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The relationship between epicardial fat volume and myocardial perfusion scintigraphy findings

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ABSTRACT

Objectives: We investigated the epicardial fat volume (EFV) between patients with normal perfusion and reversible perfusion abnormalities in the myocardial perfusion scintigraphy (MPS) in patients with suspected coronary artery disease (CAD). In addition, we aimed to investigate the relationship of automated analysis parameters obtained in the MPS SPECT examination with EFV.

Methods: A total of 295 patients (182 F, 113 M) who underwent MPS in our unit with the suspicion of CAD in the last 1 year and who had a recent thorax CT examination were included. EFV measurement in CT scans was done with Invesalius software. MPS was performed in all patients with a one-day stress and rest imaging protocol. In the stress study, imaging was performed approximately 30-45 minutes after intravenous injection of ~12 mCi Tc99m Sestamibi. Rest study imaging was performed approximately 30-60 minutes after intravenous injection of ~25 mCi Tc99m Sestamibi.

Results: Median EFV was 53.00 ml (interquartile range: 23 ml, range 17-238 ml) in patients with normal MPS, and 62.00 ml in patients with myocardial ischemia on scintigraphy (interquartile range: 53 ml, range: 25-207 ml). The EFV value was statistically significantly higher in patients with reversible ischemia on MPS compared to patients with normal scintigraphy findings ($p < 0.001$). There was a statistically significant, low, and positive correlation between EFV and summed difference score (SDS) values ($p = 0.002$, $r = 0.178$).

Conclusions: The EFV value was significantly higher in patients with reversible ischemia on MPS compared to patients with normal scintigraphy findings. Also there was a statistically low and positive correlation between EFV and SDS values. The automatic calculation of the EFV value during this examination may be a good additional parameter to detect the presence of ischemia.

Keywords: Epicardial fat volume, Tc-99m MIBI, scintigraphy, summed difference score

Coronary artery disease (CAD) can be defined as insufficient blood supply to the myocardium due to narrowing or occlusion of the coronary arteries, usually caused by atherosclerosis. CAD is one of the most important causes of mortality and morbidity all over the World [1]. It is important to determine the risk of cardiovascular disease in these patients. Although coronary angiography is considered the gold standard technique for diagnosing CAD, myocardial perfusion scintigraphy (MPS) using single-photon emission computed tomography (SPECT) with radiopharmaceutical is commonly used in the non-invasive diagnosis of obstructive CAD.

Epicardial fat (EF) is an adipose tissue located be-

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tween the myocardium and the visceral pericardium, which has some metabolic functions. EF has the same embryological origin as visceral adipose tissue and causes to release of proinflammatory cytokines which is involved in the production of atherosclerosis of the coronary arteries [2]. It has been assumed that EF has direct paracrine or vasocrine effects on the coronary arteries due to the presence of anatomical proximity and the absence of a facial barrier between them [3]. In many studies, it has been found that there is a positive correlation between epicardial fat volume (EFV) and atherosclerosis of the coronary arteries [4, 5].

Computed tomography (CT) is considered to be the preferred imaging method for the measurement of EFV due to its high spatial resolution and widespread availability. Traditionally, CT volumetric analysis of EF can be performed in non-contrast thorax CT examination, but it can also be measured with SPECT/CT hybrid cardiac gamma cameras. Low-dose CT for attenuation correction, a standard component of MPS SPECT/CT, can be used to calculate EFV without additional radiation exposure or cost [6].

In clinical practice, MPS are interpreted based on visually by assessment of radiopharmaceutical uptake. Withal, automated analysis data obtained with quantitative softwares may help in visual analysis. Quantification is an important appliance in MPS because it helps determine the severity of ischemia as well as an objective assessment. With MPS SPECT, automated analysis parameters such as summed stress score (SSS), summed rest score (SRS), summed difference score (SDS), stress, and resting mid myocardial perfusion defect percentage rates can be obtained. These parameters can provide important information about the patient's status.

