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Left Ventricular Strain and Adverse Events in Patients with Heart Failure with Preserved Ejection Fraction

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Abstract:

Background: global longitudinal strain (GLS) has clinical and prognostic significance in heart failure with preserved ejection fraction (HFpEF). Aim: evaluate left ventricular strain in patients with HFpEF and its relation with adverse events (hospitalization and mortality). **Methods:** 100 patients were admitted, as per inclusion criteria: Heart failure with preserved ejection fraction, while those with hemodynamic instability, cardiogenic shock, inadequate echogenic window, or lower ejection fraction were excluded. Every patient was evaluated using baseline transthoracic echocardiography, speckle tracking echocardiography, routine laboratory tests, history taking, demographic data gathering, and a thorough clinical examination. **Results:** The mean ± SD of the left-ventricular ejection fraction was 60.17 ± 5.29 percent, with a range of 50 to 70%. The mean ± SD of the left ventricular mass index was 79.8 ± 12.41 g/m2, with a range of 50 to 110 g/m2. With respective ranges of 25.7–40.2 mm and 38.9–57.2 mm, the mean ± SD values for the left ventricular end-systolic and diastolic diameters were 31.8 ± 2.86 mm and 47.91 ± 3.44 mm. The mean ± SD of the global longitudinal strain was -18.89 ± 3.11 percent, with a range of -13 to -23%. The mean ± SD of the global circumferential strain was -19.89 ± 3.11 percent, with a range of -14 to -24 percent. 3 months periodic follow up including assessment of clinical variables, mortality and re-hospitalization. **Conclusion**, compared to event-free heart failure with maintained ejection, individuals with an event showed much reduced global longitudinal strain and global circumferential strain.

Keywords: Left-Ventricular Strain; Adverse Events; Heart Failure; Preserved-Ejection Fraction.

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Introduction

Over 64 million individuals worldwide suffer from heart failure (HF), which has a high incidence of morbidity and death. The ejection fraction (EF), which measures the left ventricle's (LV) reduced capacity to pump blood into the systemic circulation, was traditionally used to diagnose heart failure (HF) [(1)]. But HF may also exist while LV EF is normal, which is known as HF with preserved EF (HFpEF). The frequency of HFpEF is thought to be equivalent to that of HF with decreased EF (HFrEF), and the prognosis for both groups of HF patients is similar [(2)].

However, people with HFpEF have few alternatives for treatment and diagnosis. The diastolic phase and left atrial function have been the focus of studies examining the processes in individuals with HFpEF. Furthermore, it has been shown that high LV filling pressure and diastolic dysfunction are essential components in the diagnosis of HFpEF [(3)]. Furthermore, diastolic dysfunction plays a crucial role in the course of HFpEF illness and related health effects, as shown by the independent association of higher LV filling pressure with poorer clinical outcomes in HFpEF [(4)].

The use and therapeutic significance of left ventricular global longitudinal systolic strain (GLS) in various cardiovascular disorders have been shown by a number of research conducted in recent years. Accordingly, in recent years, the function of GLS in patients with HFpEF has become more significant in this prevalent type of HF. In this context, GLS has shown value as a clinical and predictive measure for patients with HFpEF, in addition to being a sensitive measure for identifying minor myocardial anomalies. In this review, we examine the available data about GLS's therapeutic applicability in HFpEF patients and talk about the possible benefits of GLS in this complicated and diverse illness, for which there is now no proven treatment [(5)].

Assessing the prognostic usefulness of left ventricular strain and their correlation with adverse events in patients with HFpEF was the aim of this investigation.

Patients and methods

100 patients with HFpEF who were hospitalized to the Cardiology Department at Benha University Hospital between September 2023 and August 2024 were included in this observational, prospective, cohort single center research.

The patients gave their signed, informed permission. Each subject was given a secret code number and an explanation of the study's objectives. The research was completed after receiving approval from Benha University's Faculty of Medicine's Research Ethics Committee (MS 38-8-2023).

Patients with a diagnosis of HFpEF were required to be included.

Patients with HF with decreased EF, a poor echogenic window, cardiogenic shock, or hemodynamic instability were excluded.

The following procedures were applied to the patients: Complete history taking and clinical assessment: Following standard laboratory testing and electrocardiography (ECG), transthoracic echocardiography, left ventricular (LV) systolic and diastolic function, right ventricular (RV) function, and left ventricular (LV) evaluation were used to evaluate each patient. Ejection fraction (EF) and LV volumes: using echocardiography device (Philips EPIQ 7) modified Simpson's biplane approach was used to assess the left ventricular end-diastolic and end-systolic volumes. The endocardial boundaries were traced at end-diastole and end-systole, and apical four-chamber and two-chamber images were obtained. The following formula was used to determine the LVEF:

$$\text{LVEF}\ (\%) = \frac{\text{LVEDV} - \text{LVESV}}{\text{LVEDV}} \times 100$$

This technique offered a trustworthy evaluation of the LV systolic function as a whole. >50% was the normal LVEF.

