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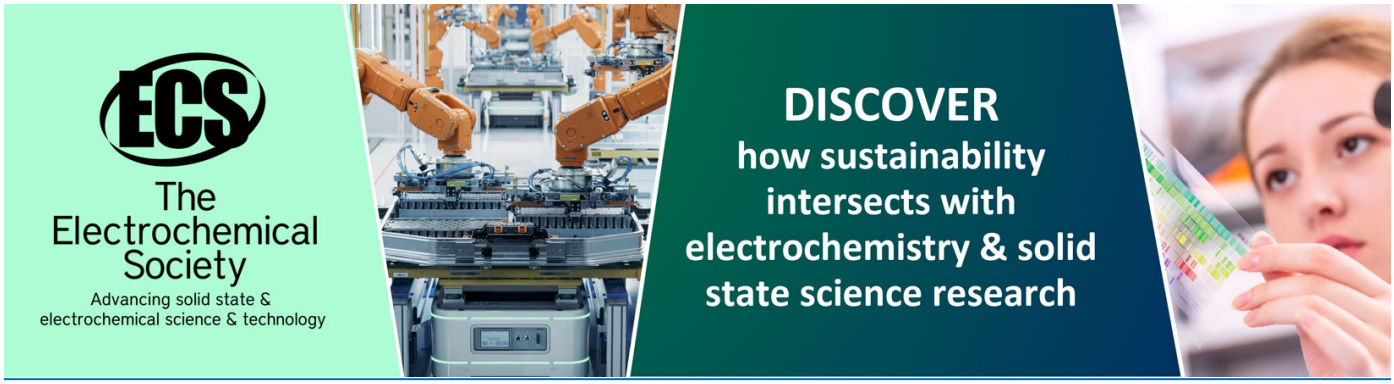

Importance of Basal Soluble ST2 and Global Longitudinal Strain 2D-Speckle Tracking Echocardiography to Detect Left Ventricle Remodeling in Post-Myocardial Infarction Patients

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Abstract. Left ventricle (LV) remodeling often occurs after acute myocardial infarction (AMI), and early detection and prompt treatment on this condition may improve prognosis of the patients. Basal soluble ST2 and Global Longitudinal Strain (GLS) 2D- speckle tracking echocardiography can detect early changes before LV remodeling occurs. This is an analytic observational study using one group pre-test and post-test design for correlation. Forty-five patients of AMI during August until December 2015 from ICCU and cardiology ward were analyzed and followed up for 12 weeks. There were 45 subjects with AMI, 38 (84.4%) patients with STEMI and seven (15.6%) patients with NSTEMI. There were significant differences of left ventricle end diastolic volume (LVEDV) baseline from 76±29.69ml/m^2 to 98.11±36.84ml/m^2 after 12 week follow-up (p=0,003). There was significant correlation between high baseline soluble ST2 with and low GLS baseline with LV remodeling (p=0.015). High baseline soluble ST2 and low GLS value can predict LV remodeling in patients with AMI.

1. Introduction

The 2009 Indonesian Health Profile issued by the Ministry of Health of the Republic of Indonesia showed that, in 2008, acute myocardial infarction (AMI) ranked as the highest cause of death in Indonesia (11.06%) [1]. Acute myocardial infarction causes regional myocardial damage that initiates systolic dysfunction. After infarction at a later stage, left ventricular (LV) remodeling occurs. This LV remodeling is associated with high cardiovascular events, including heart failure [2]. Thus, early detection of left ventricular remodeling can help to improve patient outcome.

One of the criteria for heart failure is progressive LV dilatation with Left Ventricle End Systolic Volume (LVESV)> 15% or> 20% Left Ventricle End Diastolic Volume (LVEDV) from basal values. Several epidemiological studies and clinical studies state that heart failure is a complication of 30-40% AMI cases. The incidence of LV systolic function dysfunction (LVSD) after myocardial infarction is rarely documented, but from several studies, LVSD will at least appear in 25-60% in patients with AMI, and as many as 50% of patients with LVSD will suffer heart failure. There was a strong association between heart failure and LVSD after AMI in short and long-term studies. LVSD without heart failure is also a significant condition that causes high hospital mortality in patients with acute myocardial infarction [2][3].

