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Global Longitudinal Strain and Global Circumferential Strain on Echo Heart Failure Score as 60-days Readmission Predictor in Congestive Heart Failure Patients with Left Ventricle Systolic Dysfunction in Makassar

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ABSTRACT

Introduction: *The readmission rate due to heart failure increases every year in South Sulawesi. A Frequently used method for assessing readmission is an echocardiographic examination by measuring ejection fraction. However, recent studies show that the speckle tracking parameters are more sensitive to predict readmission of heart failure patients. In this study, we assess the role of Global Longitudinal Strain (GLS) and Global Circumferential Strain (GCS) parameters on the Echo Heart Failure Score (EHFS) as a 60-days readmission predictor in heart failure patients.* ***Methods****: We included 175 patients admitted through the inpatient installation of Integrated Heart Center Dr. Wahidin Sudirohusodo General Hospital. In addition, we reviewed up to 60 days after outpatient prospectively by collecting data through medical records. The correlation between echocardiographic parameters and readmissions was*

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analyzed using the Spearman Rank Correlation. To determine each echocardiographic parameter's cut-off point, sensitivity, and specificity, we use Receiver Operating Characteristic (ROC) curve. ***Results:****GLS and GCS are very sensitive and specific parameters in predicting 60-days readmission with an area under the curve (AUC) value > 0.7. This study shows that adding GLS and GCS parameters to the EHFS increases the predicted value (AUC 0.850 vs. 0.820) and sensitivity to 79%.* ***Conclusion****: GLS and GCS parameters additional on EHFS can help predict 60-days readmission of heart failure patients with sensitivity and specificity of 79% and 83%, respectively. The present study shows that with higher GLS and GCS scores on the EHFS, the risk of readmission in heart failure patients will increase.*

1. INTRODUCTION

Heart failure is a syndrome of clinical symptoms characterized by specific symptoms such as shortness of breath, edema of the ankles, and fatigue, accompanied by signs of increased jugular venous pressure and pulmonary rales as a result of structural and or functional heart abnormality results in decreased cardiac output and or increased intracardiac pressure during rest and activity.[1] From Riskesdas Data in 2013, congestive heart failure is the leading cause of death in Indonesia, contributing to approximately 9.7% of all heart diseases. Furthermore, readmission due to congestive heart failure increases every year even though the therapy had been given optimally.[2,3,4] This fact has led to the escalation of hospitalization cost and is an essential indicator of hospital services quality.

Speckle Tracking Echocardiography (STE) is a new and non-invasive ultrasound imaging method that has the objective capability to assess the myocardium's global and regional function. This semi-automatic modality can analyze the heart's mechanical system, including coordination between myocardium and showing the longitudinal, circumferential, and radial myocardial deformation.[5] This technique is mainly based on the analysis of spots or speckles during the cardiac cycle, which combine into a functional unit, referred to as the kernel, and considered an ultrasound fingerprint that can be tracked by software during the cardiac cycle.[6,7] This system can assess strain, a linear measure of tissue deformation, and express the percentage change in length during systolic between two different points on the myocardium.[8] Several studies have shown that 2-dimensional speckle tracking Global Longitudinal Strain and Global Circumferential Strain on echocardiographic modalities are more objective to be prognostic indicators in heart failure than left ventricular ejection fraction alone.[9,10] Besides, Echo Heart Failure Score (EHFS) is used to predict mortality in European populations. The study shows that the mortality rate increases progressively and

significantly according to the increasing EHFS.[11] By this phenomenon and background, we investigate the role of Global Longitudinal Strain (GLS) and Global Circumferential Strain (GCS) by adding the parameters in EHFS as 60-days predictors of readmission in heart failure patients.

2. METHODS

Study Design

We conduct a prospective cohort in this study. The observation was carried out prospectively by collecting data through medical records and computer systems when the patients were admitted to RSUP Dr. Wahidin Sudirohusodo with congestive heart failure and left ventricular systolic dysfunction. The observation was conduct up to 60 days post-discharged to assess the 60-days readmission rate in patients with congestive heart failure. We obtained all data from physical, laboratory examinations, and echocardiographic parameters. Follow-up was conducted by phone and observation of the inpatient registration computer system. Furthermore, the STE was performed and interpreted by two independent echocardiography specialists (AFG and AFM).