For myocardial function, speckle tracking echocardiography (STE) may be performed using either QLAB Advanced Ultrasound Quantification Software (Philips)

Assessment of circumferential strain (CS): For the purpose of analyzing circumferential strain, short-axis images were obtained at the basal, mid, and apical levels. QLAB software was used to autonomously trace the endocardial boundary during end-diastole.

Assessment of the right ventricle (RV):

RV Dimensions: determined using 2D echocardiography at the midventricular level in the apical four-chamber view.

An M-mode cursor is positioned at the lateral tricuspid valve (TV) annulus in the apical four-chamber image to measure tricuspid annular plane systolic excursion (TAPSE).

To determine the peak RV systolic myocardial velocity (S'), Doppler tissue imaging is used.

Evaluation of diastolic function: LV diastolic function is determined by utilizing the mitral annular early diastolic velocity (E/e') ratio as a stand-in for LV filling pressures, tissue Doppler imaging (TDI) of the mitral annulus (e' velocity), left atrial volume index (LAVI), and mitral inflow patterns (E/A ratio). Pulsed-wave Doppler in the apical four-chamber view was used to measure mitral inflow. To assess e' velocity, TDI was done at the septal and lateral mitral annulus. The biplane area-length technique was used to quantify left atrial volume, which was then indexed to body surface area (BSA).

RV diastolic function: using the tricuspid annulus's TDI (e' velocity) and E/A ratio. Pulsed-wave Doppler was used to estimate tricuspid input in the apical four-chamber view, and TDI was used to measure e' velocity at the lateral tricuspid annulus.

Reporting and data analysis: For high-resolution imaging, Philips EPIQ 7, STE-derived strain values were used to quantify and visually evaluate myocardial deformation. Global function was reported using LVEF, GLS, and global circumferential strain for the LV, and TAPSE, S', and RV dimensions for the RV. Diastolic function was graded as normal, impaired relaxation, pseudo-normal, or restrictive based on mitral/tricuspid inflow patterns, TDI, and LAVI

STE analysis: Using QLAB software, automatic border tracing was confirmed and, if need, manually modified. For precise tracking of speckles, frame rates between 50 and 80 fps were kept constant.

Statistical analysis

SPSS v26 was used to do the statistical analysis (IBM Inc., Armonk, NY, USA). Histograms and the Shapiro-Wilks test were used to assess the data distribution's normality. The unpaired student t-test was used to assess quantitative parametric data, which were shown as mean and standard deviation (SD). The Mann Whitney test was used to evaluate quantitative non-parametric data, which were shown as the median and interquartile range (IQR). When applicable, the Chi-square test or Fisher's exact test were used to assess the qualitative data, which were shown as frequency and percentage (%). Statistical significance was defined as a two-tailed P value < 0.05.

Results:

This study carried out on 100 patients with HFpEF who were admitted to the Cardiology Department, Faculty of Medicine, Benha University Hospital. With a mean ± SD of 75.11 ± 4.78 years, the patients in the study varied in age from 66 to 85 years. A total of 67 (67%) females and 33 (33%) men were present. The mean ± SD of the BMI was 28.81 ± 4.12 kg/m2, with a range of 20 to 38 kg/m2. Of the patients, 28 (28%) had diabetes mellitus, 80 (80%) had hypertension (HTN), 14 (14%) had coronary artery disease (CAD), 10 (10%)

had acute coronary syndrome and 5 (5%) had valvular disease repair. CKD was seen in 29 (29%) individuals. Nine (9%) patients experienced a transient ischemic attack, ten (10%) experienced a stroke, nine (9%) experienced peripheral artery disease, five (5%) experienced a pulmonary embolism, sixteen (16%) experienced chronic obstructive pulmonary disease (COPD), seventeen (17%) experienced anemia, and 19 (19%) experienced obstructive sleep apnea (OSA). New York Heart Association (NYHA) classifications I–II were present in 46 (46%) and III–IV in 54 (54%) of the patients. The SBP had a mean ± SD of 153.23 ± 14.8 mmHg and varied between 120 and 180 mmHg. The DBP had a mean ± SD of 76.27 ± 9.1 mmHg and varied between 59 and 94 mmHg. The echocardiographic data of the individuals under study are shown in Tables 1 and 2. TAPSE was normal in 80 (80%) of the patients. With a mean ± SD of -18.89 ± 3.11 percent, the GLS varied from -13 to -23%. The GCS had a mean ± SD of -19.89 ± 3.11 percent and ranged from -14 to -24 percent. Thirty-one occurrences were documented.

