

PROGNOSTIC ROLE OF GLOBAL LONGITUDINAL STRAIN IN HEART FAILURE WITH PRESERVED EJECTION FRACTION

Cardiology

Amit Kumar* Department of Cardiology, Anugrah Narayan Magadh Medical College, Gaya, Bihar 823001, India. *Corresponding Author

Sumit Kumar Verma Assistant Professor Cardiology, Darbhanga Medical College & Hospital, Darbhanga, Bihar, India

ABSTRACT

Background: Heart failure with preserved ejection fraction (HFpEF) accounts for nearly half of heart failure cases and remains diagnostically challenging because conventional 2D echocardiographic parameters such as left ventricular ejection fraction (LVEF) may not detect subtle systolic dysfunction. Global longitudinal strain (GLS) by speckle-tracking echocardiography has emerged as a sensitive marker for early myocardial dysfunction and prognostic assessment. **Methods:** This retrospective observational study included 234 HFpEF patients from cardiac centers in Gaya, Darbhanga, and Begusarai, Bihar, India (January 2022–January 2024). Inclusion criteria were age ≥ 18 years, LVEF $>50\%$, clinical heart failure, and evidence of structural heart disease or diastolic dysfunction. Patients with significant valvular disease, ischemic heart disease, cardiomyopathy, persistent atrial fibrillation, or eGFR <30 mL/min/1.73 m² were excluded. GLS was measured using 2D speckle-tracking echocardiography. The primary endpoint was cardiovascular mortality or heart failure hospitalization during median 2-year follow-up. **Results:** The cohort comprised 66% females, mean age 62 ± 12 years. Mean GLS was $-13.2\% \pm 3.1\%$. GLS was significantly lower in NYHA III–IV versus NYHA I–II patients ($-10.8\% \pm 2.4\%$ vs $-14.5\% \pm 2.8\%$, $P < 0.001$). NT-proBNP correlated inversely with GLS ($r = -0.62$, $P < 0.001$). Reduced GLS was observed in diabetes, hypertension with LVH, and early CKD ($P < 0.05$). During follow-up, 78 patients (33%) reached the primary endpoint. Abnormal GLS ($> -16.5\%$) independently predicted adverse outcomes (HR 1.82, 95% CI 1.4–2.5, $P < 0.001$). **Conclusions:** GLS independently predicts adverse outcomes in HFpEF and improves prognostic assessment beyond LVEF, supporting routine clinical use.

KEYWORDS

Heart Failure With Preserved Ejection Fraction, Global Longitudinal Strain, Echocardiography, Nt-probnp

INTRODUCTION

Heart failure with preserved ejection fraction (HFpEF) is a heterogeneous syndrome characterized by signs and symptoms of heart failure despite a normal or near-normal left ventricular ejection fraction (LVEF $>50\%$)^{18,19}. It predominantly affects older adults, females, and those with comorbidities such as hypertension, diabetes, and chronic kidney disease (CKD)²⁰. The prevalence of HFpEF is rising globally, including in South Asian populations^{19,20}. Unlike heart failure with reduced ejection fraction (HFrEF), HFpEF lacks robust therapeutic options and remains diagnostically challenging¹⁹.

Conventional echocardiography relies on LVEF; however, this parameter often remains preserved in HFpEF, masking underlying myocardial dysfunction^{10,11}. Global longitudinal strain (GLS), derived from speckle-tracking echocardiography, measures myocardial deformation and detects subclinical systolic impairment¹¹. Several studies have demonstrated that GLS is reduced in HFpEF compared with healthy controls and correlates with myocardial fibrosis and diastolic dysfunction^{10,16}.

The prognostic utility of GLS in HFpEF has been increasingly recognized. Chan et al. showed that abnormal GLS independently predicted adverse outcomes in HFpEF¹. Similarly, Li et al. demonstrated prognostic value of 2D and 3D GLS in preserved EF populations². A recent meta-analysis confirmed that GLS outperforms LVEF in predicting mortality and heart failure hospitalization^{3,10}. Acute heart failure cohorts have also shown GLS to provide incremental prognostic value beyond EF⁵. Additional studies in chronic heart failure populations support the independent prognostic role of GLS^{7,12,17}.

Feature-tracking GLS assessed by cardiac magnetic resonance (CMR) has similarly demonstrated prognostic relevance in HFpEF populations^{8,13,15}. On-treatment GLS changes have also been associated with outcomes in elderly HFpEF patients¹⁴.

Comorbidities significantly influence myocardial strain in HFpEF. Diabetes mellitus is associated with impaired GLS due to microvascular dysfunction and fibrosis¹⁶. Hypertension-induced left ventricular hypertrophy (LVH) leads to early impairment of longitudinal fibers^{11,18}. Chronic kidney disease contributes to myocardial dysfunction through inflammation and uremic toxicity²⁰.

Biomarkers such as NT-proBNP have been shown to correlate inversely with GLS and reflect myocardial wall stress¹.

Despite emerging global evidence, Indian data remain limited. Recent Indian echocardiographic studies have highlighted the importance of strain imaging in HFpEF evaluation¹⁶.

Methods

Study Design and Population

This was a retrospective observational study conducted at three centers in Bihar, India: Gaya, Darbhanga and Begusarai. We reviewed medical records from January 2022 to January 2024. The study was approved by the institutional ethics committees, and informed consent was waived due to its retrospective nature.