Population and Sample

The study population was all patients admitted to Integrated Heart Center Dr. Wahidin Sudirohusodo Hospital with congestive heart failure and left ventricular systolic dysfunction. Samples that met inclusion criteria and did not meet exclusion criteria were included. Follow-up was carried out 60 days post-discharge start from November 2018 to February 2019. The echocardiography instrument used for this study was Philips® EPIC 5C series.

Objective Criteria

Echo Heart Failure Score (EHFS) is a scoring parameter consisting of several echocardiographic variables. Left Atrium Volume Index (LAVI), End Systolic Volume Index (ESVI), Deceleration Time (DT), Pulmonary Artery Systolic Pressure (PASP), and Tricuspid Annular Plane Systolic Excursion (TAPSE). EHFS assessment based on numerical, the value of 1 in each parameter if any, and 0 if not present, and then adding up each parameter, with a range of 0 to 5.[11] Speckle Tracking Echocardiography (STE) is a new non-invasive method of ultrasound imaging that has quantitative and objective capabilities in assessing the global and regional function of the cardiac myocardium. STE is semi-automatic and can analyze a complex mechanical cardiac system, such as the myocardium's coordination. It shows Global Longitudinal Strain (GLS), Global Circumferential Strain (GCS), and Global Radial Strain (GRS) myocardial deformation.[5]

Standard 4-chamber, 3-chamber, 2-chamber, and short-axis view (basal, mid, apical) were obtained using an ultrasound system by Philips ® EPIC 5C series. The echocardiography study was performed within 24 hours after admission. Speckle Tracking for the myocardial strain was perform using velocity vector imaging average from 2-chamber view, 3-chamber view, and 4-chamber view for GLS and short-axis view for GCS. In addition, digital loop and circle were acquired from apical view, 2-chamber

view, 3-chamber view, 4-chamber view, and short-axis view. GLS and GCS was the average result of each three views.

Inclusion Criteria

All participants recruited in this study were hospitalized with Heart Failure reduced Ejection Fraction (LVEF <40%), aged 18 years or older, and enabled to provide written informed consent.

Exclusion criteria

The participants were excluded with the criteria: undergoing invasive or non-invasive interventional procedures aim to correct structural cardiac disorders (such as cardiac resynchronization therapy, coronary artery bypass graft, valvular heart replacement), with permanent atrial fibrillation, and had more than nine myocardium segments with poor image quality in a subject.

Research Ethics

The research has received approval from the ethics committee of biomedical research in humans at the Hasanuddin University Faculty of Medicine and Dr. Wahidin Sudirohusodo Hospital, Makassar.

Processing and analysis of data

Mean ± standard deviation was used to determine the basic characteristics of numerical variables. Spearman Rank Correlation was used to observed the correlation between echocardiographic parameters and readmission. To assess the correlation of each echocardiographic parameter's cut-off point, sensitivity, and specificity to the readmission, the Receiver Operating Characteristic (ROC) curve was used.

3. RESULTS

There were 175 samples eligible for the study. Baseline patient characteristics are shown in Table 1 and Table 2. The majority of participants were male (n = 137; 78.3%), with a mean age of 54.4 years and ranging from 18 years to 79 years. Based on the BMI category, the subject in this study have a normal BMI, with a mean BMI of 23,87. The table above shows that risk factors such as hypertension and type 2 diabetes mellitus were not dominant, with a percentage of 46.9% and 30.9%, respectively. From the clinical presentation, we found that majority of our subject was the NYHA III group (41.7%), while the most common etiology was ischemic.

During two months of study, we found that majority of our subjects did not experience readmission (58.3%) (Table 3). From GLS and GCS parameters, we found the average value of -7.6 and -9.1, respectively. From EHFS, we discovered that most EHFS values in our subjects were 1 and 2 (22.9%). The average value of the LAVI and ESVI was above normal, 42.23 and 80.7, respectively. TAPSE value within a normal limit, specifically 1.6.