Echocardiography is an affordable examination tool that can be used to study regional and global functions of the LV in AMI. Left ventricular ejection fraction (LVEF) measured by the Simpson biplane method at hospital settings is a well-known marker for LV global function and predicts short-term or long-term morbidity and mortality in AMI patients. 2D Speckle Tracking Echocardiography (2D-STE) is a new non-invasive method of ultrasonic imaging that enables practitioners to quantitatively and objectively assess global and regional functions of myocardial, both in systolic and diastolic functions. This modality is considered more sensitive and accurate in predicting or detecting coronary heart disease. Changes in regional functions develop early, and may be detected through 2D STE. Examination with 2D STE is performed by measuring the segmental strain and strain rate (speed of myocardial deformation) [3][4]. Longitudinal strains are the earliest disturbance in ischemic conditions. Studies in patients with AMI found that longitudinal strains were associated with peak cTt levels and the extent of infarction. Longitudinal measurement of strains after reperfusion is an excellent predictor of LV remodeling, heart failure and death [5][6].

SST2 biomarkers have been included in the ACC / AHA guidelines for monitoring in patients with heart failure [7]. An increase in baseline sST2 levels> 35μg/L was an independent predictor of mortality, sudden death and heart failure in 30 days and showed the role of sST2 biomarkers in providing prognostic information in patients with acute coronary syndrome. Studies of the role of sST2 in patients with ST Myocardial Infarction Elevation (STEMI) showed an increase in initial sST2 levels ,indicating the risk of death / mortality and heart failure in patients treated with either thrombolytics or percutaneous coronary intervention therapy [8][9][10].

In this research, we aim to confirm the correlation between soluble ST 2 level and global longitudinal strain in the development of LV remodeling in patients with acute myocardial infarction.

2. Methods

This study is an analytic observational study using one group pre-test and post-test design for correlation conducted between August 2015 – December 2015. This study involved one sample group of patients with AMI who were tested twice for soluble ST2 and echocardiography: at arrival and after revascularization therapy with either thrombolytics, PCI or optimum medical therapy for 12 weeks. The study was conducted at the ICCU and cardiology ward of Dr. Soetomo General Hospital in Surabaya.

Inclusion criteria were patients aged 18 years old and over, fulfilling the criteria for AMI (increased of cardiac troponin with at least one of the following criteria symptoms: ECG changes of ischemia, imaging evidence, or thrombus found in angiography) without any signs of heart failure, being given standard AMI therapy (revascularization with PCI or thrombolytics, or optimum medical therapy), and willing to take part in the study by signing an informed consent form. Whereas the exclusion criteria were AMI patients with signs of heart failure, having a history of AMI and or heart failure, patients with co-morbidity such as sepsis, hepatic cirrhosis, anemia, acute stroke, malignancy, valvular heart disease, arrhythmia, and in critical condition. Using non-probability sampling, there were 53 eligible patients who fulfilled the required criteria.

Soluble ST2 (sST2) is measured using *Quantikine* Human ST2/IL-1 R4 Immunoassay Kit R & D System. During the research, sST2 level are measured twice: first, at arrival into the ICCU/cardiology ward, and the last is measured 12 weeks after the first measurement. Normal sST2 values range between 6.74 – 20.4ng/mL. ST2 value less than 20.4ng/mL has a low risk for left ventricle remodeling. Value of ST2 greater than 20.4ng/mL has a high risk for left ventricle remodeling. All data were analyzed using SPSS 21.0 program.

3. Results

From a total of fifty-three patients, eight patients dropped out due to mortality (two patients) and loss of follow-up (six patients), leaving forty-five patients as the subject in this study. Baseline characteristic data include gender, age, risk factors, disease diagnosis, and type of therapy (Table 1).

