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Evaluation of the Relationship Between Epicardial Fat Tissue Area and Coronary Atherosclerosis

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Abstract; In our study, it was aimed to investigating the correlation between the quantity of epicardial adipose tissue with the development of coronary atherosclerosis and coronary artery disease. In this retrospective research we used Cardiac CT Angiography images of 40 patients (age range 23-80, 30 males, 10 females). The area of epicardial adipose tissue and total calcium score values were measured. All the patients were examined for obstructive coronary artery disease. Epicardial adipose tissue areas were measured in the level of the left main coronary artery. The data obtained were analyzed with SPSS program. 13 patients were found positive for Ca score and coronary stenosis was dedected in 18 patients. There is independent correlation between the area of epicardial adipose tissue and; age and total calcium score (age: p=0.003, total calcium score: p=0.020). Based on results and statiscal analysis, the area of epicardial adipose tissue was found statistically significant among the patients, who have positive Ca score (p=0.017) and coronary artery stenosis (p=0.019). As result, based on the outcomes of this study, it can be concluded that the increase of epicardial adipose tissue has significant impact on occurence of coronary artery stenosis and calcific-atherosclerotic changes. Also, for the calculation of epicardial adipose tissue quantity, the measurement of cross section area from left main coronary artery surface is a good alternative to have an easiness of measurement as well as total volume of epicardial adipose tissue.

INTRODUCTION

Cardiovascular diseases play an increasingly important role worldwide as the major cause of mortality and morbidity. Studies conducted before the 2000s show that the mortality rate from cardiovascular diseases worldwide will increase from 28.9% to 36.3% between 1990 and 2020 [1]. In recent studies, it has been reported that the absolute number of deaths related to cardiovascular disease (CVD) increased globally and in most regions between 1990 and 2017. In the same period, the absolute number of CVD deaths among males rose from 5.9 million to 9.3 million (54% increase) and from 6 million to 8.4 million (40% increase) for women [2].

Coronary artery calcification, which is one of the known factors of coronary atherosclerosis, arises as a result of severe inflammation and proliferative changes in the vascular wall [3-6].

Atherosclerosis is a disease that can be stopped or regressed if its causes are identified and treated, and affects not only coronary vessels but all arterial structures [7]. It is a chronic inflammatory disease with a fibroproliferative character that primarily involves the intima and then the media and adventitia layers of large and medium-sized muscular arteries of varying size from the aorta to the epicardial coronary arteries [8]. In human anatomy, epicardial adipose tissue is observed more prominently in different parts of the heart. Most watched places are; the right ventricular free wall, the left ventricular free wall, the periphery of the atria and adventitia of the coronary artery branches.

During embryogenesis, epicardial and intraabdominal adipose tissues develop from brown adipose tissue [9]. The fully differentiated white adipose tissue is found in the interventricular and atrioventricular grooves in the adult heart and it extends to the apex. As the epicardial adipose tissue increases, it fills the space between the ventricles and covers the entire epicardial surface. A small amount of adipose tissue extends from the epicardial surface to the myocardium by following the adventitia of the coronary artery branches. In summary, there appears to be a functional and anatomical relationship between the fat and muscle content of the heart [10].

Atherosclerotic intimal lesions were observed more in the parts of the coronary arteries covered with epicardial adipose tissue compared to the parts surrounded by the

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myocardium[11]. Epicardial adipose tissue was measured thicker in patients with coronary artery disease and with unstable angina pectoris than in patients without coronary artery disease and in patients with stable angina pectoris [12].

Today, it is accepted that adipose tissue, which is seen as an energy store, is an important endocrine organ of the body. Adipose tissue has biological activities related to energy metabolism, neuroendocrine function and immune functions. Both the deficiency and the excess of adipose tissue have important metabolic and endocrinological consequences.

In this study, we aimed to investigate the relationship between the amount of epicardial adipose tissue and coronary calcium score value and the development of obstructive coronary artery disease in 40 patients who are in our archive and underwent Cardiac Computed Tomography (CT) Angiography.

MATERIALS and METHODS

Etical approval

The data in this study was obtained retrospectively from the hospital automation system and because of that no ethical approval was taken.

Patients

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a prior approval by the institution's human research committee. In our study, a total of 40 patients who underwent cardiac CT Angiography at the Radiology Clinic of Mustafa Kemal University from May 2009 to September 2011 were evaluated. Of the 40 patients included in the study, 10 were female, and 30 were male.

