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Correlation between Epicardial Fat Volume and the Severity of Coronary Artery Stenosis by Cardiac-CT

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ABSTRACT

Objective: *To investigate the correlation between EFV and severity of coronary artery stenosis using cardiac-CT in CAD subjects at Hasan Sadikin Hospital Bandung.* ***Methods:*** *It is an analytical observational study with a cross-sectional design using retrospective data with ANOVA and Chi-square statistical testing. The EFV and severity of coronary artery stenosis were quantified from diagnosed CAD subjects and underwent cardiac-CT in Hasan Sadikin Hospital Bandung from January2018-August 2018.* ***Results:*** *In 33 subjects there were 16 male (48.5%), 17 female (51.5%), there were 9 mild (27.3%), 9 moderate (27.3%), and 15 severe (45.5%) stenosis. Abnormal EFV (>125 ml) were 14 subjects (42.4%) found most in severe stenosis (30.3%). Chi-Square analysis showed that EFV had a significantly positive correlation with coronary artery stenosis (p=0.006), respectively.* ***Conclusion:*** *EFV demonstrated a positive correlation with the severity of coronary artery stenosis in CAD subjects using cardiac-CT at Hasan Sadikin Hospital, Bandung.*

Keywords: Cardiac-CT, EFV, Coronary artery stenosis, CAD

INTRODUCTION

Coronary artery disease (CAD) is a disorder caused by the buildup of plaque in the coronary arteries so that there is a blockage of flow in the coronary arteries that supply oxygen to the heart muscle [1-3].

The main cause of CAD is atherosclerosis, which is a chronic systemic inflammatory disease that involves the atherogenesis process and causes pathological changes in the coronary arteries which then cause stenosis so that blood flow gradually decreases [4-6].

WHO statistics in 2013 reported as many as 9.4 million deaths each year caused by cardiovascular disease with a mortality rate of 45% caused by CAD, and estimated that the number would increase to 23.3 million by 2030 [2,7]. Indonesian Basic Health Research's data (Riskesdas-Riset Kesehatan Dasar) in 2013 stated that CAD was most prevalent in the age group 65-74 years (3.6%) followed by the age group 75 years and above (3.2%), age group 55-64 years (2.1%) and age group 35-44 years (1.3%) [3,7]. Statistics from Indonesia's hospital in 2002 and 2003 showed that ischemic heart disease was the most frequent case of hospitalization and outpatient treatment compared to other heart diseases [8]. The high prevalence of CAD has increased the need for early detection and preventive interventions for atherosclerosis [9].

Clinical manifestations of CAD due to coronary artery stenosis have a broad clinical spectrum, ranging from asymptomatic, stable to the acute coronary syndrome, and causing sudden death [2,10]. Early detection of coronary disease can have a significant impact in order to accelerate prevention efforts before the onset of more severe clinical manifestations of heart disease [11].

Assessment of CAD can be established based on history, physical examination, electrocardiogram (ECG), and examination of heart markers, as well as other additional examinations such as resting ECG/activity, radionuclide scans, and coronary angiography [9].

The gold standard examination for describing the anatomy and coronary artery stenosis is coronary angiography.

Cardiac-CT with MSCT modality is a non-invasive examination and has a higher spatial and temporal resolution so that it can also assess the morphological structure around the coronary [12-14]. Achenbach, et al., study stated that MSCT had a sensitivity of 83% to 98% and specificity of 96-98% in assessing coronary artery stenosis [15].

Epicardial fat tissue (Epicardial adipose tissue, EAT) is a fat structure that anatomically directly surrounds the adventitia layer of coronary arteries, and has a local effect on coronary arteries [11,16-19]. EAT (Epicardial fat volume, EFV) volume measurements can be performed using several imaging modalities such as echocardiography, cardiac-CT with MSCT, and magnetic resonance imaging (MRI). The advantages of using cardiac-CT compared to other modalities are EFV measurements which are easier and faster and has high spatial resolution [20,21].

Epicardial fat is associated with cardiovascular risk factors, the composition of coronary artery plaques, and progression of coronary atherosclerosis [22,23]. Several studies have been conducted to see the correlation between EFV and coronary artery stenosis. Jin-Sung, et al., studied subjects with CAD in the Asian population, concluding that high EFV subjects were found in subjects with CAD with severe stenosis [24]. Research by Aslanabadi, et al., and Shehata, et al., revealed a significant association of EFV with coronary artery stenosis [11,25]. Bertaso, et al., suggested that the normal EFV value is <125 ml and not normal >125 ml [26-28].

The purpose of this study was to determine the correlation between EFV and the severity of coronary artery stenosis using cardiac CT-scan in subjects with CAD in Hasan Sadikin Hospital, Bandung.