Table 1. Subjects' characteristics

Variable		N(%)	Mean(SD)
Age	31-40	3(6.7)	
	41-50	12(26.7)	
	51-60	14(31,1)	55.47±10.13
	61-70	13(28.8)	
	71-80	3(6.7)	
Gender	Male	37(82.2)	
	Female	8(17.8)	
Risk factors	Hypertension	28(62.2)	
	Smoking	33(73.3)	
	Dyslipidemia	19(42.2)	
	Diabetes	42(93.3)	
	Coronary Artery Disease	9(20.0)	
Diagnosis	STEMI	38(84.4)	
	NSTEMI	7(15.6)	
Therapy	PCI	18(40)	
	Thrombolytic	10(22.3)	
	Conservative	17(37.7)	

Notes: ST Elevation Myocardial Infarction (STEMI). Non ST Elevation Myocardial Infarction (NSTEMI), Percutaneous Coronary Intervention (PCI)

Table 2. Characteristics of echocardiography examinations and soluble ST2 levels

Variable	*LV Remodeling* (+) N = 27	*LV Remodeling* (-) N=18	p (Mann Whitney U test)
LVEF By Biplane **(%)**	52(26-71)	51(27-64)	0.437
LVEF ***By Biplane,*** **after 12 weeks (%)**	51(29-67)	53.5(28-67)	0.610
Soluble ***ST2*** **(ng/mL)**	34(12-71)	13.5(9-29)	0.0001
Soluble ***ST2*** **after 12 weeks (ng/mL)**	11.55(2.89-40.89)	9.95(6.06-33.09)	0.30
GLS	-10.0(-20 - -3)	-13.50(-20 - -3)	0.017
GLS **after 12 weeks**	-12.0(-19 - -4)	-13.50(-20 - -6)	0.108
LVEDV **(ml/m2)**	76±29.69	76.06±27,88	0.889
LVEDV **after 12 weeks (ml/m2)**	98.11±36.84	67.56±26,26	0.003
LVESV **(ml/m2)**	40.89±23.89	39.28±22.28	0.908
LVESV **after 12 weeks (ml/m2)**	51.96±26,43	32.94±15.19	0.006

Notes: Global Longitudinal Strain (GLS), Left Ventricle End Diastolic Volume (LVEDV), Left Ventricle End Systolic Volume (LVESV)

eight 8 female patients (17.8%) participated in this study. Age range was 36 – 80 years, with 14 patients in the 51-60 years age group. The highest risk factors for acute myocardial infarction were diabetes with 42 patients (93.3%). The most common types of acute myocardial infarction were STEMI (84.4%), and NSTEMI (15.6%). Most of the patients received PCI strategy (40%), while 10

patients (22.3%) received thrombolytic therapy and 17 patients (37.7%) had been given optimum medical therapy.

From the data above, there was an increase of LVEDV from 76 ± 29.69ml/m^2 to 98.11 ± 36.84ml/m^2 in subjects with left ventricular remodeling compared to those without remodeling (p = 0.003), as well as LVESV values increased from 40.89 ± 23.89ml /m^2 to 51.96 ± 26.43ml/m^2 (p = 0.006) The basal soluble ST2 value is much higher in those who have left ventricular remodeling 34 (12-71)ng/mL (p = 0,0001). Baseline GLS values were lower in those with left ventricular remodeling -10.0 (-20 - -3) compared to those without remodeling (p = 0.017).

4. Discussion

Most of the patients in this research were male patients (82.2%), consistent with previous study that stated AMI was mostly found in male patients [3].

In this research, the incidence of left ventricular remodeling was found in 27 patients (60%), exceeding previous study by Liszka et al., possibly due to all subjects were treated with PCI, and administration of anti-remodeling drugs was more aggressive, whereas in this research almost one-third of the patients received conservative therapy because most patients had arrived with more than 24 hours after myocardial infarct onset, so that it passed the onset to reperfusion both mechanically and pharmacologically. In addition, several patients rejected reperfusion measures due to cost issues, since healthcare insurance was not widely distributed in Indonesia in 2015 [11].