Imaging methods

Coronary calcium scoring: Coronary calcium (Ca) scoring test was performed on Toshiba Aquilon 64-slice CT device (120 kV, 300 mA, 75 mAs, 250 ms rotation time). Images were created at a slice thickness of 3 mm and were evaluated after transfer to the workstation. The Agatston Scoring Method was used for calcium scoring (Figure 1). After the coronary arteries of all patients were examined one by one at the workstation, the existing calcium plaques were marked using the software program and the total calcium scores were calculated.

Cardiac CT Angiography examination: Cardiac CT Angiography examinations of all patients were performed on the Toshiba Aquilion 64-slice CT device in our hospital (120 kV, 500 mA, 1000 mAs, 400 ms rotation time). CT angiography was performed in patients with a heart rate between 60 and 70. 70-90 ml 400mg iodine / ml contrast agent was administered to the patients intravenously. ECG correlated tube flow model was used for image creation and images were reconstructed at the level of 75% of the cardiac cycle in the mid-diastolic phase.

The obtained images were transferred to the multi-slice CT device's workstation and then examined by an experienced radiologist in 3 dimensions with curved referance and MIP formats on the cross-sectional images. Patients with coronary calcium plaques were examined in terms of whether calcium plaques caused stenosis in the lumen together with the assessment of the calcium score. All patients were examined in MIP and curved reference imaging formats for non-calcific (soft) plaque that could cause filling defect (stenosis) in the lumen.

Epicardial fat measurement: Epicardial fat is located between the myocardium and the visceral leaf of the pericardium. For the measurement of epicardial fat, were used images with 3 mm slice thickness which used for calcium score measurement. Fat measurements were made at the level of the origin of the left main coronary artery from a single-slice view on the CT device console. Density threshold value was taken as (-30) - (-230) for fat voxel calculation.The amount of fat was calculated in mm² of area in the threshold density range (Figure 2).

Statistical analysis

Continuous variables were given as mean ± standard deviation (SD) and Categorical variables as %. Whether the data showed normal distribution was evaluated with the Kolmogorov-Smirnov test. Total calcium score did not show normal distribution ($p < 0.05$). Other variables (epicardial fatty area, age, gender and presence of stenosis) showed normal distribution ($p > 0.05$). Subgroup analysis was performed using Student's t test according to calcium score positivity and presence of stenosis. Independent relationship between epicardial fatty area and other variables was evaluated by multiple linear regression test (Stepwise model).

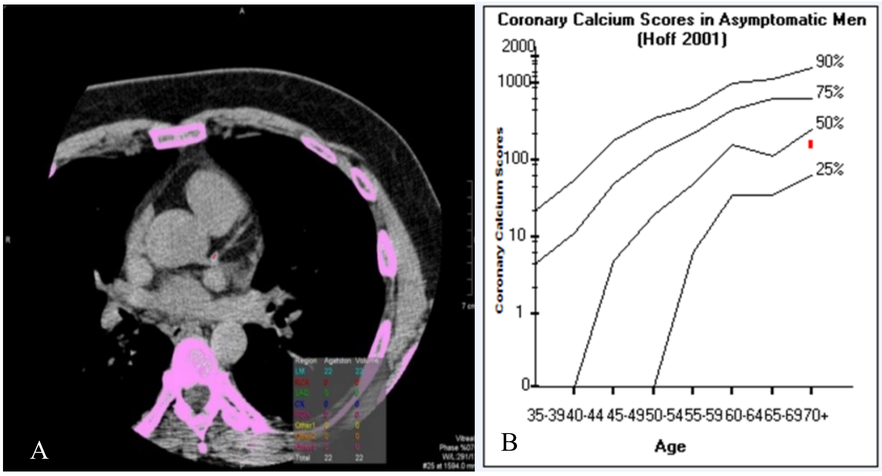

Figure 1. A and B, Coronary calcium scoring, the agatson scoring method.

