

Research of left ventricular global longitudinal strain using speckle-tracking echocardiography in patients with chronic heart failure

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Abstract

Objectives: To evaluate the characteristics of left ventricular global longitudinal strain using speckle tracking echocardiography in heart failure patients and determine the relationships between global longitudinal strain and NYHA, EF, NT proBNP in heart failure disease. **Materials and methods:** A descriptive and cross-sectional study on 97 patients with HF. The patients were examined and treated at the Hue University of Medicine and Pharmacy Hospital from May 2021 to July 2023. **Results:** The mean age was 72.08 ± 13.53 years old. The median NT-proBNP value was 1053 (366 - 2795.5) pg/ml. The mean value of EF-Simpson is $45.47 \pm 12.87\%$. The mean GLS (%) value is $-13.08 \pm 3.36\%$. GLS (%) and GLSR (1/s) progressively decreased according to NYHA heart failure level and EF ($p < 0.05$). NT-proBNP has positive linear regression correlations with GLS (%) and GLSR (1/s) ($r_1 = 0.893$, $r_2 = 0.736$, $p < 0.01$), but has a negative linear regression correlation with EF-Simpson (%) ($r_3 = -0.785$, $p < 0.01$). GLS (%) also has a strong negative linear regression correlation with EF-Simpson (%) ($r = -0.772$, $p < 0.01$, $y = 6.42 - 2.99 \cdot x$). **Conclusion:** Both GLS (%) and GLSR (1/s) have a relationship with the two classic prognostic factors, including NYHA classification and LVEF. The GLS (%) index has a stronger linear correlation with NT-proBNP when compared to EF-Simpson.

Keywords: NT-proBNP, speckle-tracking echocardiography, left ventricular global longitudinal strain, chronic heart failure.

1. INTRODUCTION

Heart failure is one of the worst health problems around the world, it has a high rate of prevalence, and this rate is also increasing gradually. In Asian countries, one study showed that the prevalence of heart failure was 1 - 3% [1]. In Vietnam, statistics from Hanoi Heart Hospital in 2016 showed that hospitalization due to heart failure accounted for 15% of the total number of hospitalized patients and the in-hospital death rate due to heart failure was about 7% [2]. Although there are many new guidelines about the diagnosis and treatment of heart failure, this disease is still a big issue in the community due to its high morbidity and mortality [3]. Therefore, besides some of the classical factors like NYHA functional classification, LVEF classification, NT-proBNP concentration, finding new markers to help with early diagnosis and risk stratification is essential in the management of heart failure patients.

Left ventricular (LV) global longitudinal strain (GLS) is a novel echocardiographic method to evaluate LV function [4]. Through the systematic measurement of global longitudinal strain (GLS), strain-based imaging allows us to detect subclinical cardiac dysfunction early, attaining a higher sensitivity compared to the traditional technique of the LVEF, assessed by

Simpson's method [5]. To support the theory of left ventricular global longitudinal strain is valuable in the diagnosis and prediction of cardiovascular events and risk of death in heart failure disease we carried out this study with 2 aims:

- To evaluate the characteristics of left ventricular global longitudinal strain using speckle tracking echocardiography in heart failure patients.

- To determine the relationships between global longitudinal strain and NYHA, EF, NT proBNP in heart failure disease.

2. MATERIALS AND METHODS

2.1. Study population

Studying 97 heart failure patients who were treated in the Hospital of Hue University of Medicine and Pharmacy during 5/2021 - 7/2023.

Inclusion criteria: Patients were diagnosed with heart failure by a cardiologist according to the latest guideline of ESC 2021 [6]. The study population was divided into 3 groups based on the value of LVEF [7].

Exclusion criteria:

- Patients reject to participate in the study
- Patients were diagnosed with COPD, renal failure, atrial fibrillation, acute coronary syndrome, acute myocarditis, and pacemakers.
- Patients had poor image quality (loss of > 3

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myocardial segments/1 section or failure to analyze one section out of 6 sections), and unclear endocardial margins.