Left ventricular remodeling in this study used the criteria for an increase in LVEDV > 20% from basal or increased LVESV > 15% from basal, as in previous studies by Hung et al., and Liszka et al., [11-12]. The value of LVEDV after 12 weeks has increased, compared with those without remodeling, the value is higher in the case of left ventricular remodeling. This is in accordance with previous studies conducted by Liszka et al., which found an increase in LVEDV and LVESV at 90 days of follow-up on subjects with AMI treated by PCI. Basal soluble ST2 levels were also found to be significant in those with left ventricular remodeling (p = 0,0001). Baseline GLS levels were also significant in those with left ventricular remodeling (p = 0.017). In a study by Sun et al. there was an increase in LVEDV after eight weeks from 36 ± 6 to 56 ± 22ml/m^2 with p <0.05, and LVESV from 20 ± 5 to 33 ± 18ml/m^2 [11][12][13].

In this study, there was a significant correlation between basal soluble ST2 levels and left ventricular remodeling (p = 0.0001 r = + 0.723). In a previous study, an increase in basal soluble ST2 was associated with changes in LVEDV after 24 weeks as measured by Cardiac Magnetic Resonance (CMR), which proved that the increase in basal ST2 soluble was associated with the occurrence of left ventricular remodeling. In this study also basal soluble ST2 was associated with low basal LVEF after IMA. Changes in ST2 after 12 weeks (ΔST2) are also associated with VLVEDV after 24 weeks.

Whereas, regarding the basal Global Longitudinal Strain (GLS), in this study it was found that GLS had a weak correlation (p = 0.015 r = + 0.362) to the incidence of left ventricular remodeling. Compared with other studies, many other studies have used STE to predict left ventricular remodeling, both with GLS, torque or circumferential associated with left ventricular remodeling. The study by Joyce et al., using STEMI patients treated with PCI, found that GLS examination at the time before the patient was discharged was a novel examination to predict the occurrence of left ventricular remodeling. In those with a decrease in GLS, left ventricular remodeling was obtained at three months and six months follow-up. Another study by Peksiene et al. found a low basal GLS –11.05 ± 4.1 in the case of left ventricular remodeling compared to those without remodeling –15.2 ± 3.2 with p <0.001 [11][14][15].

In general, longitudinal LV mechanics, which are affected mostly by the subendocardial region, are the most vulnerable components of global LV mechanics because they are highly sensitive to the presence of myocardial disease. Single assessment of longitudinal mechanics is more than enough in myocardial diseases that are still early or have not shown significant abnormalities. The subendocardial region is the most remote area in terms of perfusion, making it prone to hypoperfusion and ischemia.

5. Conclusion

Based on data analysis in our study, we conclude that there is a positive correlation between basal soluble ST2 and left ventricular remodeling after AMI, and there is a negative correlation between Global Longitudinal Strain (GLS) and left ventricular remodeling after AMI. Further research needs to be done with a longer time period to be able to see the functions of ST2 biomarkers and GLS as prognostic tools for left ventricular remodeling after AMI.

References

[1] Profil Kesehatan Indonesia 2016 *Profil Kesehatan RI 2015*

[2] Velazquez E J, Francis G S, Armstrong P W, Aylward P E, Diaz R, O'connor C M, White H D, Henis M, Rittenhouse L M and Kilaru R 2004 An international perspective on heart failure and left ventricular systolic dysfunction complicating myocardial infarction: the VALIANT registry *Eur. Heart J.* **25** 1911–9

[3] Weir R A P, Miller A M, Murphy G E J, Clements S, Steedman T, Connell J M C, McInnes I B, Dargie H J and McMurray J J V 2010 Serum Soluble ST2. A Potential Novel Mediator in Left Ventricular and Infarct Remodelling After Acute Myocardial Infarction *J. Am. Coll. Cardiol.* **55** 243–50

[4] Geyer H, Caracciolo G, Abe H, Wilansky S, Carerj S, Gentile F, Nesser H J, Khandheria B, Narula J and Sengupta P P 2010 Assessment of Myocardial Mechanics Using Speckle Tracking Echocardiography: Fundamentals and Clinical Applications *J. Am. Soc. Echocardiogr.* **23** 351–69