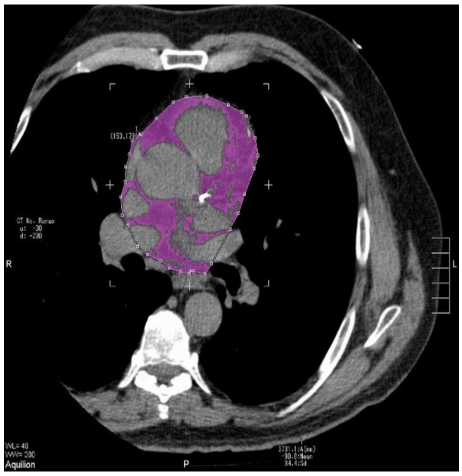

Figure 2. Epicardial adipose tissue measurement.

RESULTS

Data of a total of 40 patients were used in the study. There were 30 male and 10 female in the group. The average age of the cases was 49.52 ± 13.4 years; the age range was 23-80 years.

In the study, positivity of Ca score, total Ca score, amount of epicardial fat from the left main coronary artery level and presence of stenotic coronary artery disease were examined.

Ca score positivity was detected in 13 patients (32.5%). The mean calcium score these patients were found to be 341.92 ±.524.06

Stenosis was detected in 18 patients (45%). The number of vessels with stenosis left main coronary (LM) artery, left anterior descending (LAD) artery, circumflex (Cx) artery, right coronary artery (RCA) was examined. Stenotic changes were observed in 1 vessel in 13 patients, in 2 vessels in 3 patients; and in 3 vessels in 2 patients.

The mean epicardial adipose tissue (EAT) area was found 1173mm² 526.27 ±in 27 patients (67.5%) without Ca score positivity and 2012mm² 1064.79 ±in 13 patients (32.5%) with positive Ca scores (Table 1). Epicardial adipose tissue area in patients with positive Ca scores was statistically significantly higher (p = 0.017) than those without Ca score positivity (Figure 3).

The mean epicardial adipose tissue area was 1171mm² 595.79 ±in 22 patients (55%) without coronary artery stenosis, and 1781mm² ± 965.81 in 18 patients (45%) with coronary artery stenosis. Epicardial adipose tissue area of patients with coronary artery stenosis was found to be statistically significantly higher (p = 0.019) than those without coronary artery stenosis (Figure 4).

In multiple regression analysis, an independent relationship was found between epicardial adipose tissue area and age and total calcium score (age: p = 0.003, total Ca score: p = 0.020).

Table 1. Epicardial adipose tissue area of patients

Patients	N	Mean	SD	P
Ca score				
negative	27 (67,5%)	1173 mm^2	526,27	
pozitive	13 (32,5%)	2012 mm^2	1064,79	0,017
Stenosis				
negative	22 (55%)	1171 mm^2	595,79	
pozitive	18 (45%)	1781 mm^2	965,81	0,019

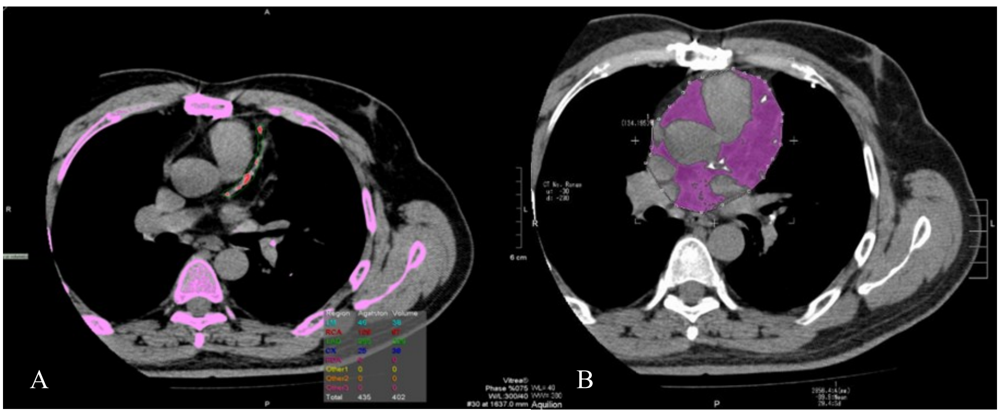

Figure 3. A, Multiple calcium plaques in LAD. **B,** Increased epicardial adipose tissue area of the same patient.