MATERIALS AND METHODS

The study population was adult subjects aged >20 years, while the study subjects were subjects with a clinical diagnosis of CAD aged >20 years who had been subjected to cardiac CT-scan examination at Hasan Sadikin Hospital Bandung, Indonesia from January 2018 to August 2018. Exclusion criteria for research subjects were subjects with incomplete data, contraindications examination by cardiac CT-scan (iodine-based contrast allergy, renal failure/creatine >1.5 mg/dl, atrial fibrillation or another unstable heart rhythm, inability to perform breath holding, hemodynamically unstable patients, pregnant females), has history of coronary artery surgery and the installation of coronary artery stents or intracardiac devices (pacemaker), difficult to assess coronary artery by cardiac CT, and subjects with a history of congenital heart abnormalities or anatomical abnormalities of the coronary arteries.

Cardiac CT-scan using Multislice CT-Scan (The Scenario SE 128-Slice, Hitachi Medical System America Inc., Twinsburg, USA) with retrospective ECG gating, and intravenous contrast Iopromide 370 mg/mL, volume 70 ml, the flow rate of 4 mL/s, and followed by saline as much as 30 mL. The region of interest (ROI) was placed within the ascending aorta and the scan was started when a CT density level reached 120 Hounsfield unit (HU) higher than the baseline CT density. The scan was performed between the tracheal bifurcation and diaphragm with the following parameters: collimation width 128 × 0.6 mm, rotation time 350 ms, tube voltage 120 kV, and maximum effective tube current 800 mA. Cardiac CT-scan image analysis using workstation post-processing (Aquarius iNtuition client ver 4.4.13, Terarecon Inc., San Mateo, California) in the form of Digital Imaging and Communications in Medicine (DICOM), data are taken mainly from the 75% RR intervals, can use data from other intervals if there were heavy motion artifacts.

Coronary plaque were identified based on cMPR (curve-multiplanar reconstruction) and MPR images with vascular analysis function, and classified as mild (25% to 49% stenosis), moderate (50% to 69% stenosis), and severe (70% to 99% stenosis) [11,25]. Assessment of the luminal diameter stenosis was assessed from the quantitative measurement of lumen narrowing, i.e., the remaining lumen at the lesion site compared to the reference lumen area using the percentage narrowing area with the formula (1-L/R) × 100 (L=area of the lumen experiencing stenosis, R=reference area) [13,14,29-32]. The coronary arteries assessed were RCA (right coronary artery), LM (main left coronary artery), LCX (circumflex left coronary artery), and LAD (descending left coronary artery). The selected coronary stenosis is the heaviest degree of stenosis between the 4 coronary arteries (Figure 1).

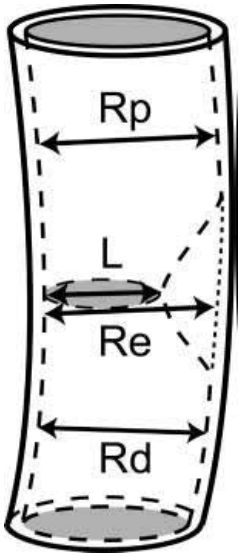

Figure 1 Illustration of measurements used to determine the severity of constriction of blood vessels. Rp is the normal lumen diameter in the proximal part of the narrowing lesion (L), Rd is the normal lumen area in the proximal part L, Re is the estimated lumen area as high as L. Rp, Re and Rd can be used as a reference area

EFV measurements were taken from contrast cardiac CT-scans image, reconstructed using the function of semi-automatic 3D fat analysis on axial slices with a thickness of 3 mm. Epicardial fat was defined as adipose tissue within the visceral epicardium. The layer of epicardium was manually tracing at each slice from the atrial appendix to the left ventricular apex. The computer will automatically construct a 3-dimensional image of the epicardium. EFV was quantified by calculating the total volume of the tissue identified in HU ranging between -250 and -30 within the pericardium (Figures 2 and 3).