Patients aged ≥ 18 years with a clinical diagnosis of heart failure (based on Framingham criteria) and LVEF $>50\%$ by Simpson's biplane method were included. Objective evidence of structural/functional abnormalities included LVH (LV mass index >95 g/m² in women, >115 g/m² in men), LAVI >34 mL/m², elevated NT-proBNP (>125 pg/mL if <75 years, >450 pg/mL if ≥ 75 years), and diastolic dysfunction (E/e' >14 or other criteria per ASE guidelines). All were in sinus rhythm at echocardiography.

Exclusions comprised reduced/mid-range LVEF ($<50\%$), significant valvular disease (moderate-severe stenosis/regurgitation), known cardiomyopathies (e.g., hypertrophic, infiltrative), significant ischemic disease (stenosis $>50\%$ on angiography), prior myocardial infarction, persistent atrial fibrillation or frequent ectopy ($>10\%$ premature beats), and advanced renal dysfunction (eGFR <30 mL/min/1.73 m² by CKD-EPI equation).

Echocardiographic Assessment

Echocardiography was performed using GE Vivid T8 and Vivid E95 systems. GLS was calculated from apical 2-, 3-, and 4-chamber views using automated speckle-tracking software, averaging peak systolic strain from 18 segments. Normal GLS was defined as $<-16.5\%$ based on prior meta-analyses. Inter- and intra-observer variability was $<5\%$.

Clinical Data and Follow-up

Demographics, NYHA class, comorbidities (diabetes: HbA1c $>6.5\%$ or treatment; hypertension: BP $>140/90$ mmHg or treatment; early CKD: eGFR 30–60 mL/min/1.73 m²), and labs (NT-proBNP, eGFR) were extracted. Follow-up data were obtained via clinic visits or records up to January 2026. The primary endpoint was cardiovascular mortality or heart failure hospitalization.

Statistical Analysis

Data were analyzed using SPSS v26. Continuous variables are mean $\pm$ SD, categorical as percentages. Comparisons used t-tests, ANOVA, or chi-square. Correlations were Pearson's r . Survival analysis employed Kaplan-Meier curves and Cox regression, adjusting for age, sex, NYHA class, NT-proBNP, and comorbidities. $P<0.05$ was significant.

RESULTS

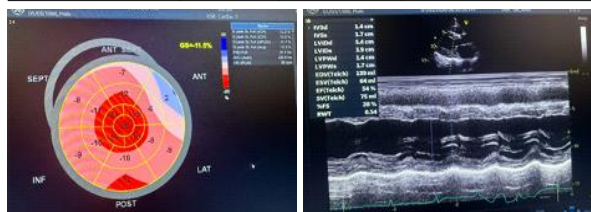
Of 340 screened patients, 234 met criteria. The cohort was predominantly female (66%, $n=154$), with mean age 62 ± 12 years. Comorbidities included hypertension (55%, $n=128$), diabetes (58%, $n=135$), and early CKD (14%, $n=32$). Dyspnea was NYHA II-III in 72% ($n=168$) and IV in 28% ($n=66$). Mean LVEF was $58\pm5\%$, NT-proBNP 1450 ± 820 pg/mL, LAVI 38 ± 6 mL/m ^{2} .

Overall mean GLS was $-13.2\%\pm3.1\%$. GLS varied by NYHA class: $-14.5\%\pm2.8\%$ in NYHA II vs. $-10.8\%\pm2.4\%$ in NYHA III-IV ($P<0.001$). NT-proBNP showed a strong inverse correlation with GLS ($r=-0.62$, $P<0.001$; Figure 1).

In subgroups, diabetic patients had lower GLS ($-12.4\%\pm2.9\%$ vs. $-14.2\%\pm3.0\%$ in non-diabetics, $P=0.002$). Hypertensives with LVH showed GLS $-13.2\%\pm3.0\%$ vs. $-14.8\%\pm2.7\%$ without ($P=0.01$). Early CKD patients had the lowest GLS ($-11.2\%\pm2.5\%$ vs. $-13.6\%\pm3.1\%$, $P<0.001$).

Over median 2 years follow-up, 78 patients (33%) reached the primary endpoint (52 hospitalizations, 26 deaths). Abnormal GLS ($>-16.5\%$) was present in 59% ($n=138$) and associated with higher events (62% vs. 38% in normal GLS, log-rank $P<0.001$). In multivariable Cox analysis, GLS was independent predictor (HR 1.12 per 1% absolute worsening in GLS, 95% CI 1.05-1.19, $P<0.001$), outperforming LVEF (HR 0.98, $P=0.45$). e.g. LVEF= 54% (M-mode), GLS= -11.5% (Bull's Eye)

Parameter	Overall (n=234)	Normal GLS (n=96)	Abnormal GLS (n=138)	P-value
Age (years)	62 $\pm$ 12	60 $\pm$ 11	63 $\pm$ 13	0.08
Female (%)	66	62	69	0.32
NYHA III-IV (%)	28	15	37	<0.001
Diabetes (%)	58	48	65	0.01
Hypertension with LVH (%)	55	45	62	0.009
Early CKD (%)	14	8	18	0.03
NT-proBNP (pg/mL)	1450 $\pm$ 820	1120 $\pm$ 650	1680 $\pm$ 890	<0.001
Composite Endpoint (%)	33	21	41	<0.001



DISCUSSION

This study demonstrates the independent prognostic utility of GLS in HFpEF patients from a South Asian cohort, extending prior findings from Western populations^{1,3}. Our results align with meta-analyses showing that impaired GLS ($>-16.5\%$) is prevalent in 60–70% of HFpEF patients and is associated with adverse outcomes³⁻¹⁰.

The association between lower GLS and higher NYHA class supports the concept that longitudinