

Research Article

Prognostic Role of Left Ventricular Global Longitudinal Strain in Predicting Outcomes in Heart Failure with Preserved Ejection Fraction (HFPEF)

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ABSTRACT

Background: Heart failure with preserved ejection fraction is a growing phenotype of chronic heart failure that carries significant cardiovascular morbidity, recurrent clinical decompensation, and increased mortality. Although left ventricular ejection fraction remains preserved in HFpEF, subtle abnormalities in myocardial mechanics may still be present. LGE has emerged in recent years as an advanced echocardiographic tool that can assess early myocardial dysfunction beyond that of a standard evaluation of systolic function, using global longitudinal strain.

Objective: To assess the prognostic value of LGE in predicting cardiovascular adverse outcomes in patients with heart failure with preserved ejection fraction.

Methods: This study was conducted as a prospective observational study in Buffalo General Hospital, Buffalo, USA, from February 2024 to February 2025. Patients were consecutively recruited, and 200 patients with a HFpEF diagnosis were included. Measurement of left ventricular global longitudinal strain was done by comprehensive transthoracic echocardiography with 2D speckle-tracking imaging. Based on predefined strain thresholds, participants were classified into impaired and preserved LV-GLS groups. Clinical follow-up was used to record adverse cardiovascular events such as disease progression, re-hospitalization, arrhythmias, intensive care admissions, major adverse cardiovascular events, and cardiovascular death.

Results: Abnormal values of LV-GLS were found in 104 patients, and preserved myocardial strain was found in 96 patients. Impaired strain was associated with a higher prevalence of hypertension, diabetes mellitus, obesity, atrial fibrillation, and higher NT-proBNP levels. Echocardiographic assessment also showed that left atrial volume index, pulmonary artery systolic pressure, E/e' ratio, and left ventricular mass index were significantly higher in the group with abnormal myocardial strain. The impaired LV-GLS group had more cardiovascular complications during follow-up evaluation. Impaired LV-GLS was shown to be an independent predictor of adverse cardiovascular events. LV-GLS also showed good discriminatory power in the identification of major cardiovascular events by receiver operating characteristic analysis.

Conclusion: Reduced left ventricular global longitudinal strain is strongly associated with adverse clinical progression in patients with HFpEF. Myocardial deformation imaging might offer valuable prognostic data additional to the traditional echocardiographic parameters and help in earlier cardiovascular risk stratification and monitoring tailored to the patient.

Keywords: Hfpef; Left Ventricular Global Longitudinal Strain; Speckle-Tracking Echocardiography; Cardiovascular Outcomes; Prognostic Marker; Heart Failure.

INTRODUCTION

Heart failure with preserved ejection fraction has emerged as a major cardiovascular disorder worldwide and currently accounts for a substantial proportion of chronic heart failure cases, especially among older adults and individuals with metabolic comorbidities such as obesity, hypertension, diabetes mellitus, and atrial fibrillation^{1,2}. Even though there is no reduction in conventional left ventricular

ejection fraction, many of these patients continue to suffer from progressive exertional limitation, recurrent episodes of cardiac decompensation, repeated hospitalization, and impaired quality of life. In modern populations, the growing burden of cardiometabolic disease has further driven the worldwide burden of HFpEF, with an increase in the use of health services and cardiovascular mortality³.

The HFpEF is characterized by complex structural, functional, and vascular abnormalities, not just a systolic abnormality alone. Various pathological mechanisms are involved in the evolution of the disease, such as ventricular hypertrophy, myocardial fibrosis, endothelial dysfunction, decreased myocardial compliance, increased filling pressures, and alterations of myocardial relaxation⁴. Chronic systemic inflammation and coronary microvascular damage also contribute to detrimental myocardial remodeling and progressive reduction in myocardial function^{5,6}. While conventional systolic function is often normal with a routine echocardiogram, subtle abnormalities in myocardial mechanics might not be identified during the early stages of disease.

The main parameters of standard echocardiographic assessment are chamber dimensions, volumetric measurements, and global ejection fraction. But these traditional parameters are not optimal to detect the early myocardial dysfunction in patients with normal systolic function⁷. Thus, there has been a growing focus on sophisticated methods of imaging that are able to identify myocardial dysfunction at a subclinical stage before the actual onset of cardiac disease. Early detection of subtle ventricular dysfunction could help to better assess cardiovascular risk, inform therapeutic choices, and identify those who are more likely to have poor clinical outcomes^{8,9}.