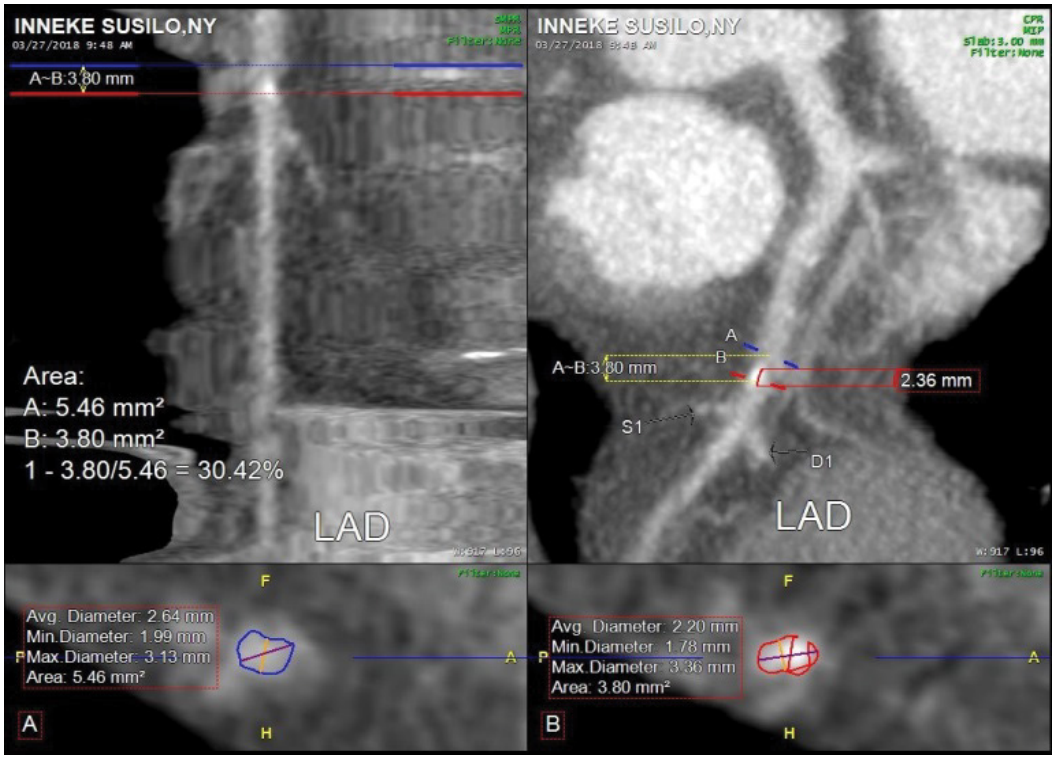

Figure 2 Coronary artery stenosis analysis by computed tomography (upper) multiplanar image shows a calcified plaque in the proximal left anterior descending artery. (A) area of reference area (mm^2); (B) area of stenosis (mm^2)

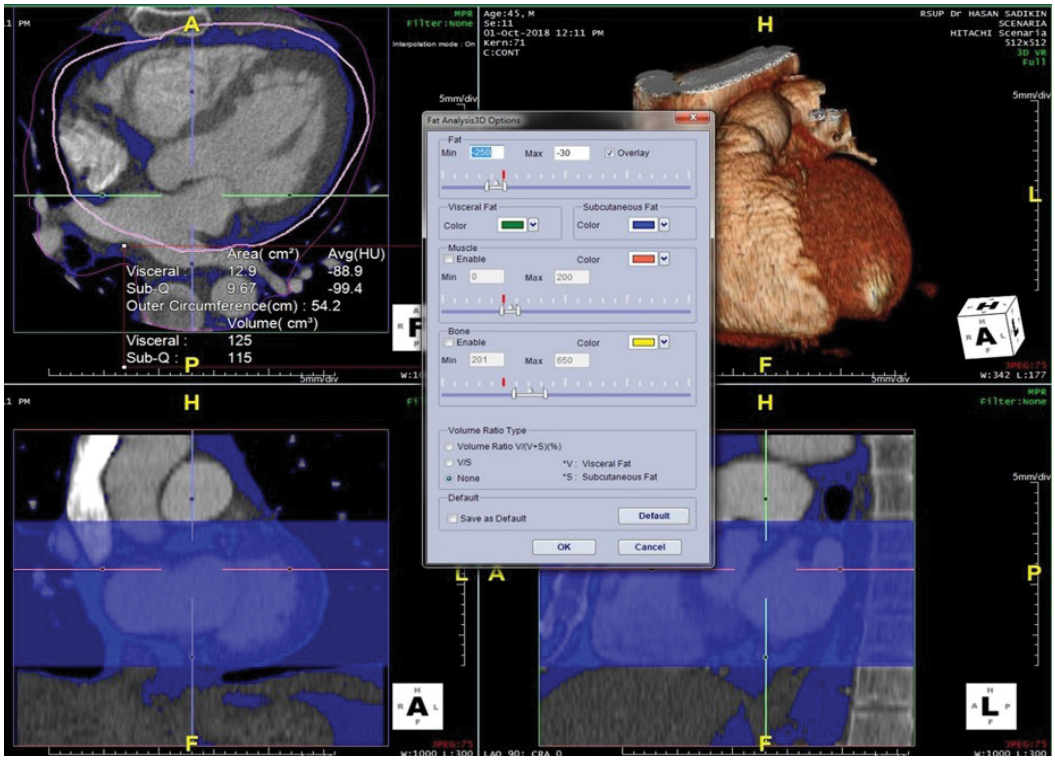

Figure 3 Semi-automated epicardial fat volume measurements using the function of 3D fat-analysis reconstruction

Statistical Analyses

The EFV data are categorized as normal and abnormal based on Bertaso, et al., a study [26]. The bivariate analysis using Chi-Square test was used to determine the correlation of EFV with the severity of coronary artery stenosis. All data analysis and processing were carried out using the Statistical product and service solution (SPSS) program for Windows version 18.0 at 95% confidence level and $p \leq 0.05$. Bivariate analysis test was carried out to test the correlation between EFV and the severity of coronary artery stenosis using ANOVA Test if EFV data were normally distributed, and Kruskal Wallis T-test was used if EFV data were not normally distributed.

