Correlation between Global Longitudinal Strain (GLS)-Left Ventricle and TEI Index (TI) with Seattle Heart Failure Model (SHFM) Score in Chronic Heart Failure Patients with Systolic Dysfunction

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Correlation between Global Longitudinal Strain (GLS)-Left Ventricle and TEI Index (TI) with Seattle Heart Failure Model (SHFM) Score in Chronic Heart Failure Patients with Systolic Dysfunction

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Abstract. Assessment of left ventricular function in patients with chronic heart failure is important for determining prognosis and treatment plans. The prognostic values of the myocardium and global ventricular functions remain unclear. This cross-sectional study included 30 subjects obtained through purposive sampling. Global longitudinal strains (GLS)is used to assess the left ventricular systolic function and Tei index (TI) is used to assess both global systolic and diastolic ventricular function. SHFM scoring was calculated based on existing patient data. The mean GLS-left ventricle value was -8.08 ± 3.98, whereas TI value was 0.65 ± 0.14. GLS-left ventricle had significant negative correlation with estimated one and five years mortality based on SHFM score (r = - 0.676 and p = 0.0001) whereas TI had a significant positive correlation (r = 0.745 and p = 0.0001; r = 0.738 and p = 0.0001). GLS-left ventricle had a significant negative correlation with an estimated one and five years mortality based on SHFM score, whereas TI had a significant positive correlation. Hence it is suggested that GLS-left ventricle and TI can be a prognostic factor.

1. Introduction

Heart failure is a significant cause of morbidity and mortality in various countries. In the last few decades, the incidence and prevalence of chronic heart failure have continuously increased. In the United States, 5.8 million people were suffering from heart failure in 2012, which is expected to increase to 8.5 million by 2030, while in the world the population of heart failure is close to 23 million, and is expected to continue to increase [1-3].

Ejection fraction (EF) of the left ventricle is the frequently used parameter to assess systolicfunction. Echocardiography, besides being a diagnostic modality, can also have prognostic value, especially parameters that assess left the ventricular function [4-5]. Previous research reported that in a population of patients with EF <45%, mortality decreased almost linearly with an increase in EF (EF <15%, mortality: 51.7%; EF 36% - 45%, mortality: 25.6%; p <0.0001) [6]. Other than being used as diagnostic tools, left ventricular function can also be used to assess the prognosis, determine treatment plans, make decisions related to the therapy of expensive non-surgical devices and assess the response to treatment. Global Longitudinal Strain (GLS) of the left ventricle assessed through Speckle Tracking Echocardiography (STE) is sensitive in determining complex left ventricular mechanics, by analyzing multidimensional myocardial deformation, which allows GLS to be a more accurate and sensitive parameter than EF in assessing left ventricular systolic function [7-9]. Stanton T *et al*. found that GLS was superior compared to EF and the Wall Motion Scoring Index (WMSI) in predicting the occurrence of all-mortality cause in patients with chronic heart failure [10].

Risk stratification is proven to provide benefits to heart failure patients in various ways as optimal management. The risk model has an essential role in facilitating patients and clinicians in understanding the condition of the disease experienced, especially about the possible outcomes. Prediction can be suboptimal if only based on a holistic assessment by the clinician alone [11]. Currently, there are many risk assessment tools which have been developed to predict the prognosis of patients with heart failure. One of multivariable risk scores that has been validated and recommended by ACCF/AHA Guidelines for the Management of Heart Failure 2013 was the Seattle Heart Failure Model (SHFM). SHFM provides an accurate estimation of mortality in patients with heart failure in 1, 2, and 5 year periods by using clinical parameters that are quickly evaluated, such as pharmacological therapy, medical devices, and laboratory characteristics [5,12].

Currently, the role of left ventricular GLS and TI in assessing mortality estimates in patients with chronic heart failure is not yet known, several studies have been carried out in several countries, but this study has never been conducted in Indonesia. This study aims to assess the correlation between left ventricular and TI GLS values with estimates of mortality within one, and five years assessed from SHFM scores, and evaluate which parameters have a stronger correlation with SHFM scores in outpatients with chronic heart failure with systolic dysfunction at Dr. Hospital Soetomo Surabaya.

2. Methods

This study was conducted at the Cardiac and Echocardiographic Room at the Dr. Soetomo General Hospital Surabaya, from February - May 2016, using purposive sampling, and obtained 30 patients with chronic heart failure who had met the inclusion and exclusion criteria. All samples were taken from the cardiac outpatients' clinic in Dr. Soetomo General Hospital Surabaya and were willing to participate in the study by signing informed consent. The Health Research Ethics Committee of Dr. Soetomo General Hospital Surabaya has agreed and stated ethical conduct for this research.