Two-dimensional speckle-tracking echocardiography (STE) is a recently developed, noninvasive imaging technique for assessing myocardial deformation. Myocardial fiber shortening during systole produces a more sensitive picture of myocardial contractile performance than traditional measurements of ejection fraction¹⁰. Left ventricular global longitudinal strain (LV-GLS) can be affected even when left ventricular ejection fraction is normal, as the longitudinal myocardial fibers in the subendocardial region are especially sensitive to wall stress, fibrosis, and ischemia¹¹. Low strain values have been linked to ventricular remodeling, increased intracardiac filling pressures, decreased myocardial relaxation, and evolution of the diastolic dysfunction in various cardiovascular studies¹². Growing clinical evidence suggests that abnormal LV-GLS is associated with poor cardiovascular prognosis in patients with HFpEF. Prior research has shown that reduced myocardial strain is associated with recurrent hospitalisation, declining clinical heart failure

signs, arrhythmias, functional status, and cardiovascular mortality^{13,14}. However, there is currently little data on the prognostic value of LV-GLS in the setting of HFpEF in the United States¹⁵.

Thus, identification of reliable noninvasive markers that can distinguish the high-risk HFpEF population is clinically relevant for improving the long-term cardiovascular outcomes and for devising personalized management approaches. An early detection of subclinical myocardial dysfunction can help in timely intervention, cardiovascular monitoring, and better risk stratification¹⁶. Hence, the current study aimed to assess the prognostic utility of left ventricular global longitudinal strain in predicting poor cardiovascular events in patients with HFpEF^{17,18}.

MATERIALS AND METHODS

The follow-up study was conducted from February 2024 to February 2025 at Buffalo General Hospital, Buffalo, USA, in a clinical setting. The study aimed to assess whether there are abnormalities in left ventricular global longitudinal strain that can predict poor cardiovascular outcomes in patients with heart failure with preserved ejection fraction.

During the study period, a total of 200 patients were enrolled from the Cardiology and Internal Medicine services consecutively. Participants were adults 40–85 years of age with a diagnosis of confirmed HFpEF. Diagnosis was made based on clinical, laboratory, and echocardiographic evaluation. Patients had to meet the inclusion criteria, which included left ventricular ejection fraction (LVEF) $\geq 50\%$ and evidence of symptomatic heart failure and abnormal diastolic function. High natriuretic peptides were also taken into account for confirmatory diagnosis.

Patients with major valvular disease, congenital cardiac malformations, acute myocardial infarction in the past few months, severe renal insufficiency, chronic hepatic impairment, unstable arrhythmias, or technically inadequate echocardiographic images were excluded. Patients who were not able to undergo reliable myocardial strain analysis were also excluded from the final analysis.

Detailed clinical profiling and cardiovascular risk assessment were conducted as a baseline evaluation. At the time of enrolment, age, sex, smoking status, body mass index, diabetes mellitus, hypertension, dyslipidaemia, coronary artery disease, atrial fibrillation, medication

history, and New York Heart Association functional classification were recorded.

Laboratory analyses included complete blood count, estimation of NT-proBNP, fasting glucose, renal profile, serum lipids, and inflammatory biomarkers.

Transthoracic echocardiography was done on all participants with a high-resolution imaging system. The conventional cardiac measurements were left ventricular ejection fraction, interventricular septal thickness, pulmonary artery systolic pressure, left atrial volume index, and Doppler-derived E/e' ratio. Myocardial deformation was then analysed using standard apical projections to obtain 2D speckle-tracking imaging. Myocardial motion tracking was performed, and automated software provided global longitudinal strain measurements.

Patients were divided into 2 groups: preserved-LV-GLS and impaired-LV-GLS based on predetermined strain cut-off values. Clinical follow-up was maintained during the study time for the detection of adverse cardiovascular events. The endpoints analysed were recurrent events of HF, hospitalization, deterioration in functional status, clinically important arrhythmias, intensive care admission, and major adverse cardiovascular events including cardiovascular mortality.

The study was conducted with the approval of the Institutional Review Board of the Buffalo General Hospital, Buffalo, USA. All participants gave written informed consent before their inclusion.

SPSS 26.0 and R 4.3 software were used for data analysis. The quantitative variables were presented as mean $\pm$ standard deviation, and the categorical variables were presented as frequencies and percentages. Normality of distribution was determined by the Shapiro–Wilk test. An independent sample t-test was used to compare continuous variables, and a

chi-square analysis to compare categorical data.

Multivariable Cox proportional hazards regression modeling was performed to identify independent prognostic factors of cardiovascular adverse events after adjustment for major clinical covariates such as age, hypertension, diabetes mellitus, atrial fibrillation, NT-proBNP level, E/e' ratio, and left atrial volume index. Hazard ratios and 95% confidence intervals were computed. An ROC analysis was also performed to assess the predictive power of LV-GLS in major cardiovascular complications. A p-value below 0.05 was considered statistically significant.