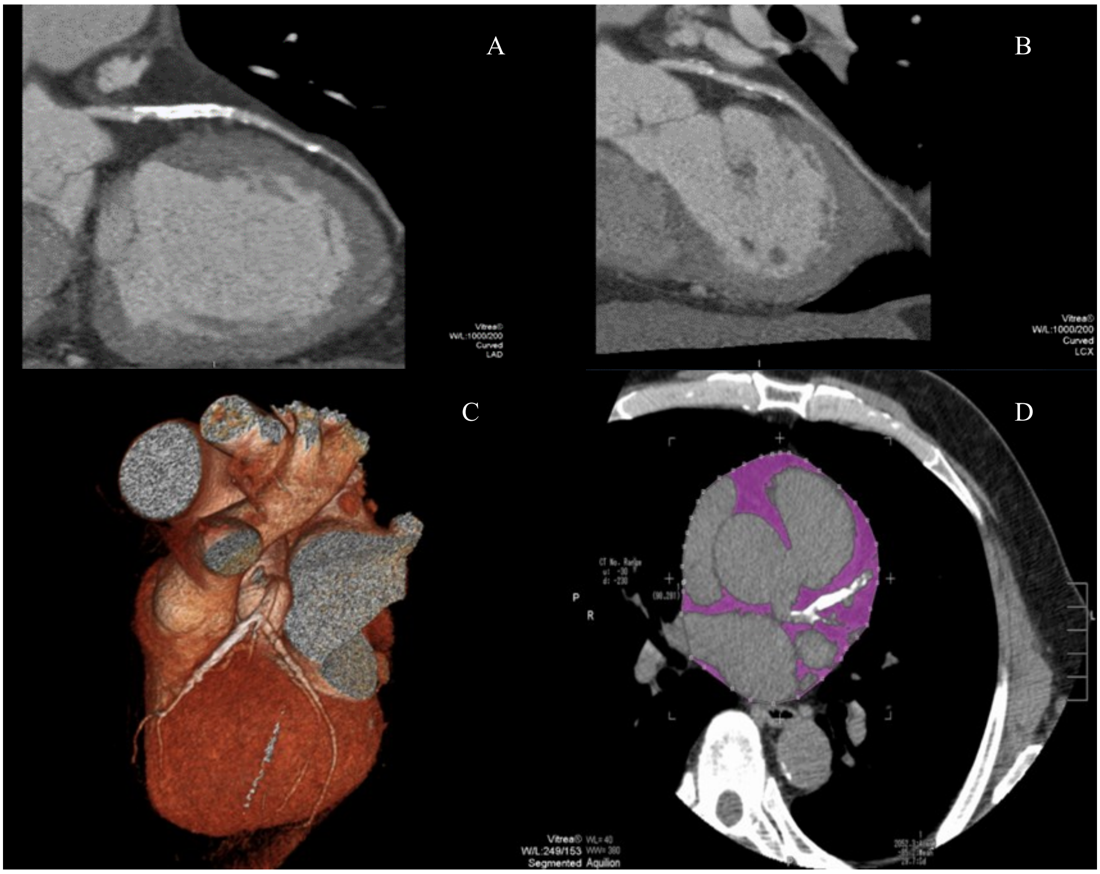

Figure 4. Patient with coronary artery stenosis and calcium score positivity. **A,** Calcific plaque formation causing lumen stenosis in LAD, **B.** Calcific plaque in Cx that does not cause significant stenosis in the lumen, **C.** Calcific plaque formation on LAD is seen in 3D image of the same patient, **D.** High amount of epicardial fat in the same patient.

DISCUSSION

Atherosclerosis is a systemic disease that causes progressive arterial stenosis and occlusion due to intimal plaques containing lipids, fibroblasts, macrophages, smooth muscle cells and extracellular substances in different proportions, affecting not only coronary vessels but all arterial structures [7].

Atherosclerosis begins early in life and progresses throughout life. The most important complications are myocardial infarction and sudden cardiac death. In addition to the known causes of atherosclerosis, epicardial adipose tissue has also been reported in recent years to cause atherosclerosis and coronary artery disease. Today, it has been proven that pericardial adipose tissue secretes more inflammatory cytokines than subcutaneous adipose tissue, and inflammation caused by these cytokines is one of the causes of coronary artery disease [13].

Epicardial adipose tissue has protective functions such as providing free fatty acids in the myocardium, protecting the myocardium against toxic levels of fatty acids, secretion of cardioprotective adipokine and preventing the torsion of coronary arteries during cardiac contraction [14]. However, when the amount of epicardial fat increases, it becomes hypoxic and dysfunctional due to increased lipolysis and inflammation and alters hemostasis. As a result, it causes atherosclerosis and the formation of atherosclerotic plaque [15].