Table 1: Demographic data, comorbid data, NYHA classification and blood pressure of the studied patients.

				n=100
Demographic data	**Age (years)**	**Mean ± SD**		75.11 ± 4.78
		Range		66 - 85
	Sex	**Male**		33 (33%)
		Female		67 (67%)
	BMI (kg/m^2)	**Mean ± SD**		28.81 ± 4.12
		Range		20 - 38
Comorbid data		**DM**		28 (28%)
		HTN		80 (80%)
		CAD		14 (14%)
		Acute coronary syndrome		10 (10%)
		Valvular disease repair		5 (5%)
		CKD		29 (29%)
		OSA		19 (19%)
		Pulmonary embolism		5 (5%)
		COPD		16 (16%)
		Anaemia		17 (17%)
		Transient ischemic attack		9 (9%)
		Stroke		10 (10%)
		Peripheral artery disease		9 (9%)
NYHA classification		**I-II**		46 (46%)
		III-IV		54 (54%)
Blood pressure		**SBP (mmHg)**	**Mean ± SD**	153.23 ± 14.8
			Range	120 – 180
		DBP (mmHg)	**Mean ± SD**	76.27 ± 9.1
			Range	59 – 94

Data presents as mean ± SD or frequency (%) . BMI: body mass index, DM: diabetes mellitus, HTN: hypertension, CAD: coronary artery disease, , CKD: chronic kidney disease, OSA: obstructive sleep apnea, COPD: chronic obstructive pulmonary disease, NYHA: New York Heart Association, SBP: systolic blood pressure, DBP: diastolic blood pressure

Table 2: Echocardiographic data, TAPSE, rhythm during echocardiography, strain characteristics and incidence of cardiac adverse events of the studied patients.

			n=100
LVEF (%)	**Mean ± SD**		60.17 ± 5.29
	Range		50 – 70
LVMI (g/m^2)	**Mean ± SD**		79.8 ± 12.41
	Range		50 – 110
LVESD (mm)	**Mean ± SD**		31.8 ± 2.86
	Range		25.7 - 40.2
LVEDD (mm)	**Mean ± SD**		47.91 ± 3.44
	Range		38.9 - 57.2
LA volume index (mL/m^2)	**Mean ± SD**		48.97 ± 10.62
	Range		31 – 70
E-wave peak velocity (cm/s)	**Mean ± SD**		85.56 ± 17.07
	Range		53.1 - 121.9
A-wave peak velocity (cm/s)	**Mean ± SD**		78.16 ± 16.94
	Range		44.1 - 114.9
Lateral e′ (cm/s)	**Mean ± SD**		8.66 ± 2.06
	Range		5.1 - 11.8
Septal e′ (cm/s)	**Mean ± SD**		6.78 ± 2.09
	Range		2.1 - 10.7
E/A ratio	**Mean ± SD**		1.1 ± 0.03
	Range		1.05 - 1.2
E/e′ average	**Mean ± SD**		11.56 ± 3.66
	Range		5.71 - 29.39
Tricuspid insufficiency (m/s)	**Mean ± SD**		2.7 ± 0.44
	Range		2 - 3.7
Estimated RV systolic pressure (mmHg)	**Mean ± SD**		33.47 ± 11.06
	Range		17 – 60
tricuspid annular plane systolic excursion(TAPSE)	**Normal**		80 (80%)
	Abnormal		20 (20%)
Strain characteristics	**GLS (%)**	**Mean ± SD**	-18.89 ± 3.11
		Range	-23 - -13
	GCS (%)	**Mean ± SD**	-19.89 ± 3.11
		Range	-24 - -14
Cardiac adverse events			31 (31%)

Data presents as mean ± SD or frequency (%) .): tricuspid annular plane systolic excursion, , GLS: global longitudinal strain, GCS: global circumferential strain

According to the occurrence of adverse events, there was no significant difference in age, sex, or BMI. In comparison to event-free HFpEF patients, HFpEF patients with an event had a substantially reduced prevalence of HTN (P value = 0.040) and a greater prevalence of DM and acute coronary syndrome (P values = 0.038 and 0.005, respectively). According to the incidence of adverse events, there was no significant difference between CAD, valvular disease repair, CKD, OSA, pulmonary embolism, COPD, anemia, transient ischemic attack, stroke, and peripheral artery disease. The occurrence of adverse events did not appreciably alter the NYHA classification. SBP was considerably lower in HFpEF patients who had an incident (P value = 0.003) than in those who did not, while DBP did not alter significantly based on the occurrence of adverse events. Echocardiographic data is shown by adverse event occurrence in Tables 3 and 4. Compared to event-free HFpEF patients, HFpEF patients with an event had significantly lower E/A ratios (P value =0.002) and significantly higher tricuspid insufficiency, LVMI, E-wave

peak velocity, A-wave peak velocity, and estimated RV systolic pressure (P values =0.028, <0.001, <0.001, <0.001, and 0.003 respectively). The occurrence of adverse events did not substantially alter the LVEF, LVESD, LVEDD, LA volume index, lateral e′, septal e′, or E/e′ average. The incidence of adverse events showed no significant difference in TAPSE.

