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Correlation of Epicardial Adipose Tissue (Eat) Thickness to Severity of Coronary Arterial Stenosis in Coronary Heart Disease Patients in Haji Adam Malik Hospital, Medan

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Abstract:-
Backgrounds: Epicardial adipose tissue (EAT) is splanchnopleuric mesoderm-derived tissue that communicates locally with coronary vessels and myocardium via paracrine and vasocrine routes. This tissue secretes pro-atherogenic and pro-inflammatory cytokines that affect cardiac function. Some studies found a significant relationship between EAT thickness and coronary artery disease (CAD).

Methods: This analytical, observational study aimed to assess the relationship between EAT thickness and coronary artery stenosis lesion severity in CAD patients of RSUP HAM. EAT thickness was measured using Doppler echocardiography by a cardiologist, while the severity of coronary artery stenosis lesion was determined by SYNTAX score. Bivariate analysis and T-test were used to analyze the difference between CAD with significant lesion and nonsignificant groups. ROC (Receiver Operating Curve) analysis was used to determine the cut-off value of EAT thickness that could predict the severity of the lesion.

Results: All 79 patients (39 CAD with significant lesion and 39 nonsignificant lesion) was dominated by male (57,6% and 42,4%). Diastole and systole EAT thickness of ≥2,75 mm, and ≥5,5 mm could predict CAD diagnoses. These cut-off points also had six times higher risk of developing significant coronary artery lesion, which was described by a SYNTAX score of > 22 [each had OR of 6,000 (IK95% 1,296-27,769)]

Conclusion: EAT thickness measurement using echocardiography could differentiate CAD with signifincant lesion with non-significant patients, and it also could predict the severity of coronary artery lesions in CAD patient

Keywords:- *Epicardial Adipose Tissue, SYNTAX, CAD.*

I. INTRODUCTION

Worldwide, CHD is the most common cause of death and its frequency continues to increase. According to the World Health Organization (WHO), the number one killer disease in the world is coronary heart disease, which is responsible for 16% of total deaths globally. Since 2000, the increase in deaths from this disease has increased from 2 million deaths to 8.9 million deaths in 2019.[1]

In Indonesia, according to the 2013 Basic Health Research data, the most common cardiovascular diseases are CHD and heart failure. The prevalence of CHD based on doctor's diagnosis or symptoms is 1.5%, and it increases with age to reach 3.6%. Not much different from CHD, the prevalence of heart failure also increases with age, from 0.5% (65 – 74 years) to 1.1% (≥75 years).[2]

In America, it is reported that the incidence of IMA-EST decreased from 133 per 100,000 in 1999 to 50 per 100,000 in 2008, while the incidence of IMANEST has remained constant or increased slightly. In Europe, the relative incidence of IMAEST has decreased and IMANEST has increased. In Sweden, the incidence rate of IMAEST was 58 per 100,000 persons per year in 2015. In other European countries, the incidence rates ranged from 43 to 144 persons per 100,000 per year.[3]

A clinical risk scoring system and coronary angiography have been developed for the identification of high-risk AMI patients. In addition, this risk stratification is also useful in establishing an appropriate management strategy and for evaluating the severity and complexity of coronary artery disease. The SYNTAX and Gensini scoring systems have been developed to determine the extent and severity of coronary artery disease.[4,5] The Global Registry of Acute Coronary Events (GRACE) scoring systems, TIMI risk scoring, and TIMI-STEMI risk scoring systems are also frequently used in clinical practice. Although this scoring system is useful, a risk stratification system that is inexpensive, non-invasive and can be widely used is still needed to identify the severity of coronary artery disease in AMI patients.[6]

A study by Akcay et al in 2019 investigated the relationship between epicardial adipose tissue thickness and the severity of acute coronary syndromes. The study took samples from patients hospitalized for AMI indications, where the severity and complexity of coronary artery disease were assessed by GRACE risk scoring, TIMI clinical, SYNTAX scoring and Gensini angiography scoring according to guidelines. While the thickness of the EAT was assessed by echocardiography, namely above the free wall of the right ventricle, perpendicular to the aortic annulus.