We purposed to compare the EFV between patients with normal perfusion and reversible perfusion abnormalities in the MPS study in patients with suspected CAD. In addition, this study aimed to investigate the relationship of automated analysis parameters obtained in the MPS SPECT examination with EFV.

METHODS

Patients who had previously undergone MPS due to suspected CAD and had recent thorax CT were included in our retrospective study. Only previous imaging of the patients was evaluated and no additional imaging was performed for the study. Informed consent of the patients was obtained before both imaging. All patients approved the use of their medical records for research purposes. This retrospective study was performed in accordance with the Helsinki Declaration.

Study Population

A total of 295 patients (182 F, 113 M) who underwent MPS in our unit with the suspicion of CAD in the last 1 year and who had a recent thorax CT examination were included in the study. There were a total of 196 people in the control group, including 70 males and 126 females. The mean age of the control group was 61.2 ± 10.1 years (range: 26-83 years). There were a total of 99 people in the patient group, including 43 males and 56 females. The mean age of the patient group was 62.9 ± 10.2 years (range: 37-92 years). Patients with a maximum heart rate below 85% of age-predicted maximum heart rate in the exercise stress test, patients with motion artifact or high extra-cardiac activity during MPS, and patients who had previous coronary vascular surgery were excluded from the study.

Computed Tomography Analysis of Epicardial Fat Volume

The non-contrast computed tomography images obtained with a 16 slice CT scanner (Alexion 16 Multi-slice, Toshiba Medical System Corporation) using the following parameters: fixed noise index of 30.9; 0.625-mm collimation; reconstruction slice thickness of 5 mm 120 kVp; variable milliamperage determined by x-, y-, and z-axis dose modulation; gantry rotation time of 0.5 seconds; and 40% ASIR. Thorax CT images of all patients were obtained from the hospital PACS system in DICOMDIR format. EFV measurement in CT scans was performed with free software. (Invesalius 3.1, Centro de Tecnologia da Informação Renato Archer, Brazil). The images obtained in DICOMDIR format were transferred into the software for quantification.

EF is defined as the adipose tissue located between the pericardium and myocardium and also surrounding the coronary arteries. The upper border of the pericardial contours was determined as the pulmonary bifurcation, and the lower border was determined as the posterior descending artery. EF within pericardium was selected by manual segmentation on sequential trans-axial slices with 5 mm slice thickness and the threshold for EF detection set between −30 HU and −271 HU. During this procedure, other adipose tissues other than epicardial adipose tissue were excluded by paying attention to the pericardial contours (Fig 1). The EFV was then calculated by software that met the threshold parameters for EF in each slice. The measurement result was obtained in ml. The operators did not have patient clinical data, such as the presence or absence of ischemia on MPS.

Myocardial Perfusion Scintigraphy Imaging

MPS was performed in all patients with a one-day stress and rest imaging protocol. In the stress study, imaging was performed approximately 30-45 min after intravenous injection of ~12 mCi Tc99m Sestamibi. In the rest study, imaging was performed approximately 30-60 min after intravenous injection of ~25 mCi Tc99m Sestamibi. MPS imaging was performed using the MEDISO Any Scan S gamma camera system (Mediso Medical Imaging Systems Ltd., Budapest, Hungary). All data collection was carried out by a double-headed SPECT system equipped with a low-energy, high-resolution collimator. The energy photopeak was set to 140 keV. Imaging was done in 64×64 matrix dimensions. Imaging was obtained by taking 64 steps from the right anterior oblique to the left posterior oblique position at 180 degrees, 3-6 degrees in each step. In all patients without contraindications, MPS was performed after a pharmacological stress test with adenosine due to the Covid-19 pandemic. In patients with contraindications for the pharmacological stress test, MPS was performed after the exercise stress test with the Modified Bruce protocol.