2.2. Study methods

- **Study design:** Cross-sectional description

- At baseline, all patients were examined by a physician and the following information was obtained: medical history, present symptoms, functional class (NYHA), medication, height, weight, non-invasive blood pressure, heart rate, and 12-lead electrocardiogram.

- Quantification of NT-pro BNP concentration is based on the principle of Sandwich immunoassay using ECUA Cobas 8000 electrochemiluminescence technology;

- On conventional echocardiography: Follow the recommendations of the American Society of Ultrasound, common echocardiographic parameters such as left ventricular systolic and diastolic diameter (Ds, Dd), left ventricular mass index (LVMI), left ventricular ejection fraction (EF) (Measured by Simpson method) [8].

- On speckle-tracking echocardiography:

+ Imaging technique: take 2D images at a frame rate of 40 - 80 frames/second or at least 40% of heart rate. Lean the patient to the left about 30 - 40 degrees, and place the probe at the apex of the heart, towards the bottom of the heart to get the

apical 4-chamber, 2-chamber, and 3-chamber view, taking 1 image from each view. The longitudinal axis section must pass through the apex of the heart (the section with the longest left ventricle).

+ Analyze results: Using offline software QLAB version 15.0. Myocardial deformation analysis were performed by two-dimensional speckle tracking in the three standard apical projections (long axis/three chambers, four chambers, two chambers). Global longitudinal strain (GLS) and global longitudinal strain rate (GLSR) were analyzed for 17 standardized segments, based on these values a mean value was calculated for each of the three apical projections and then a total LV GLS and GLSR were calculated as the average of the values from the three apical projections GLS is reported as a negative value in percentages. A value of GLS closer to zero is a sign of impaired function of the LV. In other words, the less negative the value of GLS, the worse the function of the LV. The normal range has been explored in some studies and it is reported to be in the region from -15.9 % to - 22.1% [8].

2.3. Statistical analysis

Using SPSS 20.0 software with descriptive statistics method. Evaluate the degree of correlation with the coefficient (r) according to Pearson or Spearman correlation analysis. Determine the regression line using linear regression analysis.

3. RESULT

3.1. Baseline characteristics of research participants

Table 1. Demographic, clinical, and echocardiographic characteristics

Characteristics	n = 97
Age ($\bar{X} \pm SD$)	72.08 \pm 13.53
Male (n, %)	47 (48.5)
Female (n, %)	50 (51.5)
BMI (kg/m ²) ($\bar{X} \pm SD$)	21.7 \pm 3.58
NYHA classification	
NYHA I (n, %)	10 (10.3)
NYHA II (n, %)	51 (52.6)
NYHA III (n, %)	33 (34)
NYHA IV (n, %)	3 (3.1)
NT-proBNP (pg/ml)	1053 (366 - 2795.5)
EF-Simpson (%)	45.47 \pm 12.87
LVEF classification	
HFrEF (EF \leq 40%)	34 (35.1)
HFmrEF (41% \leq EF \leq 49%)	30 (30.9)
HFpEF (EF \geq 50%)	33 (34)

The average age of the study population is 72.08 ± 13.53 and the male proportion is 48.5%, the mean value of BMI is 21.7 ± 3.58 kg/m². The group of NYHA II heart failure accounts for the highest proportion (52.6%). The median NT-proBNP value is 1053 (366 - 2795.5) pg/ml. The mean value of EF-Simpson is $45.47 \pm 12.87\%$. The proportion of the HFrEF group, HFmrEF group, and HFpEF group are 35.1%, 30.9%, and 34%, respectively.

3.2 GLS (%) and GLSR (1/s) indices on speckle-tracking echocardiography

Table 2. The value of GLS (%), and GLSR (1/s) of research participants

Index	NYHA I (n = 10)
GLS %	-17.43 ± 0.91
GLSR(1/s)	-2.09 ± 0.37

The mean GLS value and GLSR value are $-13.08 \pm 3.36\%$ and -1.5 ± 0.45 (1/s), respectively.