RESULTS

This study examined 33 research subjects (17 women and 16 men). The age of the study subjects ranged from 30-80 years (mean age 62.12 ± 9.94 years), with the largest age group of 60-69 years as many as 15 people (45.5%). The characteristics of the study subjects had normal category EFV as many as 19 subjects (57.6%), and EFV with an abnormal category of 14 subjects (42.4%). About 15 subjects (45.5%) were having severe stenosis, moderate stenosis 9 subjects (27.3%), and mild 9 subjects (27.3%).

Table 1 shows the correlation between EFV values and the severity of coronary artery stenosis in CAD subjects obtained using the ANOVA test. The results of statistical analysis using the ANOVA Test on the 95% confidence level gave a value of p=0.000 which showed a significant correlation between EFV values and the severity of coronary artery stenosis.

Table 1 Correlation between EFV values and the severity of coronary artery stenosis

Variable	Severity of Coronary Artery Stenosis			p-value*)
	Mild	Moderate	Severe	
EFV Value				
Mean (SD)	94.08 (19.15)	116.6 (19.37)	136.8 (22.45)	0.000
Median (Min-maks)	90.5 (63.9-123)	125 (83-140	137 (104-182)	
*) ANOVA Test				

Table 2 also shows that subjects with severe coronary artery stenosis had higher EFV values than subjects with moderate and mild coronary artery stenosis.

Table 2 Correlation between the EFV category and the severity of coronary artery stenosis

Variable	Severity of Coronary Artery Stenosis						p-value*)
	mild		moderate		Severe		
EFV	**n**	**%**	**N**	**%**	**N**	**%**	
Normal	9	27.3	5	15.2	5	15.2	0.006
Abnormal	0	0.0	4	12.1	10	30.3	
*) Chi-Square Test							

The calculated EFV values were then divided into 2 categories according to the Bertaso, et al., study, which was <125 ml and abnormal >125 ml, then evaluated the correlation between EFV and the severity of coronary artery stenosis as shown in Table 2, and was analyzed using Chi-Square test. The results of the analysis showed that there was a significant correlation between the EFV category and the severity of coronary artery stenosis with a value of p=0.006 ($p \leq 0.05$).

DISCUSSION

The results of this study show the characteristics of the subject at most in the age group 60-69 years, this is in accordance with the data from 2013 by Riskesdas, showed that the prevalence of CAD in Indonesia was found in the 45-74 years of age group [3]. The number of research subjects for women in this age group was almost comparable to male subjects, this is in line because women have protective endogenous estrogen, but after menopause, the incidence of CAD increases rapidly, so that it eventually becomes proportional to the incidence in men [4,33,34].

According to several existing studies such as Shehata, et al., there is a significant correlation between EFV and coronary artery stenosis levels found in both men and women [11,25]. The results of this study show the same results.

The results of this study also showed higher EFV values in subjects with severe coronary artery stenosis than those with mild to moderate stenosis. The calculated EFV values from the study subjects were divided into 2 categories according to the Bertaso, et al., study; normal <125 ml and abnormal >125 ml. The abnormal EFV was found mostly in subjects with severe stenosis, and normal EFV was found in subjects with moderate and mild stenosis. This is in accordance with Jin-Sung, et al., research which concluded that high EFV subjects were found in CAD subjects with severe stenosis [24].

The theoretical basis that supports the above results is that adipose tissue in epicardial fat has adipokine EAT, that affects blood vessel wall homeostasis; changing the function of endothelial cells, arterial smooth muscle cells, and triggering the inflammatory process, so that it can affect the development of blood vessel atherosclerosis through a vasocrine mechanism and paracrine interactions, which over time cause coronary artery stenosis in various severity [20]. The weakness of this study is that the number of samples is relatively less when compared with other studies that have similar research designs.

CONCLUSION

There is a significant correlation between value and category of EFV with the severity of coronary artery stenosis in patients with CAD who have undergone cardiac CT-scan in Hasan Sadikin Hospital Bandung, with p=0.000 and p=0.006 ($p \leq 0.05$).

Abnormal EFV categories were found to be more prevalent in subjects with severe stenosis than in subjects with moderate and mild stenosis.

DECLARATIONS

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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