Computer-Assisted Quantification of MPS

MPS images were evaluated based on a computer-assisted 17-segment model with 5–point scoring system by an experienced nuclear medicine specialist. Obtained MPS images were grouped as normal or ischemic according to the presence of ischemia signs. MPS quantitative parameters were obtained with com-

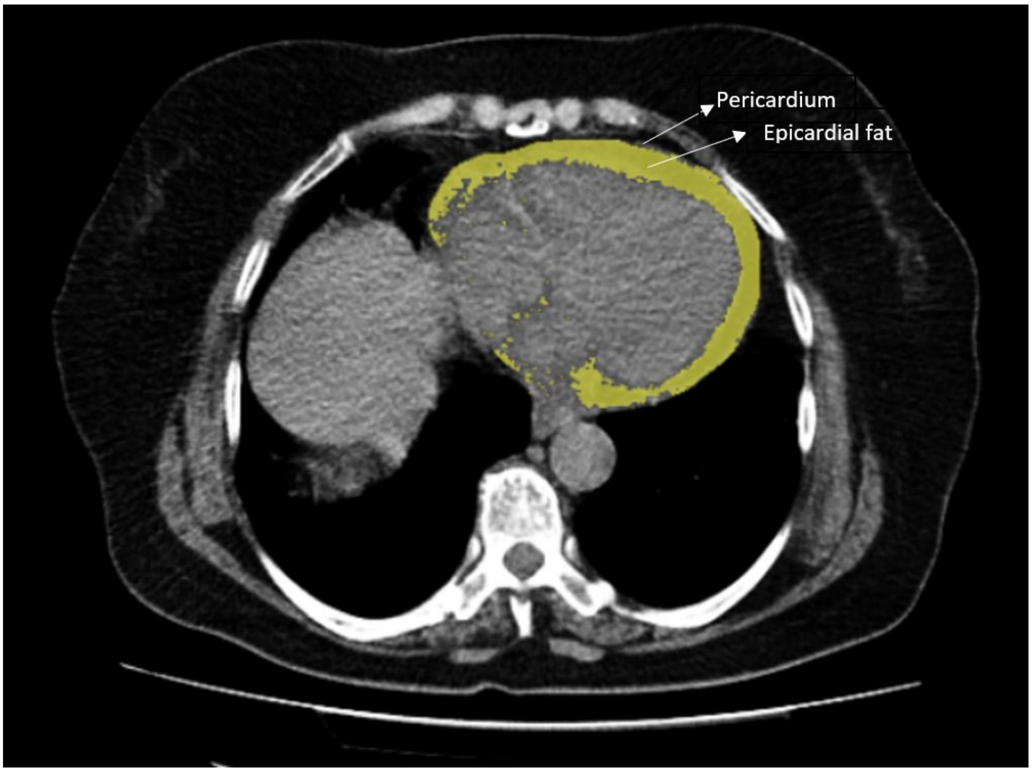

Fig. 1. Manual segmentation of epicardial adipose tissue in the pericardium, which is carried out by paying attention to the contours of the pericardium and distinguishing it from other adipose tissues. This procedure was applied to all consecutive sections. The upper border of the pericardial contours was determined as the pulmonary bifurcation, and the lower border was determined as the posterior descending artery.

mercially available software (Cedars-Sinai Quantitative Perfusion SPECT [QPS] and Quantitative Gated SPECT [QGS]). The total score at stress is called summed stress score (SSS) and reflects the extent and severity of ischemia and infarction. The difference between the SSS and SRS is called summed difference score (SDS), which reflects reversible defect.

Statistical Analysis

We used SPSS statistical software program (SPSS version 26.0, SPSS Inc., Chicago). Kolmogorov-Smirnov/Shapiro-Wilk's test was used to determine whether the data were normally distributed. The Chi-square test was used to examine the differences between categorical variables in the same patient group. While investigating the associations between non-normally distributed and/or ordinal variables, the correlation coefficients and their significance were calculated using the Spearman test. When the numerical data between two independent groups is evaluated, if the normal distribution conditions are met, the Independent Samples t-Test is used, if the normality condition is not met, the Mann-Whitney U test is used. All continuous variables were described as a mean ± SD. A p - value < 0.05 was considered statistically significant.