Table 3. The value of GLS(%), and GLSR(1/s) according to NYHA classification

Index	NYHA I (n = 10)	NYHA II (n = 51)	NYHA III (n = 33)	NYHA IV (n = 3)	p
GLS %	-17.43 ± 0.91	-14.34 ± 2.27	-10.45 ± 2.3	-6.03 ± 0.72	<0.05
GLSR(1/s)	-2.09 ± 0.37	-1.6 ± 0.36	-1.22 ± 0.34	-0.92 ± 0.21	<0.05

The mean value of GLS % and GLSR(1/s) are also different between groups, these indices of the NYHA IV group are less negative than those of the NYHA I group (-6.03 ± 0.72 vs -17.43 ± 0.91) (-0.92 ± 0.21 vs -2.09 ± 0.37). These differences are statistically significant ($p < 0.05$).

Table 4. The value of GLS (%), and GLSR(1/s) according to heart failure classification

Index	HFrEF (n = 34)	HFmrEF (n = 30)	HFpEF (n = 33)	p
GLS %	-9.81 ± 2.42	-13.9 ± 2.6	-15.7 ± 1.63	< 0.05
GLSR(1/s)	-1.15 ± 0.31	-1.52 ± 0.38	-1.84 ± 0.34	< 0.05

The values of GLS (%) and the GLSR(1/s) are also different between groups, specifically, the absolute value of GLS (%) and GLSR(1/s) of the HFrEF group is significantly lower than that of HFpEF (-9.81 ± 2.42 vs -15.7 ± 1.63) (-1.15 ± 0.31 vs -1.84 ± 0.34). These differences are statistically significant ($p < 0.05$).

3.3. Relationships between global longitudinal strain and the classic prognostic factors.

Table 5. Comparison of linear regression correlation between GLS (%), GLSR (1/s), EF-Simpson, and NT-proBNP

Index		NT-proBNP (pg/ml)			
		CHUNG (n = 97)	HFrEF (n = 34)	HFmrEF (n = 30)	HFpEF (n = 33)
GLS(%)	r1	0.893	0.742	0.706	0.774
	p	< 0.01	< 0.05	< 0.01	< 0.05
GLSR(1/s)	r2	0.736	0.363	0.513	0.438
	p	< 0.01	< 0.01	< 0.05	< 0.05
EF-Simpson (%)	r3	-0.785	-0.454	-0.38	-0.354
	p	< 0.01	< 0.01	< 0.05	< 0.05

NT-proBNP has positive linear regression correlations with GLS (%) and GLSR (1/s) ($r1 = 0.893$, $r2 = 0.736$, $p < 0.01$). By contrast, NT-proBNP (pg/ml) has a negative linear regression correlation with EF-Simpson (%), specifically, when the value of EF% decreases, the value of NT-proBNP (pg/ml) increases ($r3 = -0.785$, $p < 0.01$). Furthermore, this table also shows that the correlation between NT-proBNP (pg/ml) and GLS (%) is stronger than that of EF-Simpson(%) ($|r1| > |r3|$).

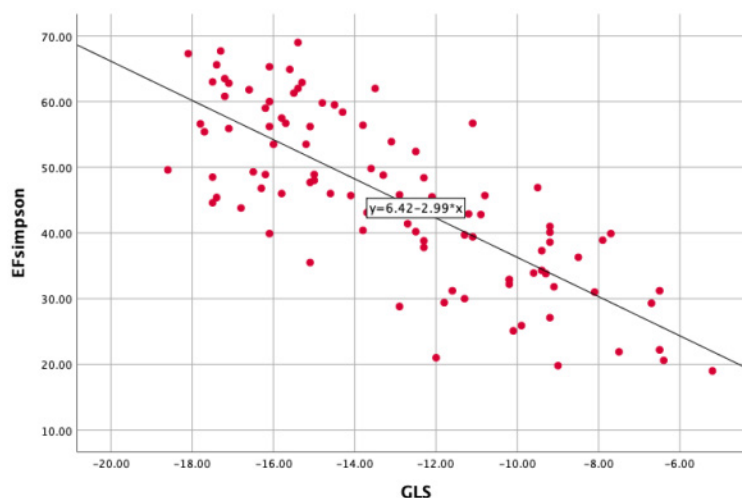


Figure 1. Linear regression correlation between GLS (%) and EF-Simpson ($r = -0.772$, $p < 0.01$)
GLS(%) has a strong negative linear regression correlation with EF-Simpson (%)
($r = -0.772$, $p < 0.01$, $y = 6.42 - 2.99 \cdot x$).