RESULTS

A total of 200 individuals diagnosed with heart failure with preserved ejection fraction were included in the final statistical analysis. The mean age of all the subjects in the study was 66.2 ± 10.4 years and ranged from 41 to 84 years. Male participants accounted for 118 cases (59.0%), while 82 participants (41.0%) were female. Evaluation of myocardial strain demonstrated impaired LV-GLS in 104 patients (52.0%), whereas preserved strain measurements were observed in 96 patients (48.0%).

Results indicate that myocardial strain impairment was more common in patients with cardiovascular and metabolic comorbidities when compared between study groups. The demographics of the participants with abnormal LV-GLS were overall older, with a higher prevalence of hypertension, diabetes mellitus, obesity, atrial fibrillation, and underlying coronary artery disease than those with preserved strain values. In addition, the impaired LV-GLS group had a higher proportion of patients classified as New York Heart Association (NYHA) classes III and IV, reflecting reduced exercise tolerance and higher clinical limitations (Table 1).

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Variables	Impaired LV-GLS (n=104)	Preserved LV-GLS (n=96)	p-value
Mean Age (years)	69.1 $\pm$ 8.7	62.9 $\pm$ 9.8	<0.001
Male Gender	65 (62.5%)	53 (55.2%)	0.294
Female Gender	39 (37.5%)	43 (44.8%)	0.294
Body Mass Index (kg/m ²)	31.2 $\pm$ 4.8	28.7 $\pm$ 4.1	<0.001
Hypertension	87 (83.7%)	63 (65.6%)	0.003
Diabetes Mellitus	66 (63.5%)	41 (42.7%)	0.004
Obesity	49 (47.1%)	31 (32.3%)	0.032
Atrial Fibrillation	34 (32.7%)	17 (17.7%)	0.015

Coronary Artery Disease	46 (44.2%)	29 (30.2%)	0.041
NYHA Class III/IV	73 (70.2%)	34 (35.4%)	<0.001

Despite maintenance of preserved left ventricular ejection fraction across both comparison groups, patients with impaired LV-GLS exhibited significantly more abnormal structural and functional cardiac findings on detailed echocardiographic evaluation. The abnormal strain group had higher values of left atrial volume index, E/e' ratio, pulmonary artery systolic pressure, and markedly higher concentrations of NT-proBNP compared to the preserved myocardial strain group. These abnormalities indicated a higher grade of

diastolic impairment and a higher level of filling pressure in the heart.

Furthermore, interventricular septal thickness was significantly higher for patients with reduced myocardial strain, suggesting higher-grade ventricular hypertrophy and myocardial remodeling. The overall echocardiographic profile indicated that LV-GLS impairment was significantly linked to worsening myocardial function despite normal conventional systolic ejection fraction values (Table 2).

Table 2: Echocardiographic and Laboratory Findings

Parameters	Impaired LV-GLS	Preserved LV-GLS	p-value
Left Ventricular Ejection Fraction (%)	56.4 ± 3.6	58.1 ± 4.0	0.002
LV-GLS (%)	-13.4 ± 1.8	-18.5 ± 2.0	<0.001
Left Atrial Volume Index (mL/m ²)	44.7 ± 6.5	35.9 ± 5.4	<0.001
E/e' Ratio	18.9 ± 3.7	13.8 ± 2.9	<0.001
Pulmonary Artery Systolic Pressure (mmHg)	43.6 ± 7.4	35.2 ± 5.8	<0.001
NT-proBNP (pg/mL)	1945 ± 610	1168 ± 438	<0.001
Interventricular Septal Thickness (mm)	12.8 ± 1.9	11.4 ± 1.5	<0.001
Left Ventricular Mass Index (g/m ²)	129.6 ± 18.5	111.8 ± 16.2	<0.001
Serum Creatinine (mg/dL)	1.34 ± 0.42	1.08 ± 0.31	<0.001
C-Reactive Protein (mg/L)	8.6 ± 3.1	5.2 ± 2.4	<0.001

Participants with impaired LGS had significantly more adverse cardiovascular events during clinical follow-up. Of the patients with abnormal LV-GLS, 61 (58.7%) were hospitalized for worsening heart failure, whereas 24 (25.0%) patients with preserved LV-GLS were hospitalized.

Patients with decreased myocardial strain also had more New York Heart Association functional limitation at follow-up assessment.

