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Peri-Coronary Epicardial Adipose Tissue and Coronary Artery Calcification as Markers of Atherosclerotic Burden in Postmenopausal Women

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ABSTRACT

Background: Peri-coronary epicardial adipose tissue (EAT) may play a role in coronary atherosclerosis via localized inflammatory and paracrine mechanisms. This study sought to evaluate the correlation between peri-coronary epicardial adipose tissue, coronary artery calcification, coronary atherosclerotic lesions, and cardiovascular risk factors in post-menopausal women.

Method: This study involved 200 post-menopausal women with suspected coronary artery disease. All participants underwent clinical evaluation, laboratory tests, coronary artery calcium (CAC) scoring, and multislice computed tomography coronary angiography. The thickness of peri-coronary EAT was assessed surrounding the left main, LAD, LCX, and RCA. Based on MSCT results, patients were put into two groups: a coronary lesion group and a control group.

Result: There were coronary lesions in 140 women. Cases with coronary lesions had CAC scores that were much higher than those of the controls (219.64±345.55 vs. 111.5±301.33; p=0.028). There was a big difference between the patient group and the control group in peri-coronary EAT around LAD, LCX, and RCA. However, there was no big difference in LM EAT. EAT around LAD, LCX, and RCA was strongly linked to significant CAC, dyslipidemia, and a positive family history, but not to age, obesity, smoking, high blood pressure, or diabetes.

Conclusion: In post-menopausal women, peri-coronary EAT had a positive correlation with CAC and coronary atherosclerotic lesions. It was also linked to certain cardiovascular risk factors, especially dyslipidemia and family history. This suggests that peri-coronary EAT could be a useful imaging marker for the burden of coronary atherosclerosis.

KEYWORDS: Epicardial adipose tissue; coronary artery calcification; multislice computed tomography; coronary artery disease; post-menopausal women.

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INTRODUCTION

Visceral adiposity (VAT) is used as a cardiovascular risk marker. Its roles in the pathogenesis of atherosclerotic diseases may be important [1].

Epicardial adipose tissue (EAT) is a part of visceral fat present surrounding subepicardial coronary arteries (CAs) and around the heart. Abdominal adipose tissue has a common embryological origin with EAT. Moreover, EAT of subjects with significant coronary artery disease (CAD) was discovered to be a cause of some inflammation mediators and demonstrated important inflammation responses that were not dependent on diabetes or body mass index (BMI) [2].

EAT has a vital role in the progression of atherosclerosis of CAs by its association with usual cardiovascular risk factors and endocrine and direct paracrine effects as well. This theory was supposed based on studies showing that atherosclerosis is absent in intramyocardial CA however present in epicardial CAs [3].

Segments of CAs, which are separated from EAT by myocardial tissue or lacking it were found to have a more protection against developing of atherosclerosis. This might be explained by the lack of fat in the myocardial CAs in comparison to epicardial CAs [4].

Multislice computed tomography (MSCT) angiography denotes a technological evolution in cardiac imaging due to improvement of temporal and spatial resolution. It allowed this technique to become an important and helpful alternative to coronary angiography in particular patients. It exhibited high specificity, sensitivity, and a very high negative predictive value, that makes it a helpful imaging modality for screening patients suspected of CAD [5].

Few studies, which evaluated EAT mainly by the use of echocardiography, exhibiting that EAT surrounding the right ventricle has a significant relation with blood pressure, waist circumference (WC), the mass of left ventricle, and insulin high levels [6].

We need a simple technique that add diagnostic tool to other risk factors without additional cost and during the same MSCT examination.

Aims of the work:
The present study aims to find the association between peri-coronary EAT and cardiovascular risk factors together with CA calcifications and atherosclerosis of CA in post-menopausal women using the MSCT.

PATIENTS AND METHODS

This institutional-based, descriptive, analytical study was conducted at National Heart Institute, Giza, Egypt, at the period from January 2022 to January 2023 on 200 females, attending the institute and suspected to have CA disease (CAD) at the post-menopausal state (A homogeneous group that is highly prone to atherosclerotic cardiovascular diseases).

Inclusion criteria:

- Post-menopausal women aged ≥50 years.
- Women attending the National Heart Institute with suspected Coronary Artery Disease and referred for multislice computed tomography coronary angiography.
- Patients eligible for coronary calcium scoring and coronary MSCT angiography.
- Patients with sinus rhythm and adequate heart rate control allowing proper MSCT image acquisition.
- Women who provided informed written consent to participate in the study.

Exclusion criteria:

- Women who miss the date of onset of menopause, or using hormonal replacement therapy or/ and oral contraceptive pills.
- Women with previous cardiovascular events (percutaneous coronary intervention, CA bypass grafting, and acute coronary syndrome).
- Women with body weight >120 kg.
- Raised creatinine level (women with creatinine ≥2 mg/dl).
- Patients having familial hypercholesterolemia.
- Patients with coronary artery calcification (CAC) score >1500 HU were excluded (because heavy calcification makes the assessment of the CAs difficult).
- Patients who had a history of thyroid dysfunction.

Every participant was subjected to detailed history taking, clinical examinations, 12-lead electrocardiography (ECG), routine laboratory workup including serum creatinine level, complete lipid profile, fasting, post-prandial blood sugar, HbA1C% level and hsCRP.

Imaging workup:

1. Calcium scoring:

The amount of calcium in the CAs was assessed with the 64-slice Toshiba Aquillion MSCT. The heart scans were taken during a single breath hold, by the use of ECG triggering at 50-80% of the R-R interval prospectively, that was dependent on the heart rate of the participant. Coronary artery calcification (CAC) quantification was done in a separated workstation by a calcium scoring software. Based on the score of Agatston et al. [7] CAC was assessed, which measures the calcified area multiplied by a factor dependent on the greatest pixel density.

The Agatston score was calculated for each of the following sites: right CA (RCA), left main (LM) CA, left circumflex (LCX) CA and left anterior descending (LAD) CA, A total score that represents the cumulative burden of calcium within all the previous sites was subsequently quantified for every subject as the final Agatston score. All the sites mentioned before were considered as potential calcifications when they had a pixel density >130 HU [7, 8].

2. Multislice computed tomography (MSCT)

The protocol of coronary arteries angiography:

A 64-slice CT scanner (Toshiba) was used to perform the scans. Breath holding was used to reduce motion artifacts. Oral β-blockers were administered when the patient's heart rate exceeded 70 beats/minute at rest. To determine the timing of acquisition, a test bolus injection was given before injecting the contrast for performing coronary CT angiography (CCTA). The retrospective ECG gating was used to perform CCTA by the following protocol: according to patient's weight the tube voltage 100–140 kV; the tube current was 560 mAs with modulating the dose; the time of gantry rotation was 0.33 s; collimation 0.6 mm, that leads to an isotropic voxel resolution of approximately 0.2 mm^3. According to body weight the contrast (Omnipaque) was adjusted (1.25 cc/kg) and was injected at a continuous rate of 6 cc/s. Reconstruction

of axial scans was performed with 0.75mm slice thickness and increment of 0.4mm. By 64 multi-slice computed coronary angiography & multi-planner reforming (MPR) technique the CAD severity was assessed in terms of number of affected vessels and coronary stenosis severity. Each artery was divided into proximal, mid, and distal parts [9].

No stenosis: was graded as (0) and defined as absence of lesions in different parts of the CAs.

Non-significant stenosis: that was graded (1) and defined as lesions with severity <50% in different parts of the CAs.
Significant stenosis: that was graded as (2) and defined as lesions with severity ≥ 50% in different segments of CAs [including the moderate and severe CA lesions].

3. Measurement of peri-coronary EAT:
The peri-coronary EAT, which surround the LM and the three main CAs were measured in the MSCT scans, by the use of a standardized method, images were transferred to the workstation with adjusting the window settings to render the EAT and pericardium visible. After that, selecting the scans with axial cuts which are perpendicular to the heart surface (to avoid overestimating EAT thickness because of obliquity). This was performed in a separate way for the main three CAs. The cuts, which had the clearest EAT layer were selected for measurement.

II. Statistical analysis:
Analysis of the recorded results by the use of the statistical package for social sciences, version 26.0 (SPSS Inc., Chicago, Illinois, USA). The following tests were performed: Chi-square (χ^2) test, Independent-samples t-test and Pearson's correlation coefficient (r) test.

RESULTS

The present study enrolled 200 females at the post-menopausal state suspected to have CAD. According to their coronary lesions, based on MSCT workup, they were classified into:

1. **Patients' group (A):** 140 females who showed CA lesions (whether significant or non-significant).
2. **Control group (B):** 60 normal females who showed no coronary stenosis.

Table (1): Risk factors prevalence comparison between patients' group (A) and control group (B).

Risk factors prevalence	Total N=200	Group (A) N=140	Group (B) N=60	t-test* χ^2 test#	P-value
Age "years": (M±SD)	57.03±4.12	57.23±4.32	56.73±3.85	0.811*	0.419**
Smoking					
Negative	162(81.0%)	107(76.4%)	55(91.7%)	5.385#	0.020&
Positive	38(19.0%)	33(23.6%)	5(8.3%)		
Hypertension					
Negative	50(25.0%)	30(21.4%)	20(33.3%)	2.571#	0.109**
Positive	150(75.0%)	110(78.6%)	40(66.7%)		
Diabetes					
Negative	126(63.0%)	84(60.0%)	42(70.0%)	1.398#	0.237**
Positive	74(37.0%)	56(40.0%)	18(30.0%)		
Dyslipidemia					
Negative	87(43.5%)	54(38.6%)	33(55.0%)	3.968#	0.046&
Positive	113(56.5%)	86(61.4%)	27(45.0%)		
Family History					
Negative	127(63.5%)	79(56.4%)	48(80.0%)	9.077#	0.003&
Positive	73(36.5%)	61(43.6%)	12(20.0%)		

*: t-test, #: Chi-square test, **: Insignificant difference, &: Significant difference.

The results of table **(1)** and figure **(1)** show that differences between the control group and patients' group are significant in terms of smoking habits (p= 0.020), dyslipidemia (p = 0.046), and family history of cardiovascular diseases (p = 0.003). The patients' group had a higher prevalence of smoking (23.6% Vs 8.3%), dyslipidemia (61.4% Vs 45.0%), and family history of cardiovascular diseases (43.6% Vs 20.0%) in comparison to the control group. On the other hand, the differences between the two groups in terms of age, hypertension, and diabetes were not significant.

Table (2): Anthropometric measures comparison between patients' group (A) and control group (B).

Anthropometric measurements	Total	Group (A) N=140	Group (B) N=60	t-test* χ^2 test#	p-value
W/H: (M±SD)	0.99±0.06	0.99±0.07	0.99±0.06	0.000*	1.000@
BMI: (M±SD)	29.37±3.1	29.5±3.18	29.16±3.01	0.72*	0.472@
Non obese	141(70.5%)	98(70.0%)	43(71.7%)	0.005#	0.946@
Obese	59(29.5%)	42(30.0%)	17(28.3%)		

*: t-test, #: Chi-square test, @: Insignificant difference. The results of table **(2)** and figure **(2)** show there were no significant differences between the two groups in terms of BMI, waist-to-hip ratio, and obesity status.

Table (3): Comparing patients' group (A) and control group (B) regarding to S. creatinine, coronary artery calcification (CAC) score, and C-reactive protein (CRP) levels.

Variables	Total	Group (A) N=140	Group (B) N=60	t-test* χ^2 test#	P-value
Creatinine: M±SD	1.02±0.15	1.02±0.16	1.03±0.14	-0.443*	0.659**
CRP: M±SD	3.48±3.96	3.83±4.85	2.94±1.99	1.84*	0.06**
CAC score: M±SD	176.39±331.31	219.64±345.55	111.5±301.33	2.223*	0.028@
CAC score:					
Non-significant	133(66.5%)	84(60.0%)	49(81.7%)	7.905#	0.005@
Significant >130 HU	67(33.5%)	56(40.00)	11(18.3%)		

*: t-test, #: Chi-square test, **: Insignificant difference, @: Significant difference.

The results of table **(3)** show that differences between the patients' group (A) and the control group (B) in terms of CAC score were significant (p= 0.028) and the proportion of individuals with significant CAC score (>130 HU) (p= 0.005). Group (A) had a higher percentage of individuals with significant CAC score (40.0% Vs 18.3%) and a higher mean CAC score (219.64±345.55 Vs 111.5±301.33) compared to group (B). However, the differences between the two groups in terms of creatinine and C-reactive protein (CRP) levels were not significant. The most significant difference was observed in the proportion of individuals with significant CAC score (p = 0.005, χ^2 = 7.905) in favor of group (A), which indicates a higher CAC burden in patients.

Table (4): Patients' group (A) Vs control group (B) regarding to CAC score of different coronary arteries.

CAC score of different CAs	Total	Group (A) N=140	Group (B) N=60	t-test	p-value
LM CAC: M±SD	16.19±43.63	24.41±53.74	3.42±11.66	4.387	0.000*
LAD CAC: M±SD	36.31±62.75	47.76±73.26	18.54±35.61	3.789	0.0002*
LCX CAC: M±SD	29.25±52.96	39.73±62.73	12.99±25.69	4.276	0.000*
RCA CAC: M±SD	48.8±87.47	62.1±97.87	28.15±64.13	2.901	0.004*

*: Significant difference.

The results of table (4) show differences between group (A) and group (B) in terms of CAC scores in all CAs, including LM (p = 0.000), LAD (p = 0.0002), LCX (p = 0.002), and RCA (p = 0.014). The patients' group (A) had higher mean CAC scores in all CAs in comparison to the control group (B), with the highest significant difference observed in LCX (t = 4.276, p = 0.000) and the lowest significant difference observed in RCA (t = -2.901, p = 0.004), both in favor of the patients' group, indicating a higher burden of CAC in patients.

Table (5): Patients' group (A) Vs control group (B) regarding to different coronary segments and lesions.

Different coronary segments and lesions	Total	Group (A) [N=140]	Group (B) [N=60]	χ^2 test#	p-value
LM					
Normal	188(94.0%)	128(91.4%)	60(100.0%)	5.471	0.065*
Non-significant	7(3.5%)	7(5.0%)	0(0.0%)		
Significant	5(2.5%)	5(3.6%)	0(0.0%)		
Prox. LAD					
Normal	130(65.0%)	70(50.0%)	60(100.0%)	46.154	<0.001 **
Non-significant	23(11.5%)	23(16.4%)	0(0.0%)		
Significant	47(23.5%)	47(33.6%)	0(0.0%)		
Mid LAD					

Normal	170(85.0%)	110(78.6%)	60(100.0%)	15.126	<0.001 **
Non-significant	9(4.5%)	9(6.4%)	0(0.0%)		
Significant	21(10.5%)	21(15.0%)	0(0.0%)		
Dist. LAD					
Normal	179(89.5%)	119(85.0%)	60(100.0%)	10.056	0.007**
Non-significant	16(8.0%)	16(11.4%)	0(0.0%)		
Significant	5(2.5%)	5(3.6%)	0(0.0%)		
Prox. LCX					
Normal	177(88.5%)	117(83.6%)	60(100.0%)	11.138	0.004**
Non-significant	7(3.5%)	7(5.0%)	0(0.0%)		
Significant	16(8.0%)	16(11.4%)	0(0.0%)		
Mid LCX					
Normal	151(75.5%)	91(65.0%)	60(100.0%)	27.815	<0.001 **
Non-significant	21(10.5%)	21(15.0%)	0(0.0%)		
Significant	28(14.0%)	28(20.0%)	0(0.0%)		
Dist. LCX					
Normal	182(91.0%)	122(87.1%)	60(100.0%)	8.477	0.014**
Non-significant	16(8.0%)	16(11.4%)	0(0.0%)		
Significant	2(1.0%)	2(1.4%)	0(0.0%)		
Prox. RCA					
Normal	184(92.0%)	124(88.6%)	60(100.0%)	7.453	0.024**
Non-significant	2(1.0%)	2(1.4%)	0(0.0%)		
Significant	14(7.0%)	14(10.0%)	0(0.0%)		
Mid RCA					
Normal	169(84.5%)	109(77.9%)	60(100.0%)	15.723	<0.001 **
Non-significant	12 (6.0%)	12(8.6%)	0(0.0%)		
Significant	19(9.5%)	19(13.6%)	0(0.0%)		
Dist. RCA					
Normal	188(94.0%)	128(91.4%)	60(100.0%)	4.057	0.044**
Non-significant	12(6.0%)	12(8.6%)	0(0.0%)		
Significant	0(0.0%)	0(0.0%)	0(0.0%)		

#: Chi-square test, ***:** Insignificant difference, ****:** Significant difference.

The results of table (5) show that the differences between the patients' group (A) and the control group (B) are significant in terms of CA lesions in various segments, including Prox. LAD ($p < 0.001$), Mid LAD ($p < 0.001$), Dist. LAD ($p = 0.007$), Prox. LCX ($p = 0.004$), Mid LCX ($p < 0.001$), Dist. LCX ($p = 0.014$), Prox. RCA ($p = 0.024$), Mid RCA ($p < 0.001$), and Dist. RCA ($p = 0.044$). group (A) had a higher proportion of significant lesions in all coronary segments in comparison to group (B), which had no significant lesions in any segment. The most significant difference was observed in Mid LCX ($\chi^2 = 27.815$, $p < 0.001$), followed by Prox. LAD ($\chi^2 = 46.154$, $p < 0.001$), indicating that patients have a higher burden of CAD.

Table (6): Relation between coronary lesions and CAC score.

Variables	Total (n=140)	Non-significant CAC<130HU (n=84)	Significant CAC ≥130HU (n=56)	χ^2 test#	P-value
LM					
Normal	128(91.4%)	77(91.7%)	51(91.1%)	6.216	0.045*
Non-significant	7(5.0%)	2(2.4%)	5(8.9%)		
Significant	5(3.6%)	5(6.0%)	0(0.0%)		
Prox. LAD					
Normal	70(50.0%)	43(51.2%)	27(48.2%)	0.749	0.688**
Non-significant	23(16.4%)	15(17.9%)	8(14.3%)		
Significant	47(33.6%)	26(31.0%)	21(37.5%)		
Mid LAD					
Normal	110(78.6%)	67(79.8%)	43(76.8%)	2.564	0.277**
Non-significant	9(6.4%)	7(8.3%)	2(3.6%)		

Significant	21(15.0%)	10(11.9%)	11(19.6%)		
Dist. LAD					
Normal	119(85.0%)	72(85.7%)	47(83.9%)	0.106	0.948**
Non-significant	16(11.4%)	9(10.7%)	7(12.5%)		
Significant	5(3.6%)	3(3.6%)	2(3.6%)		
Prox. LCX					
Normal	117(83.6%)	71(84.5%)	46(82.1%)	0.140	0.932**
Non-significant	7(5.0%)	4(4.8%)	3(5.4%)		
Significant	16(11.4%)	9(10.7%)	7(12.5%)		
Mid LCX					
Normal	91(65.0%)	71(84.5%)	47(83.9%)	0.088	0.957**
Non-significant	21(15.0%)	5(6.0%)	4(7.1%)		
Significant	28(20.0%)	8(9.5%)	5(8.9%)		
Dist. LCX					
Normal	122(87.1%)	73(86.9%)	49(87.5%)	1.428	0.490**
Non-significant	16(11.4%)	9(10.7%)	7(12.5%)		
Significant	2(1.4%)	2(2.4%)	0(0.0%)		
Prox. RCA					
Normal	124(88.6%)	77(91.7%)	47(83.9%)	3.810	0.149**
Non-significant	2(1.4%)	0(0.0%)	2(3.6%)		
Significant	14(10.0%)	7(8.3%)	7(12.5%)		
Mid RCA					
Normal	109(77.9%)	67(79.8%)	42(75.0%)	0.542	0.763**
Non-significant	12(8.6%)	7(8.3%)	5(8.9%)		
Significant	19(13.6%)	10(11.9%)	9(16.1%)		
Dist. RCA					
Normal	128(91.4%)	76(90.5%)	52(92.9%)	0.034	0.853**
Non-significant	12(8.6%)	8(9.5%)	4(7.1%)		
Significant	0(0.0%)	0(0.0%)	0(0.0%)		

#: Chi-square test, *: Significant difference, **: Insignificant difference.

The results of table (6) show a significant relation between CAC score and coronary lesions only in LM (p = 0.045). on the other hand, no significant relations were found between CAC score and coronary lesions in other coronary segments. The relation between CAC score and coronary lesions was not consistent across all segments, suggesting that the impact of CAC score on CAD may vary depending on the specific segment of CA.

Table (7): Patients' group (A) and control group (B) regarding to peri-coronary EAT.

Peri-coronary EAT	Total (n=200)	Group (A) N=140	Group (B) N=60	t-test	p-value
LM EAT	9.40±5.28	9.30±4.12	9.04±1.79	0.622	0.534*
LAD EAT	8.55±2.38	9.49±2.11	7.15±2.06	7.308	0.000**
LCX EAT	7.73±2.10	8.59±1.79	6.43±1.86	7.611	0.000**
RCA EAT	8.85±2.02	9.59±1.71	7.76±1.96	6.28	0.000**

*: Insignificant difference, **: Significant difference.

The results of table (7) show that the differences are significant between group (A) and group (B) in terms of peri-coronary EAT around LAD (p = 0.000), LCX (p = 0.000), and RCA (p = 0.000). While, the difference is non-significant the two groups regarding peri-coronary LM EAT (p = 0.534).

Table (8): Relation between risk factors according to Peri-coronary EAT.

Peri-coronary EAT	Non-significant CAC <130 HU	Significant CAC ≥130 HU	t-test	P-value
LM EAT	9.34±6.22	9.51±2.02	0.197	0.844#
LAD EAT	7.15±2.06	9.49±2.11	6.521	<0.001*
LCX EAT	6.43±1.86	8.59±1.79	6.833	<0.001*
RCA EAT	7.76±1.96	9.59±1.71	5.690	<0.001*
	Non obese	**Obese**		
LM EAT	8.90±1.93	10.59±9.28	1.725	0.087#
LAD EAT	8.51±2.38	8.64±2.41	0.295	0.768#
LCX EAT	7.76±2.10	7.65±2.14	-0.282	0.778#
RCA EAT	8.94±2.08	8.67±1.89	-0.723	0.471#
	Non smoker	**Smoker**		
LM EAT	9.38±8.50	8.31±1.40	-0.718	0.474#
LAD EAT	7.15±2.13	7.14±0.90	-0.026	0.979#
LCX EAT	6.43±1.92	6.51±1.14	0.227	0.821#
RCA EAT	7.71±2.01	8.31±1.45	1.590	0.114#
	Non hypertensive	**Hypertensive**		
LM EAT	7.89±1.34	10.01±9.95	1.161	0.248#
LAD EAT	7.07±1.91	7.19±2.15	0.277	0.782#
LCX EAT	6.30±1.66	6.50±1.97	0.509	0.612#
RCA EAT	7.76±1.63	7.76±2.13	0.000	1.000#
	Non diabetic	**Diabetic**		
LM EAT	9.82±9.76	8.14±2.76	-1.254	0.212#
LAD EAT	7.09±2.08	7.28±2.47	0.491	0.624#
LCX EAT	6.44±1.80	6.42±2.18	-0.059	0.953#
RCA EAT	7.68±1.97	7.95±2.70	0.684	0.495#
	Non dyslipidemic	**Dyslipidemic**		
LM EAT	9.91±11.11	8.58±1.78	-1.090	0.278#
LAD EAT	6.15±1.72	8.36±1.78	7.244	<0.001*
LCX EAT	5.70±1.66	7.34±1.74	5.525	<0.001*
RCA EAT	6.90±1.83	8.81±1.60	6.501	<0.001*
	Negative FH	**Positive FH**		
LM EAT	9.51±9.14	8.51±1.79	-0.841	0.402#
LAD EAT	6.94±2.04	7.96±2.06	2.921	0.004*
LCX EAT	6.22±1.82	7.26±1.92	3.273	<0.001*
RCA EAT	7.51±1.91	8.77±1.95	3.835	<0.001*

#: Insignificant difference, ***:** Significant difference.

The results of Table (8) show significant relations between peri-coronary EAT and certain risk factors. Specifically, significant relations were found between EAT around LAD, LCX, and RCA and CAC score ($p < 0.001$), between EAT around LAD, LCX, and RCA and dyslipidemia ($p < 0.001$), and between EAT around LAD, LCX, and RCA and family history of CAD ($p < 0.01$). However, no significant relations were found between EAT and other cardiovascular risk factors like obesity, smoking, hypertension, and diabetes.

Table (9): Correlation coefficient (r) between peri-coronary EAT and age.

Variables	Age "years"	
	r*	p-value
LM EAT	0.131	0.328**
LAD EAT	0.122	0.326**
LCX EAT	0.022	0.696**
RCA EAT	0.024	0.692**

:** Correlation coefficient r-test, *:** Insignificant correlation.

The results of Table (9) show no significant relation between peri-coronary EAT and age, as indicated by the non-significant p-values for all CAs (LM: $p = 0.328$, LAD: $p = 0.326$, LCX: $p = 0.696$, RCA: $p = 0.692$). The correlation

coefficients (r) are also relatively low, suggesting a weak relationship between EAT and age.

DISCUSSION

Despite the substantial mortality decrease from ischemic heart disease, it is still the leading cause of death all over the world. Approximately, 44% of this decrease was attributed to earlier recognition and amelioration of conventional CV risk factors. This stimulated the need to search in depth for more risk factors [10].

Cardiac adiposity is considered as a new CV risk factor. Peri-coronary EAT has predicted unfavorable metabolic profile and visceral adiposity. Moreover, the importance of EAT in the development of atherosclerosis of coronary arteries has gained an increasing attention [11].

CAD patients' group had a significant higher peri-coronary EAT thickness than control group in the present study (9.49 mm Vs 7.15 mm for LAD; p-value < 0.001, 8.59 mm vs 6.43 for LCX; p-value <0.001, and 9.59 mm Vs 7.76 mm for RCA; p-value <0.001), but non-significant difference was existed for left main (9.30 mm Vs 9.04 mm; p-value=0.534). The present study detected significant positive linear correlations between peri-coronary EAT and CAC score (9.49 mm with significant CAC score Vs 7.15 mm with non-significant CAC score; p <0.001 for LAD, similar results for LCX, and RCA, but non-significant difference for left main; p=0.844).

Some echocardiographic and MSCT studies support our findings and have documented a good association between EAT and coronary calcification and the CAD severity [12].

In addition to that, EAT was identified as an independent predictor for myocardial ischemia [13] and incident coronary events [14].

CAC score is a reliable predictor of atherosclerosis of the coronary arteries and correlates closely with its severity and extent [15].

A significant increase in the frequency of obstructive CAD as CAC score increases, and a CAC score >400 is significantly associated with obstructive stenosis and was not dependent on traditional CV risk factors [16]. Choi et al. [17] showed that subjects with high CAC score had more components of vulnerable plaque (plaques containing necrotic core and greater dense calcium) than those who had low score of calcium.

A strong relation between coronary calcium and atherosclerotic CAD and with the vulnerable plaque formation [18].

Furthermore, CAC score has been found as an independent predictor of outcomes of CAD, with a relative risk ratio for CAD events 2.1 (for CAC score of 1 to 100) and as high as 10 (for CAC >400) as compared to patients with a score of 0 (p <0.001) [19].

In a systematic review of 6 intravascular ultrasound (IVUS) trials, a direct relation was found between increased volume of coronary plaque and consequent adverse CV events. Each increase in standard deviation of the volume of atheroma had a more than 1.3-fold higher risk for major cardiovascular adverse outcomes, infarction of myocardium, or coronary revascularization [20].

In the present study on post-menopausal females, the major findings suggest that peri-coronary EAT is correlated to some cardiovascular risk factors, but strongly related to CAC, which suggest its role in developing coronary atherosclerosis.

In contrast, Chaowalit et al. [21] could not find a significant relationship between EAT and severity of CAD. Other studies found no significant relation between echocardiographic EAT thickness and coronary calcium score [22]. However, EAT was assessed in these studies using echocardiography which have evaluated EAT thickness on the right ventricle only or combined pericardial adipose tissue which surrounds the heart and epicardial adipose tissue and is highly affected by acoustic windows and experience of the operator. which are drawbacks of this testing method.

Discrimination between epi– and pericardial adipose tissue might be difficult by use of echocardiography [23]. The pericardium is easily discriminated by CT, so differentiation between peri- and epicardial fat is easy.

The peri-coronary EAT may have a direct rather than systemic effect due to its direct position near the wall of coronary vessel and absence of any fascia that prevent migration of bioactive mediators [24].

Waist-to-hip ratio (WHR) is a simple, inexpensive anthropometric measure which has been identified as the best predictor of abdominal fat and visceral adiposity (VAT) in a whole-body MRI study [25]. Nevertheless, Ross et al. [26] and Cornier et al. [27] found marked variability in WC measurements. Indeed, quantification of EAT is a direct marker of VAT rather than anthropometric measures that include muscle and skin, avoiding the likely confusing effect of

increased subcutaneous adipose tissue.

EAT was considered as a reliable marker of visceral adiposity [28]. Walpot et al. [29] reported a significant relation between echocardiographic thickness of EAT and MRI-measured abdominal VAT volume (p=0.01, r=0.86) and also WC (p=0.01, r=0.89).

BMI is the most common used anthropometric measure to measure total body fat, however not all adipose tissue is created equally; regional, functional and structural variations are found [30]. Various body fat compartments influence in different ways to CV risk. VAT accumulation is related to increased prevalence of, metabolic syndrome, insulin resistance and associated CV complications. However, peripheral subcutaneous fat exhibited an independent anti-atherogenic effects [31].

In this study no significant correlation has been detected between EAT and BMI. In accordance to this, prior studies found EAT is a reliable indicator of VAT, but weakly reflected the extent of obesity as measured by BMI [32].

In this study, there was no relation between peri-coronary EAT and other risk factors like hypertension, diabetes, age, and smoking.

Some studies support our findings; there was no significant relation found between EAT and hypertension [33, 34].

Iacobellis et al. [35] found no relation between EAT and age. Mohammadzadeh et al. [36] found no remarkable association was found between peri-coronary EAT and diabetes mellitus.

In contrast, Song et al. [37] measured EAT thickness on the right ventricle by echocardiography found a relation between it and diastolic blood pressure. Conte et al. [38] reported a significant relation between EAT and age. Salvatore et al. [39] demonstrated a significant relation between EAT thickness and diabetes mellitus.

Limitations of the study:

1. The study was based on a single-center experience and might be limited by the small number of patients.
2. This study was performed on females only as a homogenous group, it needs to be conducted on both males and females to compare adipose tissue properties & relations to CV risk factors in different age groups and both sexes.
3. Specific software in MSCT workstation for EAT measurement is needed as we used a traditional manual method, aiming to be a routine parameter of the results that are included in MSCT report.

CONCLUSIONS

This study showed a positive correlation between peri-coronary EAT and CAC, and with coronary arteries atherosclerotic lesions. It also showed positive correlation with some cardiovascular risk factors, as dyslipidemia, however, there was no relation between peri-coronary EAT and other CV risk factors like diabetes, age, hypertension and smoking. However, confirmation studies are recommended to support these findings among men.

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