RESULTS

Median EFV was 53.00 ml (interquartile range: 23 ml, range 17-238 ml) in patients with normal MPS, and 62.00 ml in patients with myocardial ischemia on scintigraphy (interquartile range: 53 ml, range: 25-207 ml). The EFV value was higher in patients with reversible ischemia on MPS compared to patients with

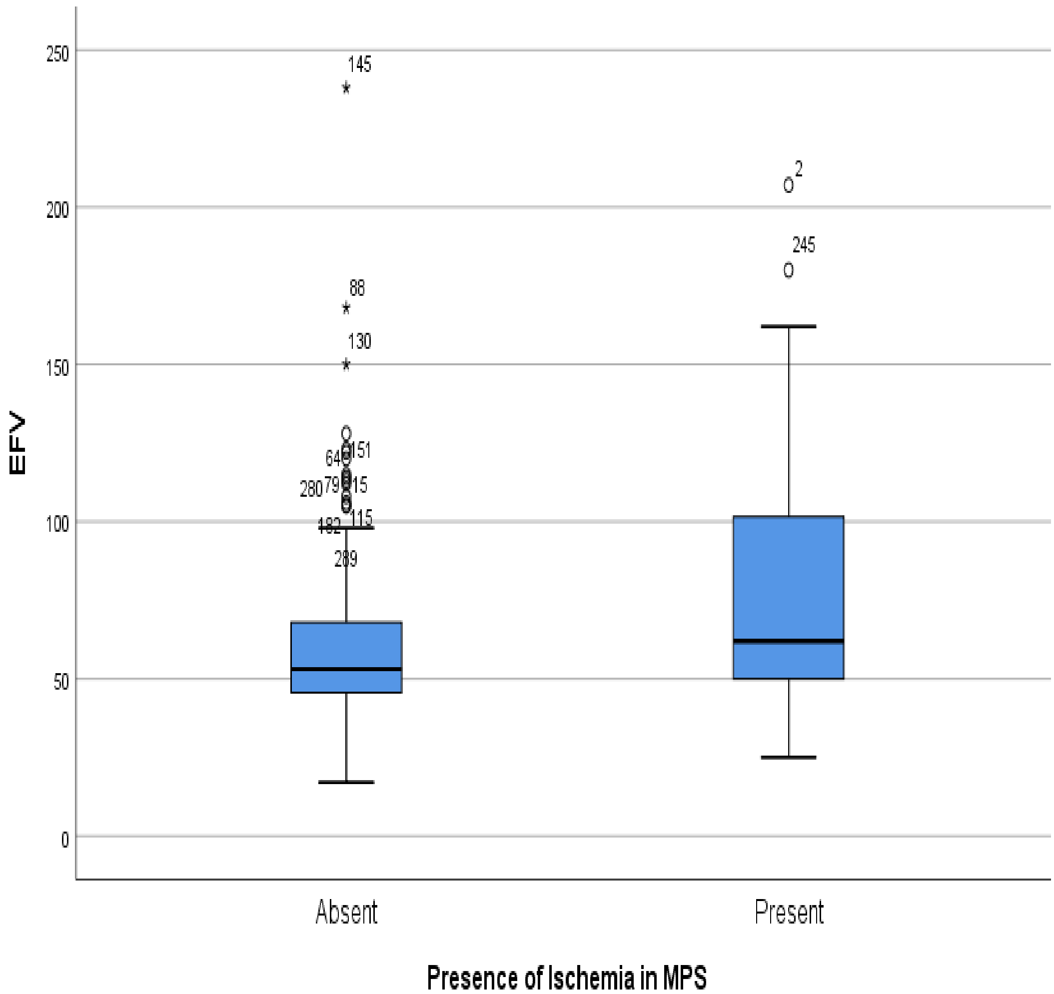

Fig. 2. The relationship between EFV and the presence of ischemia in MPS.