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After doing the research, Akcay et.al found a positive and significant correlation between the thickness of the EAT with the SYNTAX score ($r = 0.243$, $p = 0.035$) and the Gensini score ($r = 0.394$, $p < 0.001$). Multivariate linear regression analysis showed that EAT thickness could predict SYNTAX scores ($\beta = 0.06$, $p < 0.001$) and Gensini scores ($\beta = 0.04$, $p = 0.006$) in all patients.[7]

Eroglu et al compared CHD patients with individuals with normal coronary arteries and found that CHD patients had an increased EAT thickness, and this correlated with the Gensini score. Similarly, the study of Erkan et.al found a correlation of EAT with Gensini and SYNTAX scores in patients with unstable angina pectoris or myocardial infarction, and proposed that EAT could be a predictor of these conditions.[8]Gul et al also found that EAT was associated with GRACE risk scores in IMA-NEST patients and Altun et al observed a correlation between EAT and SYNTAX scores in 65 patients with ACS.[5]In addition, Ozcan et al in 2019 found an independent relationship between EAT and TIMI risk scores in APTS/IMA-NEST patients.[6]

Noldy et al concluded that epicardial adipose thickness was significantly correlated with the degree of coronary artery stenosis based on the Gensini score. It was stated that epicardial adipose thickness of 6.15 mm had a good enough ability to differentiate mild-moderate and severe stable CHD patients based on the Gensini score.[9]The author wanted to examine the relationship between Epicardial Adipose Tissue (EAT) thickness and the severity of coronary artery stenosis in patients with coronary heart disease at Haji Adam Malik General Hospital, Medan.

II. METHODS

This type of research is an observational analytic study with a cross sectional study design, which is to assess the relationship between Epicardial Adipose Tissue (EAT) thickness and the severity of coronary artery stenosis in coronary heart disease (CHD) patients treated at H. Adam Malik Hospital, Medan. This research was conducted at H. Adam Malik Hospital Medan from August 2021 to December 2021. The target population is all patients with coronary heart disease. The affordable population is coronary heart disease patients who are treated at H. Adam Malik Hospital, Medan. The sample is an affordable population that meets the inclusion and exclusion criteria, taken consecutively until the number of samples is met. The minimum sample size required in this study was 39 subjects per group so that the total research subjects were 78 people.

The inclusion criteria of this study were patients with clinical and supportive examinations as coronary heart disease (CHD) patients, namely, stable angina pectoris, APTS, IMA-EST and IMA-NEST, patients with a diagnosis of acute coronary syndrome who underwent therapy according to the recommended medical service mix in Cardiac Center H. Adam Malik General Hospital, patients with a diagnosis of coronary heart disease who underwent coronary angiography examination according to the combination of medical services available at Cardiac Center H. Adam Malik General Hospital and patients signed an informed consent letter to be included in the study.

The exclusion criteria for this study were patients with normal coronary artery angiography, patients with significant valvular disease, patients who had undergone heart valve surgery, or, IKP procedures, or coronary artery bypass surgery, patients who were pregnant and patients with echocardiographic findings that not good. Before starting the research, the researcher asked for ethical clearance from the Ethical Committee for Assessing Research Ethics, Faculty of Medicine, Universit as Sumatera Utara. Each subject who was included in the study sample was explained and asked for approval using an informed consent signed by the participants and the researcher. All samples of this study were patients with coronary heart disease (CHD) who were treated at PJT H. Adam Malik Hospital Medan (HAM) according to the inclusion and exclusion criteria.

The researcher examined the patient's medical record to see the history, physical examination, electrocardiography (ECG), blood laboratory, anthropometric examination, echocardiography and angiography, then recorded the significance of the severity of coronary artery stenosis during the patient's stay. Blood examination through the Clinical Pathology laboratory of RS. Haji Adam Malik Medan using Architech C4000 and C8000 tools. ECG assessment using Bionet Cardiotouch 3000 with a speed of 25 mm/s and an amplitude of 10 mV.

Coronary angiography examination was carried out in the cathlab room and the results of coronary angiography and the calculation of the SYNTAX score were validated by a specialist interventional heart and blood vessel specialist, while echocardiography was used to assess the thickness of the EAT which was assessed during the systolic phase (marked at the peak of the R wave on the ECG) and during the systolic phase. diastolic (marked by the end of the T wave on the EKG) taken in the parasternal long axis and parasternal short axis views about the papillary muscles performed in the Echo Poly PJT room at H. Adam Malik Hospital Medan using a GE Vivid E95 3D with an M5Sc heart probe (1.4 - 4.6). MHz) and GE VIVID VS60 with a 3SC heart probe (1.3 - 4.5 MHz) whose measurement results have been validated by a Cardiologist and Echocardiography Subspecialist.

Anthropometric examination was carried out using a measuring tape and a manual scale when the patient was treated at Cardiac Center H. Adam Malik Hospital. After all the data obtained, data processing, analysis, and hypothesis testing will be carried out using SPSS ver.24.

Statistical data processing and analysis using SPSS program. Categorical variables are represented by number or frequency (n) and percentage (%). Numerical variables are represented by a measure of the concentration of the average value (mean) and a measure of the spread of the standard deviation for normally distributed data. Meanwhile, the data that is not normally distributed is presented in the form of the median. Normality test of numerical variables on all

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research subjects with a sample of n > 50 using the Kolmogorov-Smirnov test.

Bivariate analysis to determine the difference between the two groups on the numerical independent variable and the categorical dependent variable used the Independent T-test (T-test). If the independent T-test conditions are not met, then the Mann Whitney test is used. To determine the optimal cut-off point for Epicardial Adipose Tissue (EAT) thickness on the severity of coronary artery stenosis in patients with significant and insignificant coronary heart disease, a discrimination analysis test was performed using an ROC (Receiver Operating Curve) curve analysis and the results of the analysis were presented by presenting the AUC value (Area Under Curve) and Confidence Interval 95% cut-off along with sensitivity and specificity values.

III. RESULTS

This study was followed by 78 research subjects with the aim of knowing the relationship between Epicardial Adipose Tissue (EAT) thickness and the severity of coronary artery stenosis in patients with coronary heart disease at Haji Adam Malik Hospital, Medan. Subjects were divided into two groups, namely the CHD group with significant coronary artery lesions and the CHD group with coronary artery lesions, each with the same number of 39 subjects. The majority of the research subjects were male as many as 59 people (75.5%), and the average age of the research subjects was 54 years, the characteristics of the research subjects are presented in table 1.

Based on age, the age of CHD patients with significant lesions (54.58 years) was relatively the same as the age of CHD patients with non-significant lesions (54.38 years), there was no statistically significant difference. Comparison of the proportion of CHD patients with male to female significant lesions has a ratio of 7:1 while the proportion of male to female CHD patients with non-significant lesions has a ratio of 5:3. CHD patients with significant lesions had a lower median weight (65 kg) than CHD patients with non-significant lesions (66 kg), and there was no statistically significant difference. CHD patients with significant lesions had a higher BMI, waist circumference, and upper arm circumference (UAC) than CHD patients with nonsignificant lesions and there was a statistical difference.

Based on disease history, CHD patients with significant lesions had a history of diabetes mellitus (37.8%) less than CHD patients with non-significant lesions who had a history of diabetes mellitus (62.2%), and there was a significant difference. CHD patients with significant lesions had a history of hypertension (57.1%) more than CHD patients with non-significant lesions who had a history of hypertension (42.9%), and there was no statistically significant difference. CHD patients with significant lesions had a history of hypercholesterolemia (68.4%) more than CHD patients with non-significant lesions who had a history of hypercholesterolemia (31.6%), and there was a statistically significant difference. CHD patients with significant lesions smoked (54.4%) more than CHD patients with nonsignificant lesions who smoked (45.6%), and there was no statistically significant difference.

Based on the results of lipid profile examination, the median total cholesterol level of CHD patients with significant lesions (167.51 mg/ml) was lower than the median total cholesterol level of CHD patients with non-significant lesions (177.74 mg/ml) although there was no significant difference. statistically. The median LDL level of CHD patients with significant lesions (133 mg/ml) was higher than the median LDL level of CHD patients with non-significant lesions (117.74 mg/ml) and there was a statistically significant difference. The median HDL level of CHD patients with significant lesions (35 mg/ml) was lower than the median HDL level of CHD patients with non-significant lesions (39 mg/ml), but there was no statistically significant difference. The median triglyceride levels of CHD patients with significant lesions (124 mg/ml) were lower than the median triglyceride levels of CHD patients with non-significant lesions (132 mg/ml), there was no statistically significant difference.

The median ejection fraction of CHD patients with significant lesions (43%) was lower than the median ejection fraction of CHD patients with nonsignificant lesions (57%), there was a statistically significant difference. The median EAT thickness of the diastolic phase of CHD patients with significant lesions (3 mm) was higher than the median EAT of diastolic phase of CHD patients with nonsignificant lesions (1 mm), there was a statistically significant difference. The median EAT systolic thickness of CHD patients with significant lesions (6 mm) was higher than the median EAT systolic phase of CHD patients with non-significant lesions (2 mm), there was a statistically significant difference.

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Characteristics	CHD with significant coronary artery lesions (n=39)	CHD with nonsignificant coronary artery lesion (n=39)	p-value
Age, (years)	54,58±9,36	54,38±7,81	0,917
Gender, n(%)			
Male	34 (57,6)	25 (42,4)	0,018
Female	5 (26,3)	14 (73,7)	
Weight, (kg)	65 (48-104)	66 (45-110)	0,396
Height, (cm)	165 (149-180)	165 (149-176)	0,864
IMT, (kg/m^2)	26,09±2,59	24,59±3,45	0,033
UAC, (cm)	30,92±3,68	27,94±3,28	<0.001
Waist size, (cm)	97,28±6,88	86,94±8,37	<0.001
Comorbid, Yes n(%)			
Diabetes mellitus,	14 (37,8)	23 (62,2)	0,041
Hypertension	24 (57,1)	18 (42,9)	0,173
Hypercholesterolemia	26 (68,4)	12 (31,6)	0,002
Smoke	31 (54,4)	26 (45,6)	0,202
Lab exams			
Hemoglobin (gr/dl)	13,4 (9,10-18,5)	14,3 (7,90-18,60)	0,122
Total cholesterol (mg/ml)	167,51±33,90	177,74±37,06	0,207
LDL (mg/ml)	133,17±27,39	117,28±31.93	0,021
HDL (mg/ml)	35 (10-106)	39 (18-62)	0,269
Triglyceride (mg/ml)	124 (66-416)	132 (60-326)	0,764
Fasting BGL (mg/dl)	113 (75-249)	110 (82-357)	0,956
2PP BGL (mg/dl)	132 (82-325)	145 (70-295)	0,187
Hb1AC (%)	6,10 (4,90-12,80)	6,00 (5,00-10,60)	0,606
Troponin I (ng/ml)	2,00 (0,01-26,90)	0,01 (0,01-1,50)	<0,001
CKMB (ng/ml)	71 (12-501)	20 (15-29)	<0,001
ACS, n(%)			
AP	6 (17,6)	28 (82,4)	0,029
STEMI	12 (100,0)	0 (0,0)	
NSTEMI	20 (100,0)	0 (0,0)	
UAP	1 (8,3)	11 (91,7)	
Ejection Fraction (%)	43 (22-67)	57 (33-73)	<0,001
TAPSE	20 (13-27)	21 (16-25)	0,277
Thickness *EAT* (mm)			
EAT Diastolic	3,00 (1,50-4,00)	1,00 (1,00-4,50)	<0,001
*EAT*Systolic	6,00 (3,00-8,00)	2,00 (2,00-9,00)	<0,001

Table 1: Characteristics of Research Subjects

The analysis was continued with multivariate analysis to determine the factors that most play a role as a marker of the severity of coronary artery lesions in patients with coronary heart disease. The variables included in the multivariate analysis were BMI, ALL, waist circumference, diabetes mellitus, hypertension, smoking, hemoglobin, troponin I, CKMB, total cholesterol, LDL, diastolic EAT, systolic EAT, and Ejection fraction. Based on logistic regression analysis with a backward stepwise conditional approach of 11 steps, the final results are obtained as presented in table 2.

Elevated CKMB levels had a 1.088x risk of coronary artery lesion severity, which was statistically significant with [β 0.084; OR 1.088 (CI 95% 1.022 – 1.158) p value = 0.008]. Increased diastolic EAT thickness had a 2.864x risk of coronary artery lesion severity, which was statistically significant with [β 1.052; OR 2.864 (CI 95% 1.240-6.614) p value = 0.014]. Decreased ejection fraction had a 0.865x risk of coronary artery lesion severity, which was statistically significant with [β -0.145; OR 0.865 (CI 95% 0.792-0.946) p value = 0.001].

Parameter	Coefficient beta	p-value	OR	IK 95%
CKMB (ng/ml)	0,084	0,008	1,088	1,022 – 1,158
EAT Diastolic (mm)	1,052	0,014	2,864	1,240 – 6,614
Ejection Fraction (%)	-0,145	0,001	0,865	0,792 – 0,946
Cons	1,733			

Table 2: Factors that act as markers of the severity of coronary lesions in patients with coronary heart disease

Binary Logistics Regression Test

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The graph shows that the optimal cut point for diastolic EAT is at 2.75, meaning that subjects with Epicardial Adipose Tissue (EAT) Diastolic thickness ≥ 2.75 are CHD patients with significant lesions with sensitivity 66.7%, specificity 68.4%, positive predictive value (PPV) 43.8%, and negative predictive value (NPV) 84.8%.

While the optimal cut-off point for systolic EAT is 5.5, meaning that subjects with a systolic Epicardial Adipose Tissue (EAT) thickness of ≥5.5 are CHD patients with significant lesions with sensitivity 66.7%, specificity 68.4%, positive predictive value. (PPV) 43.8%, and negative predictive value (NPV) 84.8%.