Each subject was subjected to a standard echocardiography examination and performed a calculation of left Ventricular Global Longitudinal Strain (GLS) and Tei Index (TI), as well as a calculated SHFM score when a patient is in a cardiac clinic for a regular visit. Data on sample characteristics include gender, age, risk factors, disease diagnosis, and type of therapy.

Data was collected, then managed with descriptive statistics, and presented in the form of exposures, tables, and diagrams. Data were analyzed using inferential statistics to see whether there is a relationship between variables with SPSS. The relationship between left ventricular GLS values and IT with SHFM scores was determined using the Pearson correlation test for normal data distribution or Spearman rank for abnormal data distribution. The results are significant if the value of $p < 0.05$.

3. Results

3.1 Characteristic of research subjects

The subjects obtained in this study were 30 people, consisting of 22 men (73.3%) and 8 women (26.7%). The youngest subject is 41 years, and the oldest subject is 75 years. The highest number of subjects according was in the age category 50-59 years, at 12 people (40%), followed by 60-69 years, 11 people (36.7%), then 40-49 years, 5 people (16.7%), and the least was 70-79 years, 2 people (6.7%).

The most common comorbidity was dyslipidemia with 22 people (73.3%), then hypertension and diabetes had the same number, which was found in 13 people (43.3%), smoking was found in 12 people (40%), 9 people had renal insufficiency (30%), and the least common was obesity (BMI> 30) only found in 1 person (3.3%). The most prevalent etiology of heart failure is the presence of coronary or ischemic heart disease, namely in 27 people (90%), and ischemic, dilatative cardiomyopathy was found in 3 people (10%).

Furthermore, the most given medical therapy to patients was ACEI / ARB group 27 people (90%), then statins (83.3%), beta-blockers 24 people (80%). The administration of diuretics was almost the same between furosemide and spironolactone, 18 people (60%) and 19 people (63.3%). The least administered group of drugs is digoxin 2 people (6.7%), and calcium blockers 1 person (3.3%).
The degree of heart failure in the subjects was evaluated based on the *New York Heart Association* (NYHA), most of the subjects experienced NYHA class II in 24 people (80%), then NYHA class III 5 people (16.7%), and NYHA class I 1 person (3.3%).

The characteristics of echocardiography in subjects with the lowest EF were 19%, and the highest was 45%, with an average EF of 36.2% ± 8.5. Diastolic function in all subjects was disrupted, and most were found to be abnormal relaxation, of 17 people (56.7%), then restrictive filling 8 people (26.7%), and pseudonormal 5 people (16.7%).

To determine the correlation between left ventricular GLS and SHFM score, a statistical correlation test was carried out, which began with a distribution test to determine the distribution normality of the left ventricular GLS value, and the SHFM score using seven distribution tests.

3.1.1 Correlation between Left Ventricle GLS and 1- year SHFM Score.
The Spearman correlation test was carried out between left ventricular GLS and 1-year SHFM score because one of the data was abnormally distributed. The results of the Spearman correlation test showed a significant, negative, and strong correlation between left ventricular GLS and 1-year SHFM score with p = 0,0001 (p <0.05) (Table 2).

3.2 Correlation between the Tei Index and SHFM Score
3.2.1Correlation between the Tei Index and SHFM Score of 1-Year.
The Spearman correlation test was carried out between Tei Index and 1-year SHFM score because one of the data was abnormally distributed. The results of the Spearman correlation test showed a significant, positive, and strong correlation between Tei Index and 1-year SHFM score with p = 0,0001 (p <0.05) (Table 4).

3.2.2Correlation between the Tei Index and SHFM Score of 5 Years.
The Pearson correlation test was carried out between the left ventricular GLS and the 5-year SHFM score because one of the data was abnormally distributed. Test results of the Pearson correlation showed a significant, positive, and strong correlation between left ventricular GLS and 5-year SHFM score with p = 0,0001 (p <0.05) (Table 5)

3.3 Correlation between Left Ventricular GLS and Tei Index and EF
In this analysis, the Pearson correlation test was used because all data analyzed were normally distributed. The results of the Pearson correlation test showed a significant, negative, and strong correlation between left ventricular GLS and Tei Index with p = 0,0001 (p <0.05), while the correlation between left ventricular GLS and EF was found to be significant, positive, and strong with p = 0,0001 (p <0.05) (Table 6).

