

# LEFT ATRIAL END DIASTOLIC VOLUME INDEX AS A PREDICTOR FOR MAJOR ADVERSE CARDIOVASCULAR EVENT FOR 30 DAYS AFTER ADMISSION, IN PATIENTS WITH STEMI IN HAJI ADAM MALIK GENERAL HOSPITAL MEDAN Nanda Ladita<sup>\*</sup>, Nizam Zikri Akbar, Cut Aryfa Andra<sup>1</sup>, Yuke Sarastri<sup>1</sup>, T Winda Ardini<sup>1</sup> & Harris Hasan<sup>\*</sup>

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# Abstract

**Background**: Ischemic heart disease is the leading cause of death in the world (12.8%) while in Indonesia it ranks third. The prevalence of coronary heart disease in Indonesia in 2013 is estimated to be around 883,447 (0.5%) Left Atrial Residual Volume Index, or Left Atrial End-Diastolic Volume Index (LAEDVI) is the smallest LA volume, measured at the end of the ventricular diastole. LAEDVI measurements have shown a closer correlation with LV filling pressure than LAESVI

**Purpose**: To determine Value of Left Atrial End Diastolic Index as a Predictor of Major Adverse Cardiovascular Events (MACE) for 30 days after admission, in patients with STEMI through echocardiography examination

**Method**: This study involved STEMI patients who were treated at Haji Adam Malik General Hospital Medan from March 2020 to November 2020. Each patient will undergo echocardiography and the LAEDVI values and others parameters. Observation of the occurrence of MACE on STEMI was carried out for 30 days after treatment. Multivariate analysis of independent variables with categorical dependent variables was tested by logistic regression to determine the predictive factors LAEDVI as predictors of MACE on STEMI.

**Result**: From 52 STEMI patients, there were 16 cases of MACE consisting of 11 patients with acute heart failure and 5 patients with arrhythmia. The LAEDVI value became a predictor factor that was statistically significant with OR 3.119 (CI95% 1.278-7.615) and p value = 0.012, the constant is -20.116. With cut-off point score LAEDVI against the incidence of Major Cardiovascular Events is 17.15 mL/m<sup>2</sup>.

**Conclusion**: LAEDVI is a potential tool to predict Major Adverse Cardiovascular Events (MACE) in STEMI patients.

# Introduction

ST-Elevation Myocardial Infarction (STEMI) is at the end of the spectrum for acute coronary syndrome.<sup>1</sup> Recent report from 2016 American Heart Association (AHA) reports that 15.5 million people aged  $\geq$ 20 years in the United States have coronary heart disease, the prevalence is reported to increase with age in both men and women.<sup>2</sup>

According to WHO, ischemic heart disease is the main cause of death in the world (12.8%) while in Indonesia it ranks third.<sup>3</sup> The prevalence of coronary heart disease in Indonesia in 2013 is estimated to be around 883,447 (0.5%).<sup>4</sup>

Left ventricular remodelling (LVR) that occurs after myocardial infarction is a complex process of changing the left ventricle (LV) architecture involving both infarct and non-infarct areas. Clinical manifestations of these changes include changes in size, shape and function of the heart chambers.<sup>5</sup> During ventricular diastole, the left atrium (LA) is directly exposed to LV pressure, and therefore the size of LA increases with the increasing severity of LV diastolic dysfunction. Measurement of the Left Atrial Volume Index (LAVI) is associated with the number of cardiovascular events following myocardial infarction.<sup>5,6</sup>

The Left Atrial End-Diastolic Volume Index (LAEDVI) is the smallest LA volume measured at the end of the ventricular diastole. LAEDVI measurements have shown a closer correlation with LV filling pressure than LAESVI. However, currently LAEDVI measurements are not routinely used in clinical practice, and the predictive value of clinical outcome is generally unknown.<sup>7</sup>

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This study aimed to determine the role of LAEDVI as a predictor of major adverse cardiovascular events (MACE) during admission, in patients with ST-Elevation Myocardial Infarction (STEMI) at Haji Adam Malik General Hospital Medan.

# Methods

#### **Study population**

The data of this study were taken from STEMI patients who were treated at Haji Adam Malik General Hospital Medan from March to November 2020 with consecutive sampling method. The study involved 52 STEMI patients in Haji Adam Malik General Hospital Medan, who were willing to be contacted and interviewed by telephone or face-to-face after 30 days of observation. Patients who did not undergo echocardiographic assessment <72 hours after admission, had valve abnormalities and congenital heart disease, and who could not be contacted 30 days after admission were excluded from the study subjects.

#### LAEDVI measurement and MACE evaluation

This study is an ambispective cohort study. Diagnosis of STEMI is based on the SKA guidelines from ESC and PERKI. LAEDVI values were recorded from echocardiographic examinations at <72 hours of admission in the ER and followed for 30 days after completion of treatment. MACE assessed were cardiovascular mortality, malignant arrhythmias, myocardial infarction, stroke, and acute heart failure. For patients treated before the time of the study, clinical course during treatment and MACE were collected from medical records. For patients treated during the study, observations were made during hospitalization and MACE that occurred 30 days after admission was recorded.

#### Statistical analysis

Data were analyzed using the SPSS program. Bivariate analysis for comparison between the two groups on numerical independent variables and categorical dependent variables is using the T-independent test (T-test). If the conditions for the Independent T-test are not met, the Mann Whitney test is used. Multivariate analysis of independent variables with categorical dependent variables was tested by logistic regression to determine the predictive factors of LAEDVI as predictors of MACE. The variables found to have a significance value of p < 0.05 in the multivariate analysis are shown in the form of odds ratios (ORs) with 95% confidence intervals. The variable was considered statistically significant if the p value was < 0.05.

## Results

STEMI patients who were hospitalized in RSHAM from March to November 2020 were 52 patients, with 16 patients (30.6%) experiencing Major Adverse Cardiovascular Events (MACE) and 36 other patients (69.4%) did not experience Major Adverse Cardiovascular Events (MACE). All 14 patients who experienced MACE were male. The mean age of patients was 55 years, patients who experienced MACE were younger than those who did not experience MACE. The characteristics, baseline data of the results of examination and bivariate analysis parameters of STEMI patients are presented in table 1 and 2.

<b>D</b> (	Total	MACE		
Parameter	(n=52)	Yes	No	— p value
Sex				
Male	44 (84,6)	14 (31,8)	30 (68,2)	1,000
Female	8 (15,4)	2 (25,0)	6 (75,0)	
Age	55,01±8,72	54,12±9,84	55,41±8,29	0,627
History, Yes				
Hypertension	17 (32,7)	6 (35,3)	11 (64,7)	0,863
Diabetes	12 (23,1)	2 (16,7)	10 (83,3)	0,301
Dyslipidaemia	15 (28,8)	6 (40,0)	9 (60,0)	0,508
Smoking	39 (75,0)	13 (33,3)	26 (66,7)	0,730
Vital Sign				



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HR	82,75±11,56	84,31±11,92	82,05±11,50	0,521
SBP	127,88±17,63	128,12±16,82	127,77±18,22	0,949
DBP	80 (60-100)	80 (70-100)	80 (60-100)	0,572
Laboratorium				
Hb	13,15 (5-18,5)	11,8 (8,5-14,2)	13,6 (5,0-18,5)	0,064
Ht	39,0 (20,0- 52,0)	36,5 (25,0-42,0)	40,0 (20,0-52,0)	0,141
Leucocyte	9080 (1190- 17500)	8220 (1100- 17500)	9550 (1236- 17450)	0,302
Thrombocyte	287000 (175000- 539000)	304500 (175000- 537000)	286000 (185000- 539000)	0,627
СКМВ	119 (15-744)	125 (15-744)	115(17-684)	1,000
Troponin I	4,02 (0,03- 32,0)	3,68 (0,03-32,0)	4,85 (0,03-32,0)	0,929
Ureum	30,0 (15-111)	30 (17-64)	30 (15-111)	0,504
Creatinine	0,92 (0,55- 2,72)	0,92 (0,76-2,27)	0,92 (0,55-2,72)	0,662
Natrium	$137,80\pm5,02$	137,37±5,98	138,00±4,61	0,683
Kalium	4,1 (3,2-42,0)	4,05 (3,20-5,20)	4,10 (3,20-42,0)	0,676
Chloride	103 (9,7-112)	103,0 (98,0-110)	104,0 (9,70-	0,163
Blood Glucose	111,5 (75-357)	101,5 (75-206)	112,0) 114 (82-357,0)	0,014*
2HPP Glucose	132,5 (70-325)	126 (101-219)	136,5 (70-325)	0,014
HbA1C	6 (4,9-11,6)	5,75 (4,90-8,30)	6,15 (4,9-11,6)	0,080 0,041*
Total Cholesterol	$174,59\pm40,39$	177,62±36,39	$173,25\pm42,47$	0,041
TGA	$174,39 \pm 40,39$ 125,5 (75-352)	177,02±30,39 132 (75-229)	173,23±42,47 120 (84-352)	0,722
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HDL	40,26±8,84	39,87±10,23	40,44±8,30	0,833
LDL	126,5 (60-298)	124,5 (60-191)	128,5 (80-298)	0,789
Interventions				
PCI	46 (88,5)	14 (30,4)	32 (69,6)	0,907
CABG	5 (9,6)	2 (40,0)	3 (69,6)	
Conservative	1 (1,9)	0 (0,0)	1 (100,0)	
Lesion				
1VD	28 (53,8)	8 (28,6)	20 (71,4)	0,334
2VD	14 (26,9)	3 (21,4)	11 (78,6)	*
3VD	10 (19,2)	5 (50,0)	5 (50,0)	
Culprit Lesion			- (- •,•)	
LAD	31 (59,6)	7 (22,6)	24 (77,4)	0,274
LCx	1 (1,9)	0 (0,0)	1 (100,0)	- , -
RCA	12 (23,1)	6 (50,0)	6 (50,0)	
LAD, RCA	3 (5,8)	0 (0,0)	3 (100,0)	
LAD, RCA, LCx	5 (9,6)	3 (60,0)	2 (40,0)	
STEMI Type	- (>,0)	2 (00,0)	- (10,0)	
Anterior	38 (73,1)	9 (23,7)	29 (76,3)	0,094
Inferior	14 (26,9)	7 (50,0)	7 (50,0)	5,071
Onset of STEMI	(=0,2)	. (,.)	. (,.)	