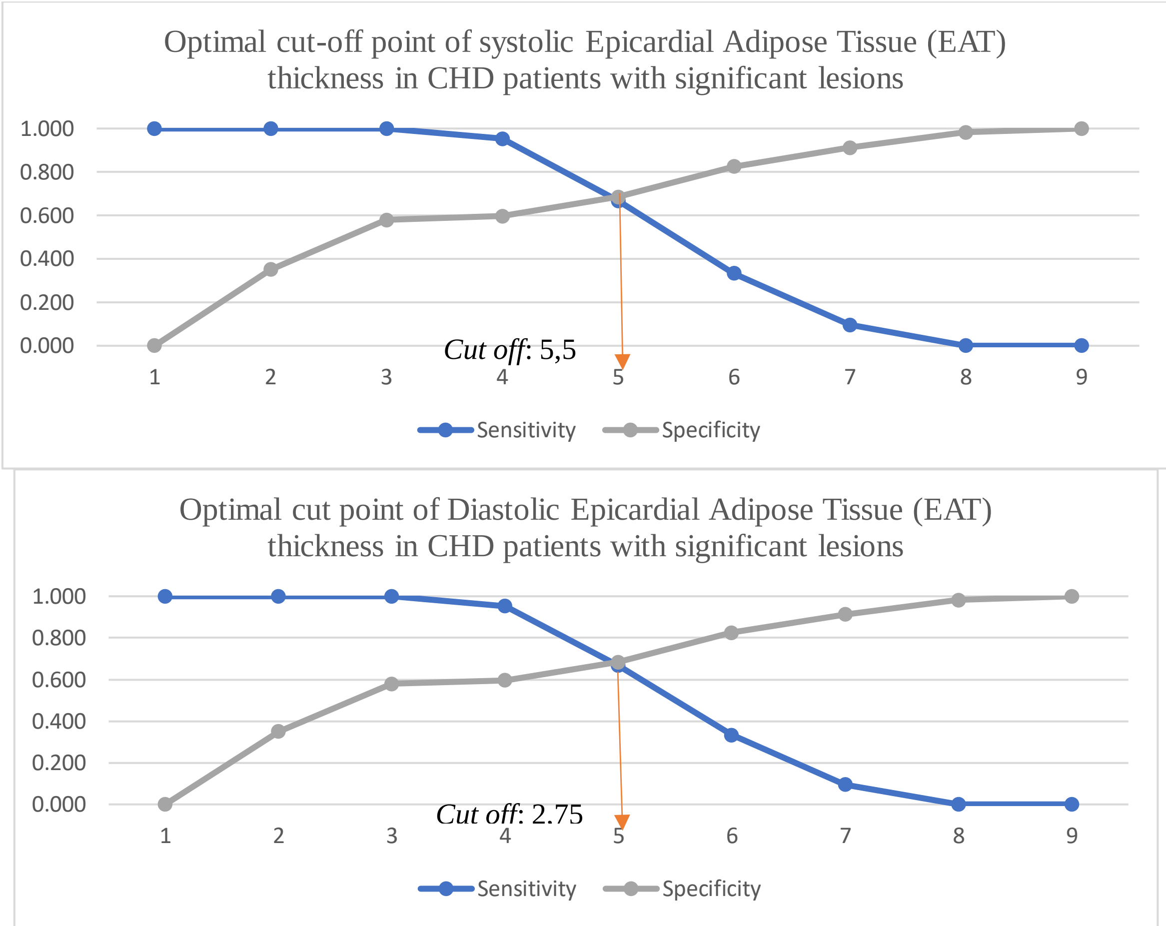

Fig. 1: Graph of sensitivity and specificity of diastolic (A) and systolic (B) Epicardial Adipose Tissue (EAT) in CHD patients with significant lesions

The severity of coronary artery lesions was assessed by a SYNTAX score which was categorized into two, namely moderate-severe >22 and low severity 22. The relationship between Epicardial Adipose Tissue (EAT) thickness in CHD patients and the severity of coronary artery stenosis in coronary heart disease patients with significant lesions at Haji Adam Malik General Hospital Medan is presented in Tables 3 and 4.

A total of 39 CHD patients with significant lesions were confirmed by angiography. A total of 27 subjects had a diastolic EAT thickness 2.75 mm, 18 subjects (46.2%) of whom had syntax>22 and as many as 12 subjects had an EAT thickness <2.75 mm and had syntax>22 as many as 3 patients (7.7%). Based on the analysis, there was a statistically significant relationship between the thickness of the diastolic EAT and the severity of coronary artery lesions in coronary heart disease patients with significant lesions with p value = 0.039 (table 4.4). Diastolic EAT 2.75 mm had a 6x risk of coronary artery lesion severity, which was statistically significant with [OR 6,000 (95% CI 1.296-27.769)].

EAT diastolic	Syntax score		Total	P-value	*OR*
	Syntax>22 (n=21)	Syntax≤22 (n=18)			
EAT≥2,75	18 (46,2)	9 (23,1)	27 (69,2)	0,039	6,000
EAT<2,75	3 (7,7)	9 (23,1)	12 (30,8)		

Table 3: Relationship between Diastolic EAT thickness and severity of coronary artery lesions as assessed by the SYNTAX score in CHD patients with significant lesions
Chi square test

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A total of 27 subjects had a systolic EAT thickness 5.5 mm, 18 subjects (46.2%) of whom had syntax>22 and as many as 12 subjects had a systolic EAT thickness <5.5 mm and had syntax>22 as many as 3 patients (7.7 %). Based on the analysis, there was a statistically significant relationship between the systolic EAT thickness description and the severity of coronary artery lesions in patients with coronary heart disease with significant lesions with p value = 0.039 (table 4.5). EAT systolic 5.5 mm had a 6x risk of coronary artery lesion severity, which was statistically significant with [OR 6,000 (95% CI 1.296-27.769)]

EAT systolic	Syntax score		Total	p-value	*OR*
	Syntax>22 (n=21)	Syntax≤22 (n=18)			
EAT≥5,5	18 (46,2)	9 (23,1)	27 (69,2)	0,039	6,000
EAT<5,5	3 (7,7)	9 (23,1)	12 (30,8)		

Table 4. Relationship between systolic EAT thickness and severity of coronary artery lesions as assessed by the SYNTAX score in CHD patients with significant lesions

Chi square test

IV. DISCUSSIONS

There is a difference between the thickness of the EAT in patients with CHD with significant lesions and CHD with non-significant lesions, so our study continued the analysis to determine the cut-off point of EAT thickness in predicting the diagnosis of CHD with significant lesions. It was found that a diastolic EAT cut-off above equal to 2.75mm can establish the diagnosis of CHD with significant lesions; with a sensitivity of 66.7% and a specificity of 68.4%. Meanwhile, the systolic EAT measurement results equal to 5.5 mm can confirm the diagnosis of CHD with significant lesions with a sensitivity of 66.7% and a specificity of 68.4%.

This finding is supported by research which found a higher mean EAT in patients who underwent angiography and found CHD with significant lesions (5.4±1.9 mm), compared to patients with CHD with nonsignificant lesions (4.4±1.8 mm).[1]In addition, a meta-analysis involving 2872 patients showed that CHD patients had an increase in EAT thickness and volume compared to subjects without CHD.[2]Xiu et.al found that the mean difference in EAT thickness between CHD and non-CHD patients was 1.57 mm (95% CI: 0.74, 2.40, P<0.00001) and the mean difference for EAT volume was 15.22 ml (95% CI: 7.58, 22.87, P<0.0001). Research by Wang et al[3]also found that increased EAT volume was associated with coronary atherosclerosis, coronary calcium scores, as well as inflammatory biomarkers of CHD. In addition, eker T et al, Aydın E et al, Alpaydın S et al, and Ozturk MT et al also found that EAT was associated with left ventricular hypertrophy, abnormal geometry of the left ventricle, microalbuminuria, carotid intima media thickness and chronic inflammatory diseases such as rheumatoid arthritis [4–7].

Previous studies have succeeded in looking at the relationship between EAT and the incidence of CHD [8–11].However, our current study conducted a deeper analysis that assessed the relationship of EAT with lesion severity with the SYNTAX score, which describes the characteristics of the lesion and its functional impact, thus illustrating the complexity of CHD. From the obtained EAT threshold values, we continued the analysis to assess whether there was a relationship between these values and the severity of coronary artery lesions which were divided into SYNTAX 22 and SYNTAX > 22. Our study found a significant relationship between diastolic and systolic EAT thickness features on the severity of arterial lesions. coronary heart disease patients with significant lesions (p = 0.039). A diastolic EAT 2.75 mm and a systolic EAT 5.5 mm each had a 6x risk of coronary artery lesion severity [OR 6,000 (CI 95% 1.296-27.769)] and OR 6,000 (CI 95% 1.296-27.769), respectively.

The results of this study are in line with the research of Erkan [12]who also found that EAT thickness as measured by echocardiography was independently associated with CHD complexity as evidenced by the SYNTAX score. Erkan et.al proposed that early identification of EAT thickness in patients with CHD could be useful for physicians to consider choosing prevention and more aggressive therapeutic strategies and offer patients to perform cardiac catheterization for early diagnosis. Erkan et al's study found that the cut-off thickness of the EAT at end-systole that could predict critical illness was 5.75 mm (with AUC 0.875; 95% KI, 0.825–0.926; P < 0.001) [12].

In addition, Gökdeniz et.al also conducted a study to examine the relationship between EAT thickness and CHD complexity in non-diabetic patients. The study found that the thickness of the EAT was significantly correlated with the SYNTAX score (r = 0.629; P < 0.001). The study also determined a threshold value of EAT thickness measured at end-diastole, which is 5mm, as a predictor of an intermediate-high SYNTAX score (AUC=0.851; 95% CI, 0.775–0.91), with a specificity of 92.2% and a sensitivity of 77.4%[13].

Research by Shambu et.al[14]also found that the EAT thickness threshold value of 4.75 mm was able to predict CHD with a sensitivity of 87% and specificity of 63%. The EAT value was measured at end-systole. However, they found that the threshold 5.2 had a better probability of predicting double-vessel-disease (DVD) and triple-vessel disease (TVD). The existence of variations in this threshold value can be influenced by several things, namely ethnic differences, traditional risk factors, and EAT measurement techniques[14].

Wang et.al[15]also reported that echocardio graphically measured EAT thickness was associated with SYNTAX scores in acute myocardial infarction patients. The mean

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EAT was found to be greater in the group with the higher SYNTAX score (≥33) than the group with the lower SYNTAX (<33), namely 5.6 ± 1.1 versus 4.1 ± 1 mm (P < 0.01). However, this study only examined patients who experienced myocardial infarction only. In contrast to the current study which has expanded the subject, namely subjects diagnosed with CHD.

