

Correlation between epicardial adipose tissue thickness and the degree of coronary artery atherosclerosis

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Background/aim: The purpose of the current study was to evaluate the thickness of the epicardial adipose tissue and its association with the degree of coronary artery disease in a group of autopsied cases.

Materials and methods: A number of 79 cases were included in the study. Five preestablished incisions of the epicardial adipose tissue (EAT) were made on each of the hearts. These five points were next to/on the path of the major coronary vessels. The degree of coronary atherosclerosis was evaluated during the autopsy.

Results: The results revealed the greatest thickness of the EAT on the incision made on the anterior and posterior wall of the right ventricle. EAT was thicker in cases presenting atherosclerosis degree I or II in two of the coronary arteries, the left circumflex artery and left main artery; on the left anterior descending artery, higher EAT thickness associated with fourth degree atherosclerosis.

Conclusion: Epicardial adipose tissue thickness was greater at the incision points situated on the right side of the heart. Greater EAT thickness was associated significantly with early atherosclerosis development in three of the coronary arteries (LCx, LMA, LADA).

Key words: Epicardial adipose tissue, coronary atherosclerosis, autopsy

1. Introduction

The epicardial adipose tissue (EAT) is located between the visceral pericardium and the myocardium. This tissue is most abundant in specific sites such as the right ventricle and the atrioventricular and interventricular sulci (1). One important role of this tissue is the secretion of proinflammatory cytokines like TNF- α , IL-6, IL-7, IL-8, or macrophages (2). In one study (3), the authors linked the presence of high levels of TNF- α produced by the EAT and the amplified vascular inflammation in a group of patients with coronary artery disease (CAD). The proximity of this tissue to the adventitia of the coronary arteries could also contribute to the inflammatory process, which afterwards leads to atherosclerosis (4). The epicardial adipose tissue thickness and the high volume of the EAT correlates, according to some studies (4,5), with the severity of CAD.

The aim of our study was to evaluate the thickness of the EAT and its association with the degree of CAD in a group of autopsied cases.

2. Materials and methods

The study includes 79 randomly selected autopsied cases from the Institute of Legal Medicine of Tirgu Mures, Romania, in the period of October–December 2015. Decomposing bodies and cases presenting adherent pericarditis were excluded.

During the autopsy, five preestablished incisions of the EAT were made on each of the hearts. These points were next to/on the path of the major coronary vessels: the right coronary artery (RCA), the left main artery (LMA), the left anterior descending artery (LADA), and the left circumflex artery (LCX). The five incisions points are presented in Figure 1.

· The first incision was performed inferior to the left appendage, on the anterior side, and measured the thickness of the EAT located on top of the left main coronary branch;

· The second incision was performed posterior and inferior to the left atrial appendage and measured the thickness of the EAT on the path of the LCX;

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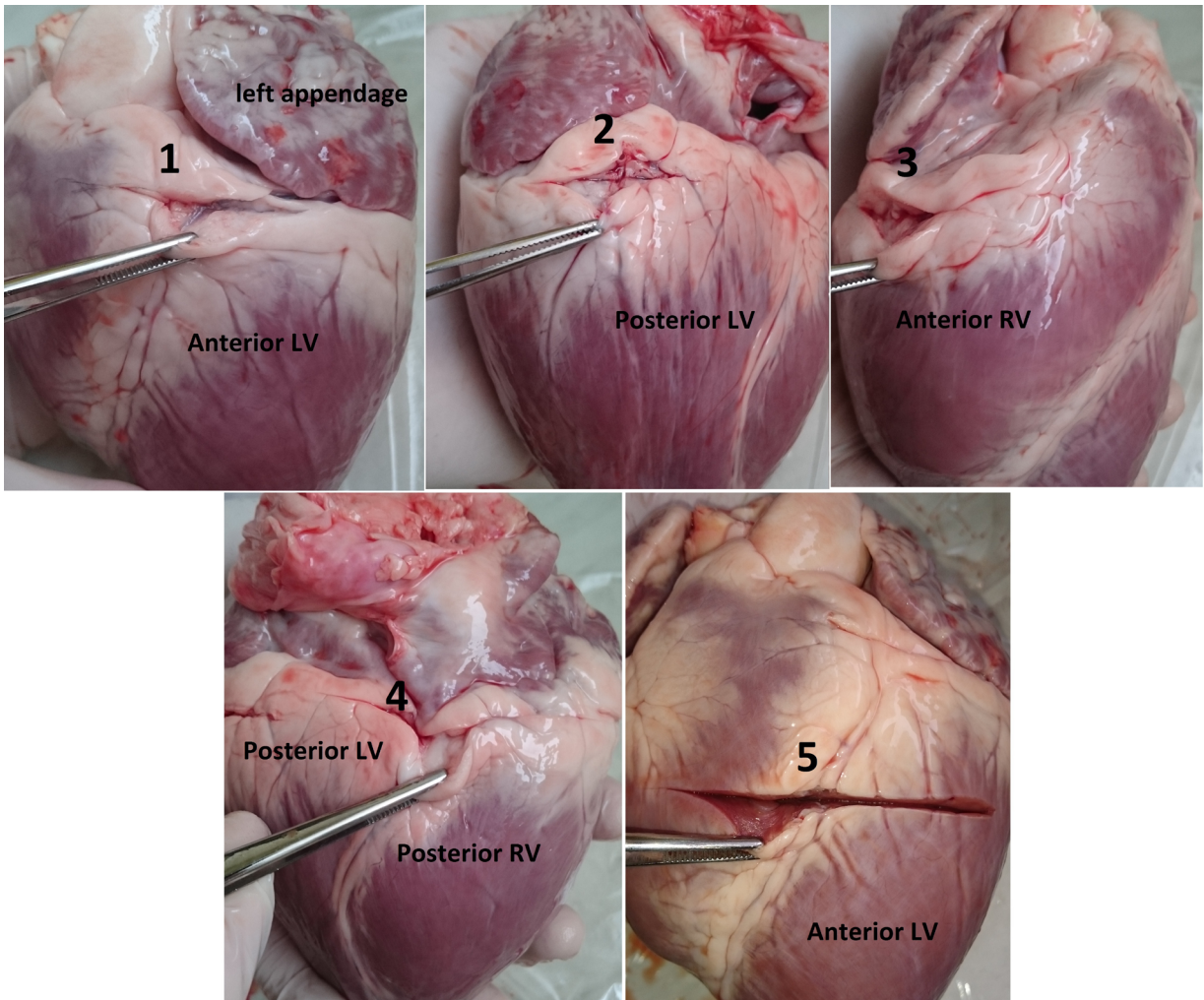


Figure 1. The five incision points used to assess the EAT thickness. LV: Left ventricle, RV: right ventricle.

- The third incision, performed under the right atrial appendage on the anterior wall, measured the EAT thickness on the emerging segment of the RCA;
- The fourth incision was located beneath and posterior to the right atrial appendage and evaluated the EAT thickness next to the path of the RCA;
- The final incision point was located on the interventricular sulcus and evaluated the thickness of the EAT on the path of the LADA.

The degree of coronary atherosclerosis was subjectively assessed during the autopsy by two forensic doctors, at least one being board-certified. All the coronary vessels were opened, and the most advanced degree of stenosis was recorded for all five points of interest, according to the five incision points.

The degree of coronary atherosclerosis was rated according to the following scale (6): Degree 0: normal, Degree I: 1%–25% stenosis, Degree II: 26%–50% stenosis,

degree III: 51%–75% stenosis, Degree IV: 76%–100% stenosis.

At the start of the autopsy, the patients were measured and weighed so that the body mass index (BMI) could be calculated. We divided the cases into 2 groups according to BMI using the World Health Organization classification (Table 1).