Table 5 displays strain characteristics based on the occurrence of adverse events. GLS and GCS were considerably poorer in HFpEF patients with an incident than in those without an event (P value <0.001). For detecting adverse events in HFpEF patients, both GLS (> -19%) and GCS (> -20%) demonstrated flawless diagnostic performance (AUC = 1.000, sensitivity = 100%, specificity = 100%). Excellent predictive accuracy was shown by the 100% PPV and NPV (P < 0.001).

Table 3: Demographic data, comorbid data, NYHA classification and blood pressure according to adverse events incidence.

			Event free (n=69)	Event (n=31)	P value
Demographic data	**Age (years)**	**Mean ± SD**	74.62 ± 4.82	76.19 ± 4.56	0.129
		Range	66 - 84	68 - 85	
	Sex	**Male**	20 (28.99%)	13 (41.94%)	0.203
		Female	49 (71.01%)	18 (58.06%)	
	BMI (kg/m^2)	**Mean ± SD**	28.49 ± 4.1	29.52 ± 4.14	0.252
		Range	20 - 36	22 - 38	
Comorbid data		**DM**	15 (21.74%)	13 (41.94%)	**0.038***
		HTN	59 (85.51%)	21 (67.74%)	**0.040***
		CAD	8 (11.59%)	6 (19.35%)	0.301
		Acute coronary syndrome	3 (4.35%)	7 (22.58%)	**0.005***
		Valvular disease repair	3 (4.35%)	2 (6.45%)	0.644
		CKD	18 (26.09%)	11 (35.48%)	0.338
		OSA	13 (18.84%)	6 (19.35%)	0.952
		Pulmonary embolism	4 (5.8%)	1 (3.23%)	1.000
		COPD	8 (11.59%)	8 (25.81%)	0.073
		Anaemia	9 (13.04%)	8 (25.81%)	0.116
		Transient ischemic attack	6 (8.7%)	3 (9.68%)	1.000
		Stroke	6 (8.7%)	4 (12.9%)	0.495
		Peripheral artery disease	5 (7.25%)	4 (12.9%)	0.453
NYHA classification		**I-II**	36 (52.17%)	10 (32.26%)	0.065
		III-IV	33 (47.83%)	21 (67.74%)	
Blood pressure	**SBP (mmHg)**	**Mean ± SD**	156.13 ± 13.75	146.77 ± 15.22	**0.003***
		Range	133 - 180	120 - 175	
	DBP (mmHg)	**Mean ± SD**	77.33 ± 9.07	73.9 ± 8.83	0.081
		Range	60 - 94	59 - 90	

Data presents as mean ± SD or frequency (%) . BMI: body mass index, DM: diabetes mellitus, HTN: hypertension, CAD: coronary artery disease, CKD: chronic kidney disease, OSA: obstructive sleep apnea, COPD: chronic obstructive pulmonary disease, *: significant as P value ≤ 0.05, NYHA: New York Heart Association, SBP: systolic blood pressure, DBP: diastolic blood pressure.

Table 4: Echocardiographic data, TAPSE and strain characteristics according to adverse events incidence.

			Event free (n=69)	Event (n=31)	P value
LVEF (%)		**Mean ± SD**	60.65 ± 5.24	59.1 ± 5.33	0.175
		Range	50 - 70	50 - 69	
LVMI (g/m^2)		**Mean ± SD**	77.99 ± 11.1	83.84 ± 14.3	**0.028***
		Range	59 - 100	50 - 110	
LVESD (mm)		**Mean ± SD**	31.61 ± 2.32	32.2 ± 3.8	0.346
		Range	27.5 - 35.6	25.7 - 40.2	
LVEDD (mm)		**Mean ± SD**	47.7 ± 2.32	48.38 ± 5.15	0.360
		Range	43.5 - 52.3	38.9 - 57.2	
LA volume index (mL/m^2)		**Mean ± SD**	48.3 ± 11.01	50.45 ± 9.71	0.352
		Range	31 - 70	36 - 68	
E-wave peak velocity (cm/s)		**Mean ± SD**	81.29 ± 16.27	95.07 ± 15.06	**<0.001***
		Range	53.1 - 111.7	63.3 - 121.9	
A-wave peak velocity (cm/s)		**Mean ± SD**	73.79 ± 15.97	87.87 ± 15.08	**<0.001***
		Range	44.1 - 102.7	55.3 - 114.9	
Lateral e′ (cm/s)		**Mean ± SD**	8.56 ± 2.09	8.88 ± 1.99	0.474
		Range	5.1 - 11.8	5.6 - 11.7	
Septal e′ (cm/s)		**Mean ± SD**	6.69 ± 2.2	6.98 ± 1.83	0.520
		Range	2.1 - 10.6	3.9 - 10.7	
E/A ratio		**Mean ± SD**	1.11 ± 0.04	1.08 ± 0.02	**0.002***
		Range	1.05 - 1.2	1.05 - 1.14	
E/e′ average		**Mean ± SD**	11.22 ± 3.9	12.33 ± 2.95	0.160
		Range	5.71 - 29.39	7.45 - 17.72	
Tricuspid insufficiency (m/s)		**Mean ± SD**	2.59 ± 0.39	2.95 ± 0.45	**<0.001***
		Range	2 - 3.2	2.3 - 3.7	
Estimated RV systolic pressure (mmHg)		**Mean ± SD**	31.29 ± 9.52	38.32 ± 12.77	**0.003***
		Range	17 - 48	21 - 60	
TAPSE		**Normal**	58 (84.06%)	22 (70.97%)	0.130
		Abnormal	11 (15.94%)	9 (29.03%)	
Strain characteristics	**GLS (%)**	**Mean ± SD**	-20.81 ± 1.2	-14.63 ± 1.23	**<0.001***
		Range	-23 - -19	-17 - -13	
	GCS (%)	**Mean ± SD**	-21.81 ± 1.2	-15.63 ± 1.23	**<0.001***
		Range	-24 - -20	-18 - -14	