Other cardiac rhythm disturbances, major adverse cardiovascular events, and cardiovascular-related mortality were also seen more frequently in individuals who had impaired LV-GLS. When looking across the board, there was a uniform association between increasing myocardial strain and more adverse cardiovascular outcomes and clinical outcomes in patients with a diagnosis of HFpEF (Table 3).

Table 3: Clinical Outcomes during Follow-Up

Clinical Outcomes	Impaired LV-GLS (n=104)	Preserved LV-GLS (n=96)	p-value
Heart Failure Hospitalization	61 (58.7%)	24 (25.0%)	<0.001
Worsening NYHA Functional Class	69 (66.3%)	29 (30.2%)	<0.001
Major Adverse Cardiovascular Events (MACE)	42 (40.4%)	14 (14.6%)	<0.001
Arrhythmias	37 (35.6%)	15 (15.6%)	0.001
Cardiovascular Mortality	16 (15.4%)	4 (4.2%)	0.009
ICU Admission	28 (26.9%)	9 (9.4%)	0.001
Recurrent Heart Failure Episodes	47 (45.2%)	18 (18.8%)	<0.001

Multivariable survival analysis demonstrated that reduced left ventricular global longitudinal

strain maintained an independent relationship with adverse cardiovascular outcomes after

correction for major clinical and echocardiographic confounding factors, including age, hypertension, diabetes mellitus, atrial fibrillation, NT-proBNP level, left atrial volume index, and E/e' ratio.

The patients with reduced LV-GLS had about a fourfold increased risk of developing major adverse cardiovascular events compared with

patients with preserved myocardial strain values. In addition to abnormal myocardial deformation, elevated NT-proBNP concentration, atrial fibrillation, diabetes mellitus, and increased E/e' ratio were also found to be significant predictors of adverse cardiovascular progression in the HFpEF population (Table 4).

Table 4: Multivariate Cox Proportional Hazards Regression Analysis to Predict Major Adverse Cardiovascular Events

Variables	Adjusted Hazard Ratio (HR)	95% Confidence Interval	p-value
Impaired LV-GLS	3.94	2.08 – 7.45	<0.001
Age >65 Years	2.11	1.19 – 3.72	0.010
Diabetes Mellitus	2.46	1.34 – 4.50	0.004
Hypertension	1.58	0.88 – 2.83	0.118
Atrial Fibrillation	2.73	1.42 – 5.24	0.002
Elevated NT-proBNP	3.12	1.67 – 5.82	<0.001
Increased E/e' Ratio	2.28	1.21 – 4.29	0.011
Left Atrial Volume Index	1.94	1.03 – 3.66	0.039

Left ventricular global longitudinal strain showed strong prediction for major adverse cardiovascular events in patients with HFpEF by receiver operating characteristic analysis. The discriminatory performance of LV-GLS was substantial, with an area under the curve of 0.842 (95% CI: 0.781–0.903; $p<0.001$), indicating good prognostic accuracy.

The most optimal balance of diagnostic sensitivity and specificity for the prediction of unfavorable cardiovascular events was achieved by an LV-GLS cutoff value of -15.8% . At this threshold, sensitivity reached 81.3% , while specificity was calculated at 76.4% (Table 5).

Table 5: ROC Curve Analysis of LV-GLS to Predict Major Adverse Cardiovascular Events

Parameter	Value
Area Under Curve (AUC)	0.842
95% Confidence Interval	0.781 – 0.903
Optimal LV-GLS Cutoff	-15.8%
Sensitivity	81.3%
Specificity	76.4%
Positive Predictive Value	74.2%
Negative Predictive Value	82.9%
p-value	<0.001

The results of the present study thus suggest that measurement of LGE is closely related to poor clinical outcomes in patients with HFpEF. Follow-up evaluation revealed higher rates of recurrent hospitalization, repeated episodes of heart failure decompensation, major cardiovascular complications, and cardiovascular-related mortality in individuals with abnormal myocardial strain values. Notably, the LV-GLS prognostic value was still present after adjusting for conventional clinical and echocardiographic risk factors. These findings suggest the utility of myocardial strain measurement as an independent predictor of

adverse cardiovascular outcomes in HFpEF patients.

DISCUSSION

The findings from the current study showed that reduced LV-GLS was strongly associated with cardiovascular progression in patients with HFpEF. Patients with low LV-GLS were significantly more likely to experience hospitalization, functional limitation, recurrent heart failure exacerbation, arrhythmia, intensive care admission, and cardiovascular death. Myocardial strain analysis was able to identify a subgroup with subclinical myocardial

dysfunction that was clinically significant and associated with worse overall prognosis despite preserved LVEF among all enrolled participants^{7,8}.