3.4 Intraobserver and interobserver variability
Assessment of intraobserver and interobserver variability was conducted using the Bland Altman method, with several (15 subjects) subjected to quite good suitability, both on left ventricular GLS examination, and TI. There were no significant differences between intraobserver and interobserver (p> 0.05).

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Table 1. Characteristics of Research Subjects.

Variable		N%	Mean(SD[a])
Age	40-49	5 (16.7)	
	50-59	12 (40)	
	60-69	11 (36.7)	58 ± 8.12
	70-79	2 (6.7)	
Gender	Male	22 (73.3)	
	Female	8 (26.7)	
Comorbidity	Dyslipidemia	22 (73.3)	
	Hypertension	13 (43.3)	
	Diabetes	13 (43.3)	
	Smoking	12 (40)	
	Renal insufficiency	9 (30)	
	Obesity (BMI[b]>30)	1 (3.3)	
HF[c] etiology	Ischemia	27 (90)	
	Others	3 (10)	
Pharmacotherapy	ACEI[d]/ARB[e]	27 (90)	
	Beta-blocker	24 (80)	
	Spironolactone	18 (60)	
	Furosemide	19 (63.3)	
	Calcium blocker	1 (3.3)	
	Statin	24 (80)	
	Digoxin	2 (6.7)	
NYHA	Class 1	1 (3.3)	
	Class II	24 (80)	
	Class III	5 (16.7)	
LV Function	EF[f] %, mean (SD)	36.2 (8.5)	
Diastolic function	Abnormal relaxation	17 (56,7)	
	Pseudonormal	5 (16,7)	
	Restrictive filling	8 (26,7)	

[a]SD: Standard Deviation; [b]BMI: Body Mass Index; [c]HF; Heart failure; [d]ACEI: Angiotensin-converting enzyme inhibitor; [e]ARB: Angiotensin-receptor blockers; [f]EF: Ejection Fraction.

Table 2. Correlation Analysis Between Left Ventricular GLS and 1-Year SHFM Score.

	Mean ± SD	Min - Max	r	p*
Left Ventricular GLS	-8,1±3,98	0 - -14,7	-0,676	0,0001
1-Year SHFM	7,3±8,69	2 – 48		

* Analyzed with the Spearman Rho Correlation test

Table 3. Correlation Analysis Between Left Ventricular GLS and 5 Years SHFM Score.

	Mean ± SD	Min - Max	r	p*
Left Ventricular GLS	-8,1±3,98	0 -14,7	-0,676	0,0001
5 Years SHFM	29,6±20,4	8 – 98		

* Analyzed with Pearson Rho Correlation test

Table 4. Correlation Analysis Between Tei Index and 1-Year SHFM Score.

	Mean ± SD	Min - Max	r	p*
Tei Index	0,65±0,14	0,43 – 0,95	0,745	0,0001
1 Year SHFM	7,3±8,69	2 – 48		

* Analyzed with the Spearman Rho Correlation test

Table 5. Correlation Analysis Between Tei Index and 5 Years SHFM Score.

	Mean ± SD	Min - Maks	r	p*
Tei Index	0,65±0,14	0,43 – 0,95	0,738	0,0001
5 Years SHFM	29,6±20,4	8 –98		

* Analyzed with the Pearson Correlation test

Table 6. Correlation Analysis Between Left Ventricular GLS and Tei Index.

	Mean ± SD	Min - Maks	r	p*
Left Ventricular GLS	-8,1±3,98	0 -14,7	-0,763	0,0001
Tei Index	0,65±0,14	0,43 – 0,95		

* Analyzed with Pearson Rho Correlation test

Table 7. Correlation Analysis Between Left Ventricular GLS and EF.

	Mean ± SD	Min - Maks	R	p*
Left Ventricular GLS	-8,1±3,98	0 -14,7	0,678	0,0001
EF	36,2±8,51	19 – 45		

*Analyzed with Pearson Rho Correlation test

4. Discussions

Assessment of prognosis in heart disease is strongly related to left ventricular systolic function, which is generally assessed with EF. Previous studies have shown that left ventricular GLS is superior to EF both in assessing left ventricular function and as a predictor of mortality and cardiovascular events [7-10]. In this study, there was a significant, positive, and strong correlation between left ventricular GLS and EF (r = 0.678, p<0.001). These results are consistent with the existing literature [13]. Research conducted by Brown in 62 post-infarct patients received a correlation significant between left ventricular GLS and EF calculated by 3D-MRI (Magnetic Resonance Imaging) [14].