Data presents as mean ± SD or frequency (%) . LVEF: left ventricular ejection fraction, LVMI: left ventricular mass index, LVESD: left ventricular end-systolic diameter, LVEDD: left ventricular end-diastolic diameter, LA: left atrial, RV: right ventricular, TAPSE: tricuspid annular plane systolic excursion *: significant as P value ≤ 0.05

Table 5: Strain characteristics according to adverse events incidence and ROC curve analysis of GLS and GCS for adverse events identification.

		Event free (n=69)	Event (n=31)	Cut-off	AUC	Sensitivity	specificity	PPV	NPV	P value
GLS (%)	**Mean ± SD**	-20.81 ± 1.2	-14.63 ± 1.23	>-19	1.000	100	100	100	100	**<0.001***
	Range	-23 - -19	-17 - -13							
GCS (%)	**Mean ± SD**	-21.81 ± 1.2	-15.63 ± 1.23	>-20	1.000	100	100	100	100	**<0.001***
	Range	-24 - -20	-18 - -14							

GLS: global longitudinal strain, GCS: global circumferential strain, *: significant as P value ≤ 0.05GLS, HFpEF: heart failure with preserved ejection fraction, AUC: area under the curve, PPV: positive predictive value, NPV: negative predictive value, *: significant as P value ≤ 0.05

Discussion:

Of individuals with clinical heart failure, around half have heart failure with preserved ejection fraction (HFpEF). Following the first hospital stay, mortality rates may reach 43%, which is comparable to those of patients with heart failure with reduced ejection fraction (HFrEF) [6].

to determine LV contractile function, 2D speckle-tracking echocardiography has become a more objective and sensitive modality than LVEF for assessing myocardial deformation. It may also be a helpful tool for the HFpEF population. Research looking into surrogate indicators of HF severity in the chronic, ambulatory HFpEF population revealed that abnormal LV GLS was linked to higher levels of natriuretic peptides and lower peak oxygen consumption (VO2), while impaired regional LV strain was linked to worse Duke Activity Status Index scores [8].

GLS has been shown to be a possible predictor of HF-related hospitalizations and cardiovascular (CV) mortality in individuals with chronic HFpEF [9].

In this study we focus on left ventricular strain and its relation with adverse events in patients with HFpEF. 3 months periodic follow up were included assessment of clinical variables including mortality and re-hospitalization.

The motivation for evaluating the usefulness of LV GLS in HFpEF is provided by the complex pathophysiology of acute HFpEF, inadequate stratification methods, and a dearth of effective treatments. Patients with acute HFpEF who were hospitalized and clinically needed diuretic medication were identified in this research [10].

The patients in our research had an average age of 75.11 ± 4.78 years. A total of 67 (67%) females and 33 (33%) men were present. The mean ± SD of the BMI was 28.81 ± 4.12 kg/m2. Which is consistent with a study conducted by Kerstens et al., in which The patients under study were 75.8 ± 6.94 years old on average. The mean BMI of the 170 (72.3%) females and 65 (27.7%) men was 29.9 ± 5.42 [7].

In our study about 28 (28%) patients had DM, 80 (80%) patients had HTN, 14 (14%) patients had CAD, 29 (29%) patients had CKD, 5 (5%) patients had pulmonary embolism and 16 (16%) patients had COPD.

In a study conducted with Buggey et al., which studied Left ventricular global longitudinal strain in patients with heart failure with preserved ejection fraction showed that 67 (60.4%) patients had DM, 105 (94.4%) patients had HTN, 68 (61.3%) patients had CAD, 61 (55%) patients had CKD, 25 (22%) patients had COPD. These findings are not consistent with that of our study [15]

Of the patients, about 46 (46%) had NYHA classification I–II, and 54 (54%) had NYHA classification III–IV. A finding consistent with Kerstens et al., which showed that around 111 patients (47.2%) had NYHA classification I–II, and 124 patients (52.8%) had NYHA classification III–IV[7].