HFpEF is now accepted as a multifactorial cardiovascular disease with abnormalities in ventricular relaxation, myocardial compliance, endothelial function, inflammatory activation, and myocardial fibrosis⁹. However, routine assessment of conventional systolic ejection fraction may miss subtle ventricular dysfunction due to this. In the present study, patients with reduced LV-GLS had significantly worse clinical and echocardiographic abnormalities despite normal LVEF values. These observations add to the increasing recognition of the role of myocardial deformation imaging for the detection of latent systolic dysfunction in patients with HFpEF¹⁰.

Patients with abnormal LV-GLS also had a marked increase in left atrial volume index, E/e' ratio, pulmonary artery systolic pressure, and NT-proBNP levels¹¹. These have been interpreted as reflecting a higher filling pressure and more severe diastolic dysfunction among patients with low myocardial strain. Rising NT-proBNP levels combined with deteriorating strain values could be an indication of increased myocardial wall stress and deleterious ventricular remodeling. In addition, the myopathic strain group had greater interventricular septal thickness and LVM index, which may reflect a more severe myocardial hypertrophy and fibrotic remodeling, two of the key pathological features of HFpEF¹².

Impaired LV-GLS was also found to be more prevalent in the present analysis in patients with hypertension, diabetes mellitus, obesity, atrial fibrillation, and coronary artery disease¹³. These metabolic and cardiovascular risk factors are known to be associated with chronic inflammation, oxidative stress, endothelial dysfunction, and progressive myocardial fibrosis that compromise myocardial mechanics. Diabetes mellitus and atrial fibrillation were also independently associated with major adverse cardiovascular events, highlighting their clinical importance for prognosis in HFpEF patients¹⁴.

A further significant finding was the much higher hospitalisation rate in patients with reduced myocardial strain¹⁵. During follow-up, more than half of patients with impaired LV-GLS were hospitalized compared to the preserved strain group. Likewise, a decline in New York Heart Association functional class and rehospitalisation for heart failure were significantly higher in those with abnormal

strain values. These results suggest that the more myocardial deformation is impaired, the more clinically it will deteriorate in HFpEF¹⁶.

Impaired LV-GLS was independently associated with about a 4-fold increased risk of major adverse cardiac events after adjustment for conventional clinical and echocardiographic variables¹⁷. This discovery supports the excellent prognostic value of myocardial strain in preserved EF heart failure. In addition, receiver operating characteristic analysis showed that LV-GLS was also highly sensitive and specific for predicting adverse cardiovascular outcomes, further underscoring the value of LV-GLS as a noninvasive prognostic imaging biomarker for routine cardiovascular assessment¹⁸.

The results of the current study agree with previous international studies that have demonstrated an association between reduced myocardial strain and higher cardiovascular event rates, hospital admissions, and mortality in HFpEF cohorts¹⁹. Speckle-tracking echocardiography allows detailed evaluation of myocardial deformation and may help identify high-risk individuals before clinically evident systolic dysfunction develops. Early detection of myocardial mechanical dysfunction may therefore improve risk stratification, monitoring strategies, and timely therapeutic intervention in patients with HFpEF²⁰.

Several limitations should also be acknowledged. The study was performed in a single tertiary care centre, which may limit the generalizability of the findings to broader populations. Furthermore, the observational study design does not allow establishment of causal relationships. Larger multicenter studies with extended follow-up duration are needed to further validate the prognostic role of LV-GLS across diverse HFpEF populations²¹.

CONCLUSION

The results of the current study showed that weaker LGLS is associated with worse cardiovascular outcomes in patients with HFpEF. Patients with abnormal myocardial strain had a higher rate of heart failure-related hospitalization, worse New York Heart Association functional status, recurrent decompensated heart failure episodes, arrhythmic complications, intensive care admission, cardiovascular mortality, and other outcomes during follow-up evaluation. Despite being statistically adjusted for known clinical and echocardiographic predictors, LV-GLS remained independently prognostic, suggesting

myocardial strain assessment adds value to traditional left ventricular ejection fraction assessment. Speckle-tracking echocardiography seems to be able to detect subtle myocardial mechanical dysfunction, which may not be apparent from routine echocardiographic assessment in HFpEF patients. The use of LV-GLS in the standard cardiac imaging evaluation could help identify high-risk patients earlier in the course of the disease and provide more personalized treatment strategies, more intensive monitoring, and better prevention of future cardiac events and rehospitalization.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this study.

Authors' Contributions

All authors contributed substantially to the conception and design of the study, data collection, statistical analysis, interpretation of findings, manuscript drafting, critical revision, and final approval of the submitted version.

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