Table 1. Clinical Profiles on Categoric Variables

Variable		n	Percentage (%)
Sex	Male	137	78.3
	Female	38	21.7
Hypertension	Yes	82	46.9
	No	93	53.1
Diabetes Mellitus Type 2	Yes	54	30.9
	No	121	69.1
NYHA Class	No	102	58.3
	I	0	0
	II	19	10.9
	III	73	41.7
	IV	83	47.4
EHFS Score	0	26	14.9
	1	40	22.9
	2	40	22.9
	3	26	14.9
	4	20	11.4
	5	22	12.6
Etiology	Ischemic	139	79.4
	HHD	9	5.1
	Valvular	8	4.6
	Cardiomyopathy	13	7.4
	PPCM	6	3.4

EHFS: Echo Heart Failure Score; HHD: Hypertensive Heart Disease; NYHA: New York Heart Association; PPCM: Peripartum Cardiomyopathy

Table 2. Clinical Profiles of Participants on Numerical Variables

	Minimum	Maximum	Mean	Std. Deviation
Baseline Characteristic				
Age	18	79	54.4	11.20
Height	142	178	162.7	6.63
Weight	40.0	723.0	73.3	76.6
BSA	1.22	2.08	1.55	0.170
BMI	16.97	40.40	23.87	3.71
SBP	90	185	125.3	17.79
DBP	57	120	78.2	12.47
Heart Rate	49	120	84.6	14.33
Laboratory Parameters				
Hb	6.7	143.0	14.68	13.27
Arum	10	249	52.5	35.15
eGFR	4.3	146	68.7	28.1
Creatinin	0.4	12.8	1.55	1.76
Echocardiography Parameters				
LAVI	13.1	90.1	42.23	13.57
EVI	26.8	190.0	80.7	32.3
DT	71.0	349.0	145.5	45.6
TAPE	0.8	2.5	1.6	0.345
PASS	21.0	97.0	42.23	13.01
LVEF	14.1	39.6	27.48	6.57
RAP	3	15	9.14	4.70
GLS	-13.8	-1.5	-7.59	2.82
GCS	-18.9	-2.5	-9.13	3.21

BSA: Body Surface Area; BMI: Body Mass Index; DBP: Diastolic Blood Pressure; DT: Deceleration Time; eGFR: estimated Glomerulus Filtration Rate; ESVI: End Systolic Volume Index; GCS: Global Circumferential Strain; GLS: Global Longitudinal Strain; LAVI: Left Atrium Volume Index; LVEF: Left Ventricle Ejection Fraction; PASP: Pulmonary Artery Systolic Pressure; RAP: Right Atrial Pressure; SBP: Systolic Blood Pressure; TAPSE: Tricuspid Annular Plane Systolic Excursion.

Table 3. Clinical outcomes of participants

Variable		n	Percentage (%)
Readmission <30 days	Yes	59	33.7
	No	116	66.3
Readmission 60 days	Yes	73	41.7

Correlation Between Echocardiography Parameters in 60-days Readmission

Speckle tracking echocardiography in this study used GLS and GCS parameters. EHFS scoring uses five parameters consisting of LAVI, ESVI, DT, TAPSE, and PASP. These parameters were analyzed for correlation using the Spearman correlation on patient readmissions in 60 days.

Table 4 shows that all parameters except PASP significantly correlate with the 60-day readmission rate. GLS and GCS parameters had a significant relationship with the readmission rate with p-value <0.05 (R = 0.253, p = 0.001; R = 0.214, p = 0.004, respectively). This finding shows that the higher the LAVI value, the probability of readmission in 60 days will increase. The ESVI parameter has a weak correlation strength and is unidirectional to the readmission incident (R = 0.293, p <0.001). This finding shows that the higher the LAVI value, the probability of readmission in 60 days will increase. The ESVI parameter has a weak correlation strength and is unidirectional to the readmission incident (R = 0.244, p = 0.001). This finding shows that the higher the ESVI value, the probability of readmission in 60 days will increase. The DT parameter has moderate correlation strength and is inversely related to the readmission incident (R -0.379, p <0.001). This finding shows that the higher the DT value, the low likelihood of readmissions in 60 days. The TAPSE parameter had moderate correlation strength and was inverse for the readmission event (R -0.310, p <0.001). PASP parameter does not show a significant correlation with readmissions in 60 days (R = 0.001, p = 0.993).