In our study the LVEF had a mean ± SD of 60.17 ± 5.29 percent. The mean ± SD of the LVMI was 79.8 ± 12.41 g/m2. the mean ± SD values for the LVESD and LVEDD were 31.8 ± 2.86 mm and 47.91 ± 3.44 mm respectively. the mean ± SD of the LA volume index 48.97 ± 10.62 mL/m².

A findings consistent with a study conducted with Kerstens et al., The mean LVEF was 60.0 ± 7.06, the mean was LVMI was 80.3 ± 19.4, and the mean LVESD and LVEDD were 31.9 ± 4.31 and 47.2 ± 5.35, respectively [7]. 47.3 was the LA volume index (37.8–58.8) [7].

Research has shown that HFpEF patients who have negative outcomes, such hospitalization or death, have lower GLS and GCS values than those who don't have any events. For example, studies show that patients with HFpEF often have impaired GLS, which is linked to higher levels of indicators of cardiac stress and fibrosis, highlighting its prognostic

significance. According to these results, individuals with HFpEF are more likely to have adverse events if they have underlying myocardial dysfunction, which is indicated by decreased GLS and GCS [11].

Prior prognostic studies in HFpEF examined systolic function in connection to adverse outcomes in addition to diastolic indicators [8, 12]. In a study conducted by Kerstens et al., peak strain was not substantially linked to long-term adverse outcomes after accounting for various variables[7]. These results are consistent with some, but not all, of the earlier research [8, 10, 13, 14]. The variation in research procedures might be one reason for these contradictory results.

GLS throughout hospitalization, whereas the studies showing a correlation measured strain when acute heart failure patients were admitted. According to [15], individuals hospitalized for HF are more likely to have adverse effects in the future than stable ambulant patients, and strain may be more compromised during the acute episode than when HF is stable.

This might be one of the reasons why research vary from one another. While previous studies focused on readmission or change in EF with strain as a continuous variable [10, 14]. According to [13] was the only one to incorporate mortality, albeit with a predetermined cut-off value for impaired strain.

Compared to event-free HFpEF patients, HFpEF patients with an event had significantly lower E/A ratios (P value =0.002) and significantly higher tricuspid insufficiency, LVMI, E-wave peak velocity, A-wave peak velocity, and estimated RV systolic pressure (P values =0.028, <0.001, <0.001, <0.001, and 0.003 respectively) .[7] revealed that throughout the course of 2.9 (1.75–4.11) years of follow-up, a total of 73 events—that is, 39 HF hospitalizations (53%) and 34 deaths (47%).

Nakagawa et al., found that early diastolic characteristics, including E/e′, were linked to worse outcomes in HFpEF[16].

Mechanistically speaking, research analyzing diastolic function usually measured cardiac relaxation [e.g. LV stiffness (e.g. LV late diastolic pressures or deceleration time) and LV systolic pressure decline or mitral annulus early diastolic velocity (e′)] [17].

It is known that HFpEF affects LV stiffness, which is often assessed late in diastole [18]. A protracted LV pressure decline in HFpEF was shown in earlier research to highlight the significance of early diastole and LV relaxation. Furthermore, it was shown that early diastole echocardiographic indicators were a strong predictor of HFpEF diagnosis [12, 18].

Furthermore, our findings imply that clinical development in individuals with HFpEF is influenced by anomalies in cardiac dynamics during early diastole, which may be connected to LV relaxation and, in turn, LV filling. These changed cardiac dynamics may be caused by structural alterations (such as myocardial fibrosis and steatosis), altered titin phosphorylation, altered calcium hemostasis, inflammation, and/or mitochondrial function.

For detecting adverse events in HFpEF patients, both GLS (> -19%) and GCS (> -20%) demonstrated flawless diagnostic performance (AUC = 1.000, sensitivity = 100%, specificity = 100%). Excellent predictive accuracy was shown by the 100% PPV and NPV (P < 0.001).

Shinzato et al., showed that GLS and GCS have become essential instruments for the non-invasive diagnosis and classification of HFpEF, holding up the possibility of customized treatment plans. Notwithstanding their promise, it is essential to integrate these biomarkers into conventional diagnostic procedures in an organized manner [6].

However, there is little information on biomarkers, clinical, or echocardiographic

factors that could indicate worse short-term post-discharge outcomes. Additionally, the majority of research on the correlation between HFpEF echocardiographic factors and clinical outcomes has focused on diastolic dysfunction measurements in chronic HFpEF patients [19–22].

Therefore, LV GLS may be a new tool for identifying high-risk individuals with distinct cardiac pathophysiology for possible therapies before discharge. It may be used to identify a subgroup of acute HFpEF patients with poorer short-term outcomes, regardless of diastolic dysfunction.