Table 1. Correlation of EFV with SSS, SRS, SDS, age and extent values

		SRS	SDS	SE	RE	Age	SSS
EFV	**Pearson Correlation Coefficient**	**0.240**	**0.178**	**0.262**	**0.236**	**0.227**	**0.254**
	p value	**< 0.001**	**0.002**	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**

EFV = epicardial fat volume, SDS = summed difference score, SRS = summed rest score, SSS = summed stress score, SE = stress extent, RE = resting extent

normal scintigraphy findings ($p < 0.001$) (Fig. 2).

The median SDS was found to be 5.00 (range: 0-23) with reversible ischemic patients and 0.00 in patients with normal MPS. The SDS value was statistically significantly higher in patients with reversible ischemia on MPS compared to patients with normal scintigraphy findings ($p < 0.001$). There was a statistically significant, low, and positive correlation between EFV value and SDS values ($p = 0.002$, r = 0.178).

There was a statistically low and positive correlation between EFV and age ($p < 0.001$), r = 0.227). There was no statistically significant correlation between EFV and gender ($p > 0.05$). When ischemic patients were evaluated alone, no statistically significant correlation was found between EFV and SSS, SRS, SDS, and percentage of extent ($p > 0.05$). (Table-1). When the relationship between the presence of myocardial ischemia and age is investigated; While the mean age of patients with myocardial ischemia was 62.9 years, the mean age was 61.3 years in patients without ischemia, and there was no statistically significant relationship between age and presence of myocardial ischemia (p > 0.05) (Table-2).

DISCUSSION

In our study, the EFV value was statistically significantly higher in patients with reversible ischemia on MPS compared to patients with normal scintigraphy findings ($p < 0.001$). There was a statistically significant, low and positive correlation between EFV value and SDS values ($p = 0.002$, r = 0.178).

Kilambi *et al*. [6] compared EFV between patients with normal perfusion and reversible perfusion abnormalities in the MPS. According to the study of Kilambi *et al*. [6], patients with reversible perfusion defects had an increased total EFV compared to patients with normal myocardial perfusion in MPS ($p < 0.001$). In the same study, a statistically significant relationship was found between age and the presence of myocardial ischemia [6].

With the development of technology in recent years, the use of SPECT/CT hybrid gamma cameras has become widespread. At the same time, false-positive findings can be minimized because attenuation correction can be made with cardiac SPECT/CT gamma cameras. In the study of Khawaja *et al*. [7], the relationship between EFV and the presence of is-

Table 2. Age, gender distributions, and EFV in the study groups with regard to the presence of ischemia in MPS

	Normal MPS (n = 196)	Ischemic MPS (n = 99)	*p value*
Age (years), (mean ± SD)	61.2 ± 10.1	62.9 ± 10.2	0.245
Gender, n (%)			0.198
Male	70 (61.9)	43 (38.1)	
Female	126 (69.2)	56 (30.8)	
EFV (mL, median)	53.00	62.00	0.000375
SDS	0	5	< 0.001

MPS = myocardial perfusion scintigraphy, EFV = epicardial fat volume, SDS = summed difference score chemia in the vascular territories was evaluated in patients who underwent MPS with SPECT/CT cardiac gamma cameras. In this study, patients without perfusion defects had a total EFV of 99.8 ± 82.3 cm3, which was lower than those with ischemia (156.4 ± 121.9 cm3; p = 0.001 versus controls). Nevertheless, EFV is similar to those with fixed perfusion defects that are compatible with myocardial infarction [7].

Although EFV in vascular regions separately not evaluated in this study, we investigated the relationship between the presence of myocardial ischemia and EFV. Our results were similar to these studies. The EFV values of patients with ischemia in MPS examination were significantly higher than those without ischemia ($p < 0.001$). Moreover, positive correlation was found between the SDS values obtained as a result of MPS examination and EFV ($p = 0.002$, r = 0.178).