MPI or TI is an index that can globally describe both systolic and diastolic ventricular function , and is easy to do, and is not affected by heart rate, blood pressure, and the severity of mitral valve regurgitation. Some studies also mention that TI can have prognostic value for various heart diseases[15]. In this study, the average value of TI in heart failure patients was 0.65±0.14, with the lowest value of 0.43 and the highest value of 0.95. The data from this study were not much different from the research conducted by Bruch and his colleagues on 81 patients with heart failure with NYHA class ≤ 2. The results of the average TI value were 0.60 ± 0.18, other than that the results of the study stated that TI values >0.47 could be used to identify the presence of congestive heart failure with a sensitivity of 86% and specificity of 82% [16].

In this study, left ventricular GLS was found to have a significant, negative, and strong correlation with TI (r = -0.763, p <0.001). This correlation is in line with a recent study by Sørensen, in 1088 outpatient type 1 diabetes patients who did not have a history of previous heart disease, and where GLS was significantly correlated with TI (p <0.001) [15].

SHFM is a model developed to predict mortality, or survival at 1, 2, and 5 years in patients with chronic heart failure. SHFM consists of various clinical, laboratory, and therapeutic variables, where each of these variables has a prognostic value and has been recognized by AHA as one of the predictive scores in heart failure that has been well validated[5,12]. This study is the first study conducted in Indonesia that correlates between myocardial deformity (left ventricular GLS) and cardiac time interval (TI) markers with prognostic indicators obtained from a multivariable risk assessment tool (SHFM score). In this study, the selected SHFM score became the prediction of 1-year and 5-year mortality because it was made more aware of mortality or 1-year survival, and it is essential in clinical practice considerations in determining candidate patients who deserve further therapy such as ICD / CRT-D installation. Or even determine the heart transplant candidate. Five-year mortality prediction is used to assess predictions of mortality over a longer period so that it can be used when educating and explaining disease status in patients.

In this study, there was a significant, negative, and strong correlation between left ventricular GLS and 1-year, and 5-year SHFM mortality scores with both having the same values, with r = -0.676, p <0.001. The results of this study are in line with the research conducted by Rangel in 54 chronic heart failure patients with systolic dysfunction (EF≤45%), which obtained a significant correlation between left ventricular GLS and SHFM score which estimated the value of life expectancy (r = −0.41, p = 0.002) [9]. The results of this research also support the cohort study of 1,065 HFrEF patients with an observation period of 22-57 months and a median of 40 months conducted by Sengeløv and colleagues. The results showed that GLS left ventricle was an independent predictor of mortality after adjusting the age, sex, BMI, total cholesterol, mean arterial pressure, heart rate, ischemic cardiomyopathy, percutaneous transluminal coronary angioplasty, coronary artery bypass graft surgery, noninsulin-dependent diabetes mellitus, and conventional echocardiographic parameters (hazard ratio (HR): 1.15, 95% confidence interval (CI)) [17]. In this study, a significant, positive, and strong correlation was found between Tei Index and 1-year SHFM score (r = 0.745, p <0.001), and 5- year SHFM score (r = 0.738, p <0.001). This research is the first study to analyze the correlation between TI and SHFM scores, which is a model prognostic score consisting of various validated prognostic variables. There have been several previous studies that analyzed TI correlation with other prognostic variables such as EF, BNP, and NYHA, and all found significant correlations [18,19].

Harjai et al., investigated the prognostic value of TI in heart failure patients with EF <30%, followed by a period of 24 ± 19 months, assessed as the endpoint of death due to any cause, and heart transplantation. During the study, 28 patients died (49%), and two patients (3.5%) underwent a heart transplant. A strong correlation was found between TI values >1.14 and long-term outcomes and proved independent of other clinical and echocardiographic variables that have been shown to have prognostic value [20]. Sørensen et al. researched the general population and got results showing that TI is a significant prognosticator (p <0.05) for Major Adverse Cardiac Event (MACE) [15].

Some limitations of this study are that the results of this study are supported by a model prognostic score without prospective cohort. Hence, further validation is still required. However, despite SHFM being a well-validated prognostic model score in patients with chronic heart failure, outpatient care, based on a variety of variables that have been known to have prognostic value in patients with heart failure. In this study, STE-2D strains evaluated were only assessed retrospectively, and both radial and circumferential strains were not assessed.

5. Conclusion

GLS-left ventricle had a significant negative correlation with an estimated one and five years mortality based on SHFM score, and it is suggested that GLS-left ventricle and TI can be a prognostic factor.

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