In contrast to earlier research that demonstrated LV GLS to be a significant predictor of clinical outcomes like death or hospitalizations in individuals with chronic HFpEF, the association between LV GLS and these outcomes was no longer statistically significant after one year [13, 23-25].

Regarding the whole time of follow-up in our study, a total of 31 events (31%) were recorded including: i.e. 24 HF hospitalizations (77.4%) and 7 deaths (22.6%)

In a study conducted by Yixia Lin et al., which evaluate the Prognostic Value of LV Global Longitudinal Strain by Speckle-Tracking Echocardiography in Patients With HFpEF showed that After a median follow-up of 17.6 months, 150 patients experienced adverse outcomes (44.77%) [30].

Shah et al. discovered that in 447 chronic patients, abnormal LV longitudinal strain was a predictor of both CV death and a composite of HF hospitalizations, CV death, or aborted cardiac arrest. After adjusting for this, they discovered a correlation between higher LV GLS and mortality rates 30 days after discharge [13]. Even up to five years after discharge, death rates after hospitalization for acute HFpEF are reported to be comparable to those for HFrEF [26-28].

LV GLS was linked to higher mortality (HR 1.19 per 1% increase; 95% CI 1.00–1.42; P = 0.046) and a nominal increase in the composite endpoint of mortality or rehospitalization at 30 days (HR 1.08 per 1% increase; 95% CI 0.99–1.18; P = 0.08), according to [29]'s findings. Mortality (HR 1.02 per 1% increase; 95% CI: 0.96–1.08; P = 0.56) and a composite of mortality or rehospitalization (HR 1.03 per 1% increase; 95% CI: 0.98–1.08; P = 0.20) at 1 year did not statistically significantly correlate with LV GLS.

Conclusion:

Left ventricular global longitudinal strain (GLS) and Global circumferential strain (GCS) are important markers of myocardial dysfunction. GLS and GCS showed perfect diagnostic performance for identifying adverse events in HFpEF patients including mortality or HF hospitalization with high positive and negative predictive value.

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Conflicts of interest

No conflicts of interest

References

1. Savarese G, Becher PM, Lund LH, Seferovic P, Rosano GMC, Coats AJS. Global burden of heart failure: a comprehensive and updated review of epidemiology. Cardiovasc Res. 2023;118(17):3272-87.
2. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. Corrigendum to: 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2021;42(48):49-55.
3. Shah SJ, Borlaug BA, Kitzman DW, McCulloch AD, Blaxall BC, Agarwal R, et al. Research Priorities for Heart Failure With Preserved Ejection Fraction. Circulation. 2020;141(12):1001-26.