Data analysis was performed with EpiInfo software and SPSS (demo version); ANOVA, Welch ANOVA, and post hoc tests were used with a confidence limit of 95%. $P < 0.05$ was considered statistically significant. Continuous variables are reported as mean \pm standard deviation (SD) and categorical variables as observed number of patients.

3. Results

The mean age of the studied group was 58 ± 14 years, with a male to female ratio of 3.4:1 (61 male cases and 18 female cases). The mean BMI of the 79 cases was 28.9 ± 5.63 kg/m².

Table 1. Distribution of cases according to BMI.

Group	Classification	BMI (kg/m ²)	Cases
1	Normal	18.5–24.99	14
2	Preobese	25–29.99	36
	Obese class I	30–34.99	19
	Obese class II	35–39.99	8
	Obese class III	≥40	2

The mean thickness and the median of the EAT at the 5 incision points are presented in Table 2. A total of 395 incisions were made on the 79 studied cases, with a mean thickness of 0.84 ± 0.2 cm.

The degree of coronary atherosclerosis in each of the coronary arteries is presented in Figure 2.

Regarding the first incision and the coronary artery beneath (left main artery), the ANOVA test result was $P = 0.003$; there was a significant difference between the mean thicknesses of the EAT and the degree of coronary atherosclerosis, as presented in Table 3. The post hoc test used (Tamhane – equal variance – Levine test = 0.09) showed a statistical difference between the mean thickness of EAT in the cases presenting first and second degrees of atherosclerosis, with higher thicknesses in cases with second degree atherosclerosis. There was no association between the BMI and the degree of coronary atherosclerosis of the left main coronary artery.

Concerning the second incision located on top of the LCX artery, the Welch ANOVA test result was $P = 0.05$. The post hoc test (Games–Howell test – unequal variance – Levine test = 0.01) revealed significant differences between the mean thicknesses of the EAT in the cases presenting no atherosclerosis with first degree atherosclerosis, with higher mean values in cases with first degree atherosclerosis (Table 3).

The degree of coronary atherosclerosis in the left circumflex artery was associated with the mean BMI of the cases and the ANOVA test showed a result of $P = 0.014$.

Table 2. The mean thickness and median of the EAT at the 5 incision points

	Mean EAT thickness \pm SD (cm)	Median
First incision	0.90 ± 0.41	0.80
Second incision	0.67 ± 0.32	0.60
Third incision	1.03 ± 0.54	1.00
Fourth incision	1.00 ± 0.45	1.00
Fifth incision	0.59 ± 0.29	0.50

Using the Tukey HSD post hoc test, the difference of BMI was observed between cases presenting first and third degree coronary atherosclerosis (BMI: 27.8 kg/m^2 vs. 35.1 kg/m^2). The mean values of the thickness of the EAT in the second incision site did not associate statistically with the BMI.

The third incision of the EAT was performed on top of the first segment of the RCA, and the ANOVA test revealed a P-value of 0.183. The result has no statistical significance, with no difference between the atherosclerosis degree of the right coronary artery and the mean EAT thickness (Table 3).

Regarding the fourth incision, located on the path of the RCA, the ANOVA test result was $P = 0.86$, without statistical significance (Table 3).

For the final incision, located on the interventricular sulcus, on top of the path of the LADA, the homogeneity Levine test result was 0.01 and the Welch ANOVA P-value was 0.001, statistically significant. The post hoc test (Games–Howell) revealed a difference between second degree, third degree, and fourth degree atherosclerosis, with the highest thickness of EAT in the cases with second degree atherosclerosis.

4. Discussion

Atherosclerosis has been identified as a chronic inflammatory disease (7), but a relatively limited number of studies focus on the relationship between the EAT and coronary atherosclerosis. The published studies evaluate the atherosclerosis degree and the EAT thickness or volume using imaging methods, while few of them explore this link in postmortem cases. The thickness of the EAT can be precisely measured and the degree of coronary atherosclerosis can be accurately evaluated during autopsy.