Table 4. Correlation Between Echocardiography Parameters and EHFS in Predicting 60-days Readmission

Echocardiography Variable	Correlation Coefficient (R)	p-value
LAVI	0.293	<0.001
ESVI	0.244	0.001
DT	-0.379	<0.001
TAPSE	-0.310	<0.001
PASP	0.001	0.993
GLS	0.253	0.001
GCS	0.214	0.004
EHFS	0.554	<0.001

DT: Deceleration Time; EHFS: Echo Heart Failure Score; ESVI: End Systolic Volume Index; GCS: Global Circumferential Strain; GLS: Global Longitudinal Strain; LAVI: Left Atrium Volume Index; PASP: Pulmonary Artery Systolic Pressure; TAPSE: Tricuspid Annular Plane Systolic Excursion

Correlation Between EHFS Scoring System and Readmissions in 60 Days

The EHFS score consists of five echocardiography parameters, as described above. In this study, the Spearman analysis evaluates the EHFS scoring system's correlation and 60-days readmission incidence. The results showed that there were a strong correlation and a unidirectional relationship between the EHFS score and the incidence of readmissions within 60 days ($R > 0.5$; $p < 0.001$) (Table 4).

Sensitivity and Specificity of Various Echocardiographic Parameters on Readmission in 60 days

In ROC curve analysis for the GLS parameter, we found that GLS was a good predictor for readmission incidence within 60 days (Area Under Curve (AUC) = 0.704 ; $p < 0.001$) (Figure 1a). The analysis proves that GLS has excellent sensitivity and specificity in predicting readmission incidence in 60 days. Table 4 demonstrates that the GLS cut-off value to readmission in 60 days was -6,55, where a value higher than this predicted higher readmission incidence.

The GCS parameter in this study has excellent sensitivity and specificity in predicting the incidence of readmission in 60 days (AUC = 0.705 ; $p < 0.001$) (Figure 1b). The cut-off value of GCS is -9.95 (Table 5), with higher values than this cut-off predicts a higher incidence of readmission.

LAVI has excellent sensitivity and specificity in predicting readmission incidence in 60 days (AUC = 0.716 ; $p = 0.040$. (Figure 1c). The cut-off value of LAVI is 42.4 (Table 5).

ESVI and TAPSE have a role as predictors of readmission within 60 days with a p-value of 0.001. ROC curve analysis (Figure 1d and 1e) of ESVI and TAPSE parameters showed good sensitivity and specificity for predicting readmission within 60 days (AUC = 0.3-0.7 (0.651 and 0.331, respectively). The cut-off value of ESVI is 87.56 mL / m^2, while TAPSE is 1.55 cm (Table 5).

The DT parameter in this study had a very high specificity level for the readmission incidence within 60 days but had a very low sensitivity (AUC = 0.279 ; $p < 0.001$) (Figure 1f). Therefore, the cut-off value of DT is 136 (Table 5).

In addition, the ROC curve analysis test was carried out on the EHFS variable toward readmission incidence in 60 days (Figure 2). Results found that the EHFS has excellent ability in predicting 60-days readmission incidence (AUC > 0.7 (0.820) with a cut-off value of 2.51 (Table 5).

Table 5. Various Parameters in Predicting 60-days Readmission and EHFS as 60-days Readmission's Predictor

Parameters	AUC	p	95% CI		Cut off value
			Lower Bound	Upper Bound	
GLS	0.704	<0.001	0.625	0.784	-6.55
GCS	0.705	<0.001	0.629	0.781	-9.95
LAVI	0.716	0.040	0.639	0.793	42.4
EVI	0.651	0.001	0.568	0.733	87.56
TAPE	0.331	<0.001	0.248	0.413	1.55
DT	0.279	<0.001	0.201	0.358	136.0
EHFS	0.820	0.034	0.754	0.886	2.51

AUC: Area Under the Curve; CI: Confidence Interval; DT: Deceleration Time; EHFS: Echo Heart Failure Score; ESVI: End Systolic Volume Index; GCS: Global Circumferential Strain; GLS: Global Longitudinal Strain; LAVI: Left Atrium Volume Index; PASP: Pulmonary Artery Systolic Pressure; TAPSE: Tricuspid Annular Plane Systolic Excursion