In the light of the information obtained, a positive correlation was found between epicardial adipose tissue thickness and coronary artery disease and metabolic syndrome [10].

In studies using MDCT, atherosclerotic plaque development and coronary stenosis were investigated using parameters such as epicardial adipose tissue volume, epicardial adipose tissue thickness, and pericoronary fat amount. In the literature, volumetric measurements have been used in most of the examinations made for the amount of epicardial adipose tissue. However, a software program is required for the calculation of total adipose tissue volume and the calculation takes a long time.

In a study by Oyama et al., single-section epicardial fat area measurement and epicardial fat volume were examined, and fat area measurements taken from the levels of the right pulmonary artery, left main coronary artery, right coronary artery and coronary sinus were compared with the total epicardial fat volume. In this study, it was reported that the level that showed the most correlation with epicardial fat volume in relation to coronary artery disease (CAD) was the left main coronary artery level [16]. In our study, we used the area measurement over a single section at the level of the left main coronary artery in epicardial adipose tissue examinations.

Many studies have reported high epicardial adipose tissue volume in patients with calcium plaque formation. In the study conducted by Nakanishi et al., It was thought that an increase of 15% or more in epicardial adipose tissue volume caused an increase in coronary calcium score [17]. In another study conducted with 515 patients, it was found that the calcific plaque formation was significantly increased in patients with epicardial adipose tissue volume above 100 ml compared to those below 100 ml. In addition, in this study, it was reported that epicardial adipose tissue volume increased in patients with coronary stenosis over 50% and calcium score above 400 [18].

Also, although there are different studies [19, 20] reporting a significant positive relationship between coronary calcium score and epicardial adipose tissue volume and epicardial adipose tissue thickness in the literature, in another study Aslanabadi et al. measured epicardial fat volume, pericardial fat volume and epicardial fat thickness and they found a significant linear relationship between coronary calcium score and pericardial fat volüme. However, it has been reported that there is no significant correlation between epicardial fat volume and coronary calcium score [21].

In our study, epicardial adipose tissue area was significantly increased in patients with positive coronary calcium scores.

In many studies in the literature using epicardial fat volume, pericardial fat volume and epicardial adipose tissue thickness, a strong positive correlation was found between coronary artery stenosis and ischemic lesions and the amount of adipose tissue [13,15,19,21]. In the study conducted by Du et al., pericardial fat volume was found to be higher in patients with significant stenosis and ischemic lesions compared to those without [22]. In another study with 70 patients; patients were divided into 3 groups as with no atherosclerosis, with non-obstructive atherosclerosis and with obstructive atherosclerosis, and founded that in the third group, epicardial and pericoronary fat thickness was significantly higher [23].

In this study, we investigated the relationship between coronary calcium plaque formation and coronary artery stenosis with epicardial adipose tissue. We also examined the predictability of coronary artery disease by measuring the epicardial adipose tissue area.

In our study, the epicardial adipose tissue area of patients with Ca score positivity and coronary artery stenosis was found to be statistically significantly higher. The findings we have obtained by measuring the epicardial adipose tissue area and the results of the studies conducted by measuring the total adipose tissue volume are consistent. Our findings support that the increase in epicardial adipose tissue increases the development of calcium plaque in coronary arteries and coronary artery disease, as in the literature.

There are several limitations in our study. Routine clinical follow-up of our cases was not performed and their relationships with traditional atherosclerotic risk factors such as diabetes and HT and anthropometric parameters such as BMI were not evaluated. The presence of these risk factors and parameters may have affected the cardiovascular risk profile and the amount of epicardial adipose tissue. In our study, only CT findings were evaluated.

CONCLUSION

As a result, an independent relationship was found between the amount of epicardial adipose tissue and coronary calcium score positivity. Epicardial adipose tissue area was found to be significantly higher in patients with coronary artery stenosis and positive coronary calcium score. In the light of these findings, it can be concluded that epicardial adipose tissue increase is effective in the development of coronary artery stenosis and calcific-atherosclerotic changes in coronary arteries.

In addition, it is thought that the measurement of a single cross-sectional area from the left main coronary artery level in calculating the amount of epicardial adipose tissue may be a good alternative to total epicardial adipose tissue volume calculations due to easier measurement.

Conflict of interest

The authors declare that they have no conflict of interest.

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