Clinical observations suggest that the proximal part of the coronary arteries is more deeply embedded in the epicardial fat, than the distal part, so that this condition makes the condition more prone to atherosclerosis. This situation is related to the small amount of periadventital adipose tissue, which is a continuation of the EAT . tissue[16]. Vela et.al[17] demonstrated the importance of this periadventitial adipose tissue in the development of atherosclerosis, and highlighted the presence of macrophage aggregation in this tissue.

The EAT tissue produces large amounts of proinflammatory and pro-atherogenic mediators.[18–20]. On the other hand, adiponectin, which exerts anti-atherogenic effects through improved endothelial function and mitigating inflammation, has decreased expression in EAT tissues of CHD patients[20].

Research by Bagheri et.al [21]found that creatinine was significantly associated with the prevalence and severity of CHD, as determined by the presence of narrowing of the coronary artery lumen (>70%) [odds ratio 1.79 (1.47-2.20), p<0.001; and F(3,528)= 3.0, p=0.03]. Several mechanisms are involved in the association of serum creatinine with an increased risk of CHD[22]. Muscle is a major source of serum creatinine, and is also a target organ for insulin[23,24]. It is proposed that serum creatinine levels may be an indicator factor for diabetes and CHD. Several studies have reported that creatinine correlates with inflammatory markers[25,26].

In this study, it was found that an increase in CKMB levels had a 1.031x risk of coronary artery lesion severity, which was statistically significant with [β 0.031; OR 1.031 (CI 95% 1.007 – 2.056) p value = 0.011]. As previously noted, creatine kinase (CK) is a cytosolic protein involved in mitochondrial phosphate transport. CK has three different dimeric forms, namely MM, MB, and BB. Prior to the use of troponins, CK-MB was a cardiac enzyme that was used as the standard for the diagnosis of myocardial infarction. CK is found in all otto tissue and is not specific for myocyte injury only, but CK-MB is relatively specific for myocardial tissue. CK-MB can be found in serum within 4-6 hours of the onset of myocardial ischemia, but can also be up to 12 hours. The presence of increased levels of CK-MB should be interpreted as a danger where there is muscle injury, especially the heart muscle[27].

Decreased ejection fraction was also found to have a 0.798x risk of coronary artery lesion severity, which was statistically significant with [β -0.233; OR 0.792 (CI 95% 0.684-0.918) p value = 0.002]. This study supports a previous study conducted by Li et.al who conducted a cohort study of CHD patients who were established for 15 ± 12 months, and patients were divided into a group with left ventricular ejection fraction (LVEF) 0.50 and a low LVEF group (LVEF< 0.50). From the analysis results, it was found that compared to the group with normal LVEF, the lower LVEF group had a more severe degree of coronary artery stenosis (Gensini score: 62.85±41.45 vs. 47.68±33.26, P<0.05)[28].

In this study, it was found that DM patients were found more in CHD patients with non-significant lesions. This may be due to the small number of patients involved in this study, so it does not really describe the state of the patient's metabolic disorders, especially diabetes mellitus as a whole. In addition, in this study we did not further analyze the onset, duration, and treatment of diabetes mellitus in patients. As is well known, clinical risk factors that indicate an increased risk of cardiovascular disease in diabetic patients are age over 40 years for men and 50 years for women and a long duration of diabetes; where there is an 85% increase in risk for every additional 10 years of diabetes mellitus duration. In addition, treatment-treated diabetes mellitus patients with HbA1c levels below 6% successfully demonstrated reduced cardiovascular-related risks. Unfortunately, the variables mentioned above have not been included in the analysis in this study, and are expected to be additional material for future research.[24,28]

V. CONCLUSION

In this study, we concluded that there was a significant relationship between systolic and diastolic Epicardial Adipose Tissue (EAT) values in CHD patients with significant lesions and CHD with non-significant lesions (p < 0.001). The cut off point of Diastolic EAT thickness was 2.75. mm and EAT Systolic thickness 5.5 mm in predicting the incidence of significant coronary artery stenosis in coronary heart disease patients. Diastolic EAT 2.75 mm and systolic EAT 5.5 mm had a 6x risk of coronary artery lesion severity with a SYNTAX score > 22 which was statistically significant in CHD patients with significant lesions.

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