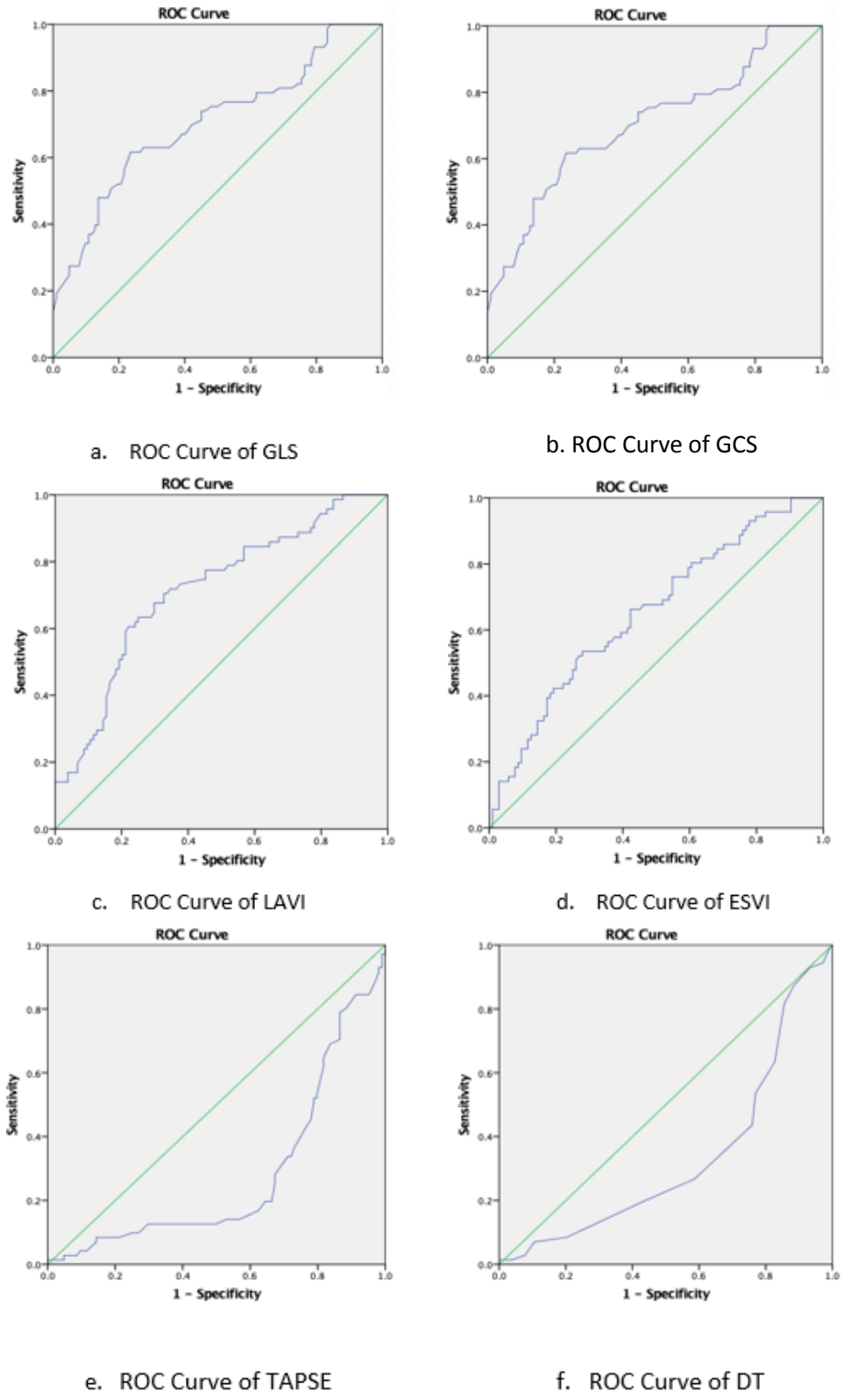

Figure 1. ROC Curve of 60-days Readmission Predictor Parameter. GLS, GCS, and LAVI show high sensitivity and specificity in predicting 60-days readmission, while ESVI and TAPSE show moderate sensitivity and specificity in predicting 60-days readmission. DT has very high specificity but low sensitivity in predict 60-days readmission.