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121	10(265)	4 (01 1)	15(700)	0.401
<12 hours	19 (36,5)	4 (21,1)	15 (78,9)	0,401
>12 hours	33 (63,5)	12 (36,4)	21 (63,6)	
Killip				
Ι	43 (82,7)	16 (37,2)	27 (62,8)	0,056
II	7 (13,5)	0 (0,0)	7 (100,0)	
III	1 (1,9)	0 (0,0)	1 (100,0)	
IV	1 (1,9)	0 (0,0)	1 (100,0)	
GRACE Score	105,0±19,89	101,62±18,27	$106,5\pm 20,64$	0,420
Low Risk	26 (50,0)	7 (26,9)	19 (73,1)	0,841
Moderate Risk	24 (46,2)	9 (37,5)	15 (62,5)	
High Risk	2 (3,8)	0 (0,0)	2 (100,0)	
MACE, Yes				
AHF	11 (21,2)	11 (100,0)	0 (0,0)	1,000
Arrhythmia	5 (9,6)	5 (100,0)	0 (0,0)	
MI	0 (0,0)	0 (0,0)	0 (0,0)	
Stroke	0 (0,0)	0 (0,0)	0 (0,0)	

Data are presented as mean  $\pm$  SD if distributed normally, and presented median (minimum-maximum) if not normally distributed. \*P value < 0.05 is statistically significant.

	Table 2. Baselin	ne Characteristics			
<b>D</b> (	Total	MA	MACE		
Parameter	(n=52)	Yes	No	— p value	
Echocardiography					
TAPSE, (mm)	20,0 (13-25)	20 (15-24)	20,5 (13-25)	0,322	
LAEDVI, (mL/mm <sup>2</sup> )	$15,15\pm6,65$	22,63±4,27	11,28±3,59	<0,001*	
LAESVI, (mL/mm <sup>2</sup> )	23,42 (10,4- 39,8)	41,54 (33-48,2)	21,16 (10,4- 39,8)	<0,001*	
EF, (%)	46,76±14,36	37,56±14,92	50,86±12,21	0,001*	
LVEDD	46,5 (33-65)	50 (38-64)	44 (33-65)	0,006*	
LVESD	29 (17-55)	32,5 (22-55)	26,5 (17-53)	0,008*	
IVSS	16,76±4,17	15,12±4,25	17,5±3,97	0,061	
IVSD	14 (8-19)	13 (8-17)	13,75 (8-19)	0,206	
LVPWD	11 (7-18)	11 (7-17)	11 (7-18)	0,547	
LVPWS	15 (8-23)	15 (9-23)	17 (8-23)	0,142	
FS	32 (12-58)	24,25 (12-49)	38,5 (15-58)	0,001*	

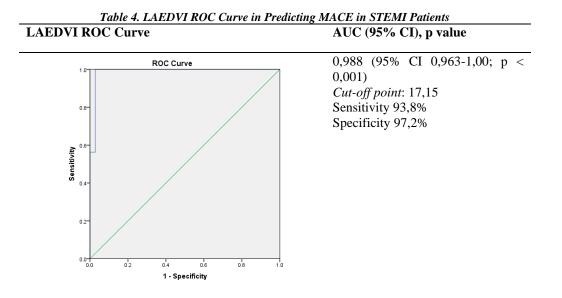
Multivariate analysis is used to determine which factors predict the incidence of MACE in STEMI patients, presented in table 3. The selected parameter bivariate analysis result variables with p value < 0.25 are included in the logistic regression analysis of the incidence of MACE, obtained until the last step in step 3, the LAEDVI variable. It was found that the LAEDVI variable alone was a predictor factor that was statistically significant with OR 3.119 (CI95% 1.278-7.615) and p value = 0.012, with constant of -20.116.

Table 3. Mul	tivariate Analysis of	Risk Factors f	or MACE Predic	tors in STEMI P	atients
Variable	Coefficient	p value	OR	95% CI (n	nin-max)
Step 1 <sup>a</sup> :					
LAEDVI	0,639	0,240	1,895	0,653	5,502
LAESVI	0,186	0,387	1,204	0,791	1,834

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EF	0,018	0,777	1,019	0,896	1,157
Step 2 <sup>a</sup> :					
LAEDVI	0,605	0,228	1,831	0,685	4,899
LAESVI	0,201	0,317	1,223	0,825	1,813
Step 3 <sup>a</sup> :					
LAEDVI	1,138	0,012	3,119	1,278	7,615
Constant	-1,008				

To determine the LAEDVI *cut-off point* percentage that can predict the incidence of MACE in STEMI patients, the ROC analysis was performed as presented in table 4. LAEDVI has a very strong relationship with the incidence of MACE with AUC of 0.988 and is statistically significant (p value < 0.001).



Visualization to determine the LAEDVI cut-off point for the incidence of MACE in STEMI patients is presented in Figure 1. The intersection of the curve of sensitivity of 93.8% and specificity of 97.2% obtained a cut-off point of the LAEDVI value for the incidence of MACE, 24.00 mL/mm<sup>2</sup>. Patients with LAEDVI value of  $\geq$ 17.15 mL/mm<sup>2</sup> may likely to experience a Major Adverse Cardiovascular Event (MACE).

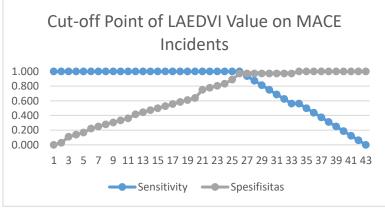


Figure 1. LAEDVI cut-off point on the incidence of MACE in STEMI patients



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### Discussion

This study found that LAEDVI could be a predictor factor for MACE and was statistically significant, though LAESVI did not show the same results. Based on echocardiography, the value of LAEDVI, LAESVI, LVEDD, LVESD, EF, and FS there is a statistically significant differences between STEMI patients who experienced MACE compared to those who did not experience MACE. LAEDVI value of patients who experienced MACE was higher  $(22.63 \pm 4.27 \text{ ml/mm}^2)$  compared to the LAEDVI value of patients who did not experience MACE  $(11.28 \pm 3.59 \text{ ml/mm}^2)$ . Multivariate analysis showed that the LAEDVI variable alone was a statistically significant predictor factor (OR 3.119 [95% CI 1.278-7.615], p value = 0.012, constant -20.116).

LAEDVI can describe the LV end-diastolic pressure better, because during diastole, LA remains exposed to LV pressure. Therefore, LAEDVI reportedly better describes LV filling pressures and elevated pulmonary wedge pressures, with a greater prognostic value than LAESVI.<sup>8</sup>

A study by Thadani et al. reported an almost 6-fold increase in the hazard ratio for the cardiovascular care category between the highest and lowest quartile of LAEDVI values. This hazard ratio value is higher than that found in LAESVI, which is only 4.85 times the difference between the lowest and highest quartiles.<sup>9</sup> Left atrial enlargement is a strong predictor of long-term MACE, and left atrial dilatation has been shown to predict all causes and cardiovascular mortality, atrial fibrillation, and heart failure.<sup>7</sup>

In this study, the LAEDVI cut-off point for the incidence of MACE was found to be 17.15 mL/mm<sup>2</sup>, meaning that a patient with LAEDVI value of  $\geq$ 17.15 mL/mm<sup>2</sup> may likely to experience MACE.

## Conclusion

LAEDVI is a predictor factor for MACE in STEMI patients and is statistically significant. The mean LAEDVI value in STEMI patients who experienced MACE was  $22.63 \pm 4.27$  ml/m<sup>2</sup>. LAEDVI cut-off point for the incidence of MACE was found to be 17.15 mL/mm<sup>2</sup>, meaning that a patient with LAEDVI value of  $\geq$ 17.15 mL/mm<sup>2</sup> may likely to experience MACE.

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