In the current study, we aimed to measure the epicardial fat tissue located on top of or on the path of the main coronary arteries in order to identify a possible link between the thickness of the tissue and the degree of coronary atherosclerosis in a group of autopsied cases. This association was mentioned in a few studies (8–10), where the authors measured the EAT by using computer tomography, and higher values correlated with advanced coronary atherosclerosis. In the present study, the results were partially different; thus, greater EAT thickness was associated with low degrees (I or II) of coronary atherosclerosis of some arteries (left main trunk, left circumflex artery, and left anterior descending artery).

Similar results to the ones presented in our study were reported by Mahabadi et al. (11), with 3367 patients included in their study. The authors evaluated the coronary atherosclerosis and quantified the EAT using CT imaging. The authors concluded that the epicardial fat tissue may have an initial promoter effect on early

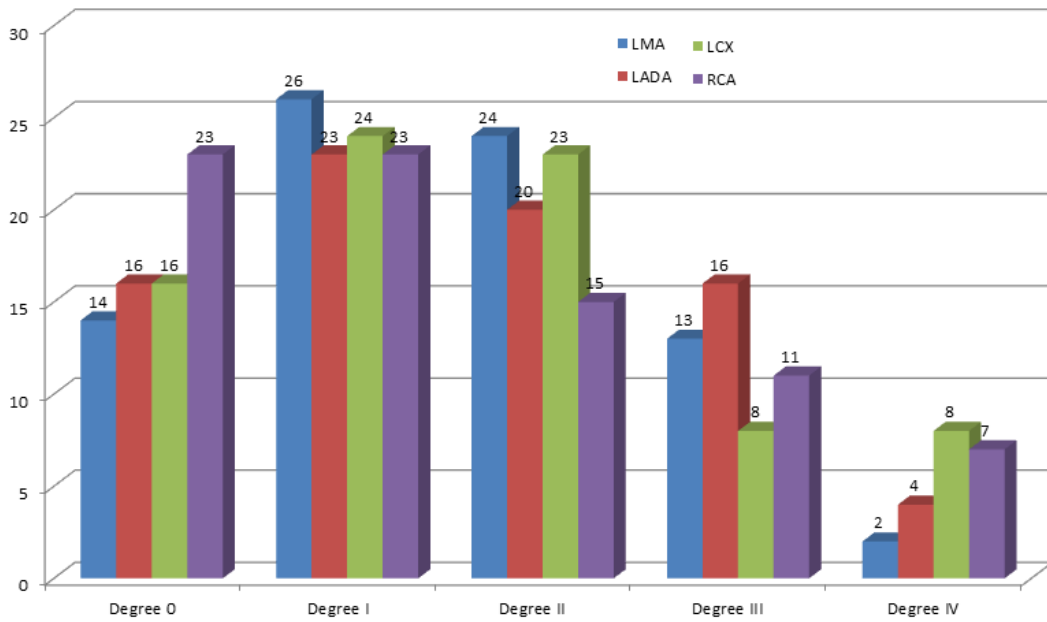


Figure 2. The degree of coronary atherosclerosis. RCA: Right coronary artery, LMA: left main artery, LADA: left anterior descending artery, LCX: left circumflex artery.

Table 3. Thickness of EAT and the degree of coronary atherosclerosis.