DT: Deceleration Time; ESVI: End Systolic Volume Index; GCS: Global Circumferential Strain; GLS: Global Longitudinal Strain; LAVI: Left Atrium Volume Index; ROC: Receiver Operating Characteristic; TAPSE: Tricuspid Annular Plane Systolic Excursion.

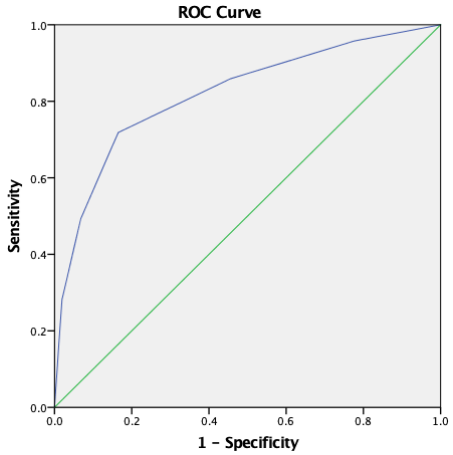

Figure 2. EHFS' ROC Curve toward 60-days Readmission. EHFS has excellent ability in predicting 60-days readmission incidence with AUC > 0.7 (0.820).

EHFS: Echo Heart Failure Score; ROC: Receiver Operating Characteristic

Table 6. The role of GLS dan GCS in EHFS as 60-days Readmission's Predictor

AUC (C)	p	95% C.I.		Cut-Off Value
		Lower Bound	Upper Bound	
0.850	<0.001	0.791	0.909	3.50

AUC: Area Under the Curve; CI: Confidence Interval; EHFS: Echo Heart Failure Score; GCS: Global Circumferential Strain; GLS: Global Longitudinal Strain

Correlation between GLS, GCS on EHFS toward 60 days-Readmission

GLS, GCS, and EHFS are parameters with excellent sensitivity and specificity levels. ROC curve shows that the addition of GLS and GCS parameters to EHFS is the stronger predictor value of EHFS to predict readmission in 60 days, due to better the AUC value (0.850 vs. 0.820) (Figure 3). GLS and GCS will gain one point if their value is positive than the cut-off value, respectively. The cut-off value is 3.50 (Table 5).

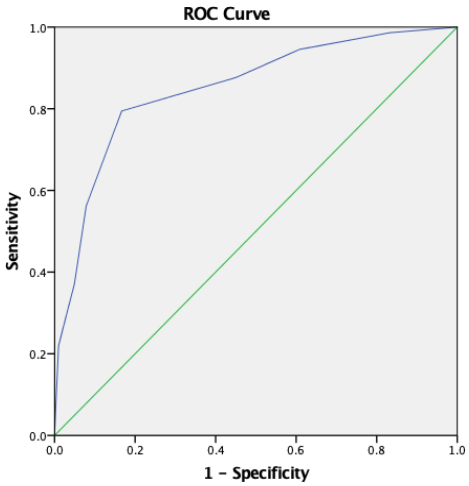

Figure 3. GLS and GCS' ROC curves on the EHFS score toward the incidence of 60-days Readmission show a better AUC value (0,850) with the additional GLS and GCS parameter to EHFS.

EHFS: Echo Heart Failure Score; GCS: Global Circumferential Strain; GLS: Global Longitudinal Strain; ROC: Receiver Operating Characteristic.

4. DISCUSSION

Speckle Tracking Echocardiography (STE) is a new and non-invasive ultrasound imaging method that has the objective capability to assess the myocardium's global and regional function and is an accurate prognostic indicator, especially in heart failure. The parameters used in this study were GLS and GCS. Studies show that GLS> -6.1 and GCS> -7.7 are associated with higher heart failure readmission rates.[9,12] Echo Heart Failure Score consists of five parameters, ie. LAVI, ESVI, DT, TAPSE, and PASP. These five parameters have a strong ability to predict mortality from heart failure. EHFS value ≥ 3 has a hazard ratio of 3.58 compared to EHFS < 3. EHFS is expected to improve the predictive ability and determine risk stratification in systolic heart failure patients.[11]