4. Smiseth OA, Morris DA, Cardim N, Cikes M, Delgado V, Donal E, et al. Multimodality imaging in patients with heart failure and preserved ejection fraction: an expert consensus document of the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2022;23(2):34-61.
5. Kosmala W, Sanders P, Marwick TH. Subclinical Myocardial Impairment in Metabolic Diseases. JACC Cardiovasc Imaging. 2017;10(6):692-9.
6. Shinzato MH, Santos N, Nishida G, Moriya H, Assef J, Feres F, et al. Left ventricular and atrial myocardial strain in heart failure with preserved ejection fraction: the evidence so far and prospects for phenotyping strategy. Cardiovascular Ultrasound. 2024;22(1):4.
7. Kerstens TP, Weerts J, van Dijk AP, Weijers G, Knackstedt C, Eijsvogels TM, et al. Association of left ventricular strain–volume loop characteristics with adverse events in patients with heart failure with preserved ejection fraction. European Heart Journal-Cardiovascular Imaging. 2023;24(9):1168-76.
8. Shahim A, Hourqueig M, Donal E, Oger E, Venkateshvaran A, Daubert JC, et al. Predictors of long-term outcome in heart failure with preserved ejection fraction: a follow-up from the KaRen study. ESC heart failure. 2021;8(5):4243-54.
9. Kleinnibbelink G, van Dijk AP, Fornasiero A, Speretta GF, Johnson C, Sculthorpe N, et al. Acute exercise-induced changes in cardiac function relates to right ventricular remodeling following 12-wk hypoxic exercise training. Journal of Applied Physiology. 2021;131(2):511-9.
10. Park JJ, Mebazaa A, Hwang IC, Park JB, Park JH, Cho GY. Phenotyping heart failure according to the longitudinal ejection fraction change: myocardial strain, predictors, and outcomes. Journal of the American Heart Association. 2020;9(12):e015009.
11. DeVore AD, McNulty S, Alenezi F, Ersboll M, Vader JM, Oh JK, et al. Impaired left ventricular global longitudinal strain in patients with heart failure with preserved ejection fraction: insights from the RELAX trial. European journal of heart failure. 2017;19(7):893-900.
12. Ma C, Luo H, Fan L, Liu X, Gao C. Heart failure with preserved ejection fraction: an update on pathophysiology, diagnosis, treatment, and prognosis. Braz J Med Biol Res. 2020;53(7):11-22.
13. Shah AM, Claggett B, Sweitzer NK, Shah SJ, Anand IS, Liu L, et al. Prognostic importance of impaired systolic function in heart failure with preserved ejection fraction and the impact of spironolactone. Circulation. 2015;132(5):402-14.
14. Romano S, Mansour IN, Kansal M, Gheith H, Dowdy Z, Dickens CA, et al. Left ventricular global longitudinal strain predicts heart failure readmission in acute decompensated heart failure. Cardiovascular ultrasound. 2017;15:1-6.
15. Buggey J, Alenezi F, Yoon HJ, Phelan M, DeVore AD, Khouri MG, et al. Left ventricular global longitudinal strain in patients with heart failure with preserved ejection fraction: outcomes following an acute heart failure hospitalization. ESC Heart Fail. 2017;4(4):432-9.
16. Nakagawa A, Yasumura Y, Yoshida C, Okumura T, Tateishi J, Yoshida J, et al. Predictors and outcomes of heart failure with preserved ejection fraction in patients with a left ventricular ejection fraction above or below 60%. Journal of the American Heart Association. 2022;11(15):e025300.
17. Nagueh SF. Left ventricular diastolic function: understanding pathophysiology, diagnosis, and prognosis with echocardiography. JACC: Cardiovascular Imaging. 2020;13(1 Part 2):228-44.
18. Pfeffer MA, Shah AM, Borlaug BA. Heart failure with preserved ejection fraction in perspective. Circulation research. 2019;124(11):1598-617.
19. Persson H, Lonn E, Edner M, Baruch L, Lang CC, Morton JJ, et al. Diastolic dysfunction in heart failure with preserved systolic function: need for objective evidence: results from the CHARM Echocardiographic Substudy–CHARMES. Journal of the American College of Cardiology. 2007;49(6):687-94.
20. Ohtani T, Mohammed SF, Yamamoto K, Dunlay SM, Weston SA, Sakata Y, et al. Diastolic stiffness as assessed by diastolic wall strain is associated with adverse remodelling and poor outcomes in heart failure with preserved ejection fraction. European heart journal. 2012;33(14):1742-9.
21. Zile MR, Gottdiener JS, Hetzel SJ, McMurray JJ, Komajda M, McKelvie R, et al. Prevalence and significance of alterations in cardiac structure and function in patients with heart failure and a preserved ejection fraction. Circulation. 2011;124(23):2491-501.
22. Rossi A, Cicoira M, Florea VG, Golia G, Florea ND, Khan AA, et al. Chronic heart failure with preserved left ventricular ejection fraction: diagnostic and prognostic value of left atrial size. International journal of cardiology. 2006;110(3):386-92.
23. Wang J, Fang F, Yip GW-K, Sanderson JE, Feng W, Xie J-M, et al. Left ventricular long-axis performance during exercise is an

important prognosticator in patients with heart failure and preserved ejection fraction. International Journal of Cardiology. 2015;178:131-5.
24. Pellicori P, Kallvikbacka-Bennett A, Khaleva O, Carubelli V, Costanzo P, Castiello T, et al. Global longitudinal strain in patients with suspected heart failure and a normal ejection fraction: does it improve diagnosis and risk stratification? The international journal of cardiovascular imaging. 2014;30:69-79.
25. Stampehl MR, Mann DL, Nguyen JS, Cota F, Colmenares C, Dokainish H. Speckle strain echocardiography predicts outcome in patients with heart failure with both depressed and preserved left ventricular ejection fraction. Echocardiography. 2015;32(1):71-8.
26. Toma M, Ezekowitz JA, Bakal JA, O'Connor CM, Hernandez AF, Sardar MR, et al. The relationship between left ventricular ejection fraction and mortality in patients with acute heart failure: insights from the ASCEND-HF T rial. European journal of heart failure. 2014;16(3):334-41.
27. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. New England Journal of Medicine. 2006;355(3):251-9.
28. Tribouilloy C, Rusinaru D, Mahjoub H, Souliere V, Levy F, Peltier M, et al. Prognosis of heart failure with preserved ejection fraction: a 5 year prospective population-based study. European heart journal. 2008;29(3):339-47.
29. Buggey J, Alenezi F, Yoon HJ, Phelan M, DeVore AD, Khouri MG, et al. Left ventricular global longitudinal strain in patients with heart failure with preserved ejection fraction: outcomes following an acute heart failure hospitalization. ESC heart failure. 2017;4(4):432-9.
30. Yixia Lin, Mingxing Xie, Li Zhang, , Yanting Zhang, Peige Zhang , Xin Chen, et al. Prognostic Value of LV Global Longitudinal Strain by 2D and 3D Speckle-Tracking Echocardiography in Patients With HFpEF. American Heart Association Journal. 2025;18(2): e016975.

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