4. DISCUSSION

- Baseline characteristics

The average age of the population in our study was 72.08 ± 13.53 years, the same as the study of Nguyen Duy Toan (2022), which studied 70 patients with heart failure had a mean age of 78.61 ± 8.24 years [9]. There was a difference in the gender ratio between our study and related studies, specifically, in our study, the proportion of women was higher than that of men (51.5% vs 48.5%). The mean value of BMI was 21.7 ± 3.58 kg/m², equal to the results of Nguyen Duy Toan's research and Yuta Seko's research [9, 10].

Regarding functional classification (NYHA), which includes 4 levels of symptoms. Specifically, the patients who have no symptoms or aren't restricted in daily activities are classified into group NYHA I. Those who have severe symptoms making them completely restricted in daily activities are classified into the group NYHA IV. In our research, the group of NYHA II accounted for the majority of the study population, at 52.6%; followed by the group of NYHA III and NYHA I, with 34% and 10.3%, respectively; and finally the NYHA IV group, at only 3.1%. This result was similar to the result in the research of Vibhu Parcha (2021) (NYHA II group accounts for 53.2%) and the research of Damian Kaufmanni (2019) (NYHA II group accounts for 66%) [11, 12].

Theoretically, NT-proBNP is released from the myocardium when there is increased ventricular wall tension and increased filling pressure [13]. Quantify NT-proBNP concentration is a conventional test that was widely used in clinical to evaluate heart failure

patients, because it is easy to measure and analyze, and can confirm or rule out the diagnosis of heart failure, predicting which patients have the risk of developing heart failure [7]. In our study, the median value of NT-proBNP was 1053 (366 - 2795.5) pg/ml, which was quite similar to the study by Hirohiko Motoki (2012) (1158 (452 - 3399) pg/ml) [14].

In our study, the mean value of EF-Simpson was $45.47 \pm 12.87\%$. When classifying the study population based on LVEF classification, the proportions of the HFrEF group, HFmrEF group, and HFpEF group were 35.1%, 30.9%, and 34%, respectively. This characteristic was similar to the research of Yuta Seko (2020), which had the rates of each group at 37.8%, 18.8%, and 43.4%, respectively [10].

- GLS (%), GLSR (1/s) indices on speckle-tracking echocardiography

Each ventricular wall was subsequently subdivided into three segments (4-chambers, 2-chambers, 3-chambers) to realize the creation of 17 segments covering the whole myocardium. Longitudinal strain curves were built for each segment and the maximum value was determined. The GLS and GLSR are then computed as the average of all 17 segments [15]. The mean GLS value and GLSR value in our study were $-13.08 \pm 3.36\%$ and -1.5 ± 0.45 (1/s), respectively. These values were lower than the normal reference values (normal values $-15.9\% - -22.1\%$). This result was also quite similar to the results of other studies, specifically, the study of Hirohiko Motoki (2012) had a mean value of GLS is $7.1 \pm 3.3\%$ [14]; the study of Damian Kaufmanni (2019) had a median value of GLS is -12.3% (-9.7%

-14.7%) [12]. These studies had lower GLS values than our study due to the difference between the proportion of HFReEF and HFPeEF patients and the rate of NYHA groups (group NYHA I-II accounts for the majority of the study population).

When studying the role of GLS (%) and GLSR (1/s) in prognosis the patients with heart failure, our research found that the indices GLS (%) and GLSR (1/s) were related to two prognostic factors, including NYHA class and heart failure subgroup according to LVEF. Specifically, the NYHA IV group had less negative mean GLS (%) and GLSR (1/s) values than the NYHA I group (-6.03 ± 0.72 vs -17.43 ± 0.91) and (-0.92 ± 0.21 vs -2.09 ± 0.37).