In this study, GLS parameter showed a very sensitive and specific characteristic in predicting the incidence of 60 days readmission in patients with heart failure (AUC = 0.704; p-value < 0.001; cut-off = -6.55). This finding shows that the value of GLS begins to be significant as a predictor of readmission if the value is getting positive from -6.55. This finding is in line with a study by Park et al., which shows that GLS with a value more positive than -8% shows a worse prognosis than the LVEF parameter alone.[12] Study by Romano et al. found that the GLS parameter was a predictor of heart failure patients with a GLS value> -6.41 having the highest readmission rate.[13] Study by Mignot et al. with a population with systolic dysfunction (EF <45%) showed that GLS can be used in patients with left ventricle dysfunction and is excellent for risk stratification in Heart Failure reduced Ejection Fraction (HFrEF) patients with better accuracy than LVEF only with a cut-off value above - 7%, GLS can predict cardiac events and prognosis.[14]

In this study, the GCS parameter showed a very sensitive and specific characteristic in predicting the incidence of readmission within 60 days (AUC value = 0.705 ; p <0.001; cut off -9.95). This finding shows that the GCS value begins to be significant as a

predictor of readmission if the value is getting positive from -9.95. These results are in line with Zhang et al. that found a significant correlation between low GCS values and mortality rates in patients with systolic heart failure. A value of > -6.1 is a predictor of high mortality heart failure patients.[9]

In this study, EHFS has strong correlation strength of R > 0.5 (0.55) and excellent ability to predict readmissions within 60 days (AUC = 0.820; p = 0.034). EHFS value began to be significant as a predictor of readmission if the value was above 2.51. The sensitivity and specificity of EHFS for predicting 60-days readmission are 71% and 84%, respectively. These results are in line with the cohort study of Carluccio et al., where the mean EHFS score was 1.9 ± 1.5 for a mean of 34 ± 23 months (median 34 months, interquartile range 13-53), there were 224 (30%) deaths from all causes of death. The mortality rate (x 100 patients/year) was progressively and significantly increased with increasing EHFS (p < 0.0001). The high-risk group patients (EHFS ≥ 3) had low survival rate (log-rank test 100.2, P < 0.0001). Compared to the low-risk group, high-risk patients had an up to a four-fold increase in the risk of death (Hazard Ratio (HR) 3.58, 95% CI 2,623 - 4,548, P <0.0001).[11] This study shows that the addition of GLS and GCS parameters to EHFS will increase the readmission predictor value, comparing to EHFS parameter alone. An increased AUC value proved this finding from 0.820 to 0.850. The sensitivity value also increased to 79%. GLS and GCS parameters can increase the sensitivity because quantification of myocardial deformation was measured by the distance between 2 points on the heart muscle during the contraction and relaxation phase of the myocardium. If there is a reduction in shortening of the heart muscle fibers, it reflects impaired contractility. The present study shows that these parameters start to be significant as a predictor of readmission if the value is more than 3.5.

Limitations

There are several limitations to our study. The echocardiographic examination was not performed in the outpatient setting, and hence, we could not determine whether there was a change in echocardiographic parameters during the treatment. In addition, other parameters that could lead to readmissions, such as adherence to treatment and post-hospitalization patient's lifestyles, were not evaluated. We also did not conduct a study in a population of mid-range and preserved LVEF, so we could not determine the role of GLS and GCS in that population. Technically, there were no barriers in methodology for data collection.

5. CONCLUSIONS

GLS and GCS parameters additional on EHFS can predict the 60-days readmission of heart failure patients with sensitivity and specificity of 79% and 83%, respectively. Thus, this study shows that the risk of readmission in heart failure patients will increase with the higher GLS and GCS scores on the EHFS.

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Conflict of Interest Statement:

The author declares that the case report was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Supplementary files

Table S1. Pharmacotherapy received by participants during the study.

		n	Percentage (%)
Furosemide	Yes	163	12
	No	12	6.9
Ace inhibitor	Yes	146	83.4
	No	28	16.0
Beta-Blocker	Yes	56	32.0
	No	118	67.4
Spironolactone	Yes	74	42.3
	No	100	57.1
Digoxin	Yes	36	20.6
	No	138	78.9