون من آمراض الشريان التاجى.