Ath. (degree)	Mean ± SD	Median	IQR	Mean ± SD	Median	IQR	Mean ± SD	Median	IQR	Mean ± SD	Median	IQR	Mean ± SD	Median	IQR
0	0.80 ± 0.47	0.60	1.0	0.55 ± 0.20	0.60	0.2	0.82 ± 0.42	0.80	0.7	0.99 ± 0.57	0.80	1.0	0.47 ± 0.26	0.45	0.3
I	0.77 ± 0.37	0.80	0.6	0.86 ± 0.39	0.80	0.6	1.03 ± 0.64	0.90	1.1	1.05 ± 0.35	1.00	0.6	0.53 ± 0.25	0.50	0.4
II	1.17 ± 0.38	1.30	0.5	0.62 ± 0.23	0.50	0.3	1.14 ± 0.60	1.10	0.6	0.89 ± 0.45	0.80	0.5	0.74 ± 0.38	0.65	0.6
III	0.84 ± 0.31	0.80	0.6	0.63 ± 0.22	0.70	0.4	1.12 ± 0.54	1.10	0.8	1.00 ± 0.51	1.00	0.2	0.64 ± 0.19	0.60	0.4
IV	0.50 ± 0.00	0.50	-	0.50 ± 0.32	0.40	0.7	1.31 ± 0.24	1.50	0.5	1.07 ± 0.11	1.10	0.2	0.40 ± 0.00	0.40	-
	Left main artery (first incision)			Left circumflex artery (second incision)			Right coronary artery – emerging part (third incision)			Right coronary artery – middle part (fourth incision)			Left anterior descending artery (fifth incision)		

atherosclerosis rather than a sustained effect, mostly due to a mismatch between the secretion of proinflammatory and antiinflammatory mediators.

In another recently published study evaluating the degree of coronary atherosclerosis during autopsy (12), the authors correlated the presence of coronary atherosclerosis to the thickness and volume of EAT on postmortem CT scans for a total of 116 patients. Their results suggest a strong link between high volumes of EAT and ≥50% stenosing atherosclerosis. The thickness of the EAT according to their classification (no stenosis, <50% stenosis, 50% stenosis), was proportionally increasing with the coronary atherosclerosis degree.

The Framingham study (13) did not report a link between EAT and the coronary atherosclerosis degree

evaluated via coronary artery calcification score after cardiovascular risk factor adjustment. The authors sought to determine a possible correlation between the pericardial adipose tissue, metabolic risk factors, and vascular calcification. Their results showed that there is a stronger link between pericardial adipose tissue and visceral abdominal adipose tissue than other cardiovascular risk factors. Vascular calcification was associated with intrathoracic and pericardial adipose tissue, probably due to a local toxic effect exerted on the vasculature. The authors stated in their results that the pericardial adipose tissue correlated with many cardiac risk factors (high BMI, hypertension, and low HDL-cholesterol levels).

After studying the current literature, in most studies, a clear distinction between the epicardial, pericardial,

paracardial, and intrathoracic adipose tissue was not made, and sometimes the terms seemed to be wrongly used (13–15). Although most of the studies reported a link between the quantity of adipose tissue and coronary atherosclerosis, we suggest a better definition of the tissue being measured.

In many studies, all linear measurements of EAT showed a significant association with obesity. In one study conducted with 34 postmenopausal women, the highest degree of association was reported between increased BMI and the area of epicardial fat measured next to the right ventricle. The increased quantity of EAT was also linked to the presence of metabolic syndrome and diabetes mellitus (16,17). Metabolic syndrome has a high prevalence in patients with CAD. In a study conducted with 574 patients presenting with acute coronary syndrome, metabolic syndrome was present in 50.9% patients, women being more frequently diagnosed with this disorder than men (66.3% vs. 47.3%; $P < 0.001$) (18).

In another study, the authors aimed to test the hypothesis that increased EAT thickness can be used as a marker for the presence and the severity of CAD (19). They enrolled 150 patients (100 with CAD and 50 without CAD), who underwent 2D echocardiography and coronary angiography, and they compared EAT thickness with angiographic findings. Their results showed that EAT thickness was significantly increased in patients with CAD in comparison to those without CAD (6.9 ± 1.5 mm vs. 4.4 ± 0.8 mm; $P < 0.001$).

More and more studies suggest that measuring central obesity or total body fat content may be more appropriate in determining the cardiovascular risk than using the body mass index alone (20).

In conclusion, EAT thickness was greater at the incision points situated on the right side of the heart. Greater EAT thickness was associated significantly with early atherosclerosis development in three of the coronary arteries (LCX, LMA, LADA). BMI was associated with high degrees of atherosclerosis in the LCX artery but was not associated with an increased thickness of EAT.

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