[5] Ryczek R, Krzesiński P, Krzywicki P, Smurzyński P and Cwetsch A 2011 Two-dimensional longitudinal strain for the assessment of the left ventricular systolic function as compared with conventional echocardiographic methods in patients with acute coronary syndromes *Kardiol. Pol. (Polish Hear. Journal)* **69** 357–62

[6] Sjøli B, Ørn S, Grenne B, Ihlen H, Edvardsen T and Brunvand H 2009 Diagnostic Capability and Reproducibility of Strain by Doppler and by Speckle Tracking in Patients With Acute Myocardial Infarction *JACC Cardiovasc. Imaging* **2** 24–33

[7] Park Y H, Kang S-J, Song J-K, Lee E Y, Song J-M, Kang D-H, Kim Y-H, Lee C W, Hong M-K and Kim J-J 2008 Prognostic value of longitudinal strain after primary reperfusion therapy in patients with anterior-wall acute myocardial infarction *J. Am. Soc. Echocardiogr.* **21** 262–7

[8] Yancy C W, Jessup M, Bozkurt B, Butler J, Casey D E, Drazner M H, Fonarow G C, Geraci S A, Horwich T, Januzzi J L, Johnson M R, Kasper E K, Levy W C, Masoudi F A, McBride P E, McMurray J J V, Mitchell J E, Peterson P N, Riegel B, Sam F, Stevenson L W, Tang W H W, Tsai E J and Wilkoff B L 2013 2013 ACCF/AHA Guideline for the Management of Heart Failure *J. Am. Coll. Cardiol.* **62** e147–239

[9] Sabatine M S, Marrow D A and Higgins L J 2008 Complementary roles for biomarkers of biomechanical strain, ST2 and NT-proBNP, in patients with ST-elevation myocardial infarction *Circulation* **117** 1936–44

[10] O'Malley R G, Bonaca M P, Scirica B M, Murphy S A, Jarolim P, Sabatine M S, Braunwald E and Morrow D A 2014 Prognostic performance of multiple biomarkers in patients with non-ST-segment elevation acute coronary syndrome: Analysis from the MERLIN-TIMI 36 trial (Metabolic Efficiency with Ranolazine for Less Ischemia in Non-ST-Elevation Acute Coronary Syndromes-Thrombolysis in Myocardial Infarction 36) *J. Am. Coll. Cardiol.* **63** 1644–53

[11] Liszka J, Haberka M, Tabor Z, Finik M and Gąsior Z 2014 Two-dimensional speckle-tracking echocardiography assessment of left ventricular remodelling in patients after myocardial infarction and primary reperfusion *Arch. Med. Sci. AMS* **10** 1091

[12] Hung C L, Verma A, Uno H, Shin S H, Bourgoun M, Hassanein A H, McMurray J J, Velazquez E J, Kober L, Pfeffer M A and Solomon S D 2010 Longitudinal and circumferential strain rate, left ventricular remodelling, and prognosis after myocardial infarction *J. Am. Coll.*

Cardiol. **56** 1812–22
[13] Sun J P, Niu J, Chou D, Chuang H-H, Wang K, Drinko J, Borowski A, Stewart W J and Thomas J D 2007 Alterations of regional myocardial function in a swine model of myocardial infarction assessed by echocardiographic 2-dimensional strain imaging *J. Am. Soc. Echocardiogr.* **20** 498–504
[14] Joyce E, Hoogslag G, Leong D, Debonnaire P, Katsanos S, Schalij M J, Marsan N A, Bax J J and Delgado V 2013 Association between global left ventricular longitudinal strain and left ventricular remodelling after STEMI *J. Am. Coll. Cardiol.* **61** E855
[15] Zaliaduonyte-Peksiene D, Simonyte S, Lesauskaite V, Vaskelyte J, Gustiene O, Mizariene V, Jurkevicius R, Jariene G, Tamosiunas A and Zaliunas R 2014 Left ventricular remodelling after acute myocardial infarction: Impact of clinical, echocardiographic parameters and polymorphism of angiotensinogen gene *JRAAS - J. Renin-Angiotensin-Aldosterone Syst.* **15** 286–93