Tamarappoo *et al*. [8] measured pericardial fat volume from non-contrast thorax CT images taken within the last 6 months of 73 patients with ischemia and 146 patients without ischemia in the SPECT scan. The mean PFV of the ischemic group was significantly higher ($p = 0.0003$). In addition, no significant difference between patients with ischemia and control patients without ischemia in terms of age, gender, and BMI were found. According to the results of this study, myocardial ischemia and pericardial adipose tissue were found to be associated with each other in patients without known coronary artery disease, and it was stated that pericardial fat volume could be used during risk stratification [8]. Janik *et al*. [9] also measured the EFV and coronary artery calcium scores (CAC) of patients who underwent Rb-82 PET/CT with a suspect of myocardial ischemia. Both parameters were significantly higher in patients with ischemia ($p < 0.01$). In addition, EFV values showed a better correlation with ischemia findings than with CAC (r = 0.47 vs r = 0.28, $p < 0.01$) [9]. In a similar study, Otaki *et al*. [10] investigated the relationship between EFV and CAC with impaired myocardial flow reserve (MFR) in Rb-82 PET/CT scans. Both the EFV and CAC values were significantly higher in patients with impaired MFR ($p = 0.01$). According to the results of this study, EFV was determined as the only independent predictor of impaired MFR [10]. Although there were some differences in methods, the results presented in these studies were in parallel with our findings.

In their study in 194 patients with suspected coronary artery disease in 2021, Yu *et al*. [11] showed that those with obstructive disease had higher EFV values ($p < 0.001$). Sun *et al*. [12] demonstrated that indigenous individuals had significantly higher EFV than nonindigenous individuals in Australia and supported the possibility that EAT may result in the greater burden of cardiovascular disease in indigenous populations. Moharram *et al*. [13] concluded that EAT thickness was significantly associated with BMI in European patients from New Zealand, but not in Maori/Pacific patients; this showed that the same BMI level showed different risk in different ethnic groups. These studies also show that EFV is associated with obesity and obviously, cardiovascular risk factors.

When all these studies were evaluated together, it was found that although epicardial fat volume was measured by different methods and myocardial ischemia was revealed by different tests, it was associated with cardiovascular risk factors. Some authors have calculated CAC to EFV in their studies, while others have shown its relevance to clinical situations. In our study, we demonstrated that there is a significant relationship between quantitative values such as SDS and SRS obtained in MPS and EFV.

Limitations

There are several limitations in our study that should be noted. First of all, our study was of a retrospective nature and the cases could not be followed up. The majority of our patient population in terms of gender consisted of female patients, and this leads to a gender imbalance. Coronary artery calcium scoring was not performed in our study. In addition to the patients who underwent MPS, no confirmation was made with coronary angiography. This study was a single-center study and reflects local patient population data only. In addition, SPECT/CT was not used in our study. Instead, SPECT images and recent CT images were used.

CONCLUSION

The EFV was higher in patients with reversible ischemia on MPS compared to normal patients. Also low and positive correlation between EFV and SDS values was found. SPECT/CT gamma cameras are currently used for MPS imaging. Epicardial adipose tissue volume can be easily calculated from low-dose CT imaging images used for attenuation correction during this hybrid imaging examination. The automatic calculation of the EFV value during this examination may help to detect the presence of ischemia. However, studies with a larger patient population with a prospective study design are needed.

Authors' Contribution

Study Conception: SÖ, SAE; Study Design: SÖ, SAE; Supervision: SÖ, SAE; Funding: SÖ, SAE; Materials: SÖ, SAE; Data Collection and/or Processing: SÖ, SAE; Statistical Analysis and/or Data Interpretation: SÖ, SAE; Literature Review: SÖ, SAE; Manuscript Preparation: AEY and Critical Review: SÖ, SAE.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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