The research by Nguyen Thi Kieu Ly (2022) also showed that the absolute value of GLS (%) also gradually decreased with increasing NYHA class ($p < 0.01$) [16]. Besides, when grouping patients according to LVEF, the average GLS (%) and GLSR (1/s) values of the HFReEF group were also less negative than that of the HFPeEF group (-9.81 ± 2.42 vs -15.7 ± 1.63) (-1.15 ± 0.31 vs -1.84 ± 0.34). These differences were statistically significant ($p < 0.05$). This result was similar to the research of Nguyen Duy Toan (2022) [9].

- Relationships between global longitudinal strain and the classic prognostic factors.

Our research results show that there was a very strong positive correlation between GLS (%), GLSR (1/s), and NT-proBNP concentration with a correlation coefficient is $r_1 = 0.893$; and $r_2 = 0.736$, respectively ($p < 0.01$). And when separately analyzing all 3 heart failure groups HFReEF, HFmrEF, and HFPeEF, we also demonstrated that the GLS (%) index had a strong correlation with NT-proBNP concentration with a correlation coefficient of $r = 0.742$, respectively; $r = 0.706$; $r = 0.774$ ($p < 0.01$), respectively. These results were also true for the GLSR (1/s) index. Two studies by Ayako Yoneyama (2008) and Mads Ersboll (2012) both agreed that there was a strong positive correlation between NT-proBNP and GLS(%), with $r = 0.75$, $r = 0.62$, respectively, ($p < 0.0001$) [17, 18].

By contrast, our research demonstrated that NT-proBNP (pg/ml) had a strong negative linear regression correlation with EF-Simpson (%), specifically, when the value of EF% decreased, the value of NT-proBNP (pg/ml) increased ($r_3 = -0.785$, $p < 0.01$). Similarly, Faida O's (2012) study also found that there was a strong negative correlation between NT-proBNP and EF - Simpson with $r = -0.83$, $p = 0.0001$ [19].

On the other hand, when evaluating the group of patients with HFPeEF, it was noted that the average

GLS (%) value of this group was $-15.7 \pm 1.63\%$, which was less negative than the conventional normal value ($-15.9\% - -22.1\%$). In other words, in the group of patients with HFPeEF, although there was no decrease in EF value, there was a relative decrease in the value of GLS (%). Furthermore, our study also showed the correlation between NT-proBNP (pg/ml) and GLS (%) was stronger than that of EF-Simpson(%) ($|r_1| > |r_3|$). These results support the hypothesis that GLS(%) is a useful index as an early diagnostic and prognostic marker in heart failure patients even when EF is still normal. Because, in patients with reduced ventricular systolic function, GLS decreases but EF remains within normal limits because of compensation of circumferential motion. Mads Ersboll's (2012) study on acute MI patients also showed that NT-proBNP levels were more closely related to GLS (%) than LVEF, and in patients with HFPeEF, GLS was superior to LVEF in identifying increased NT-proBNP concentrations [18].

The GLS (%) index in our research also has a strong negative linear regression correlation with EF-Simpson (%) with $r = -0.772$, $p < 0.01$, $y = 6.42 - 2.99^a x$). Similar to us, Mads Ersboll's study (2012) on 611 patients with acute MI also found that there was a fairly strong correlation between GLS and EF ($r = -0.66$, $p < 0.0001$) [18]; research by Hirohiko Motoki (2012) also showed similar results (quite close correlation between GLS and EF - Simpson with $r = -0.66$, $p < 0.0001$) [14].

5. CONCLUSION

Both GLS (%) and GLSR (1/s) have a relationship with the two classic prognostic factors, including NYHA classification and LVEF. GLS (%) has a strong negative linear regression correlation with EF-Simpson (%). The correlation between GLS (%) and NT-proBNP (pg/ml) is stronger than that of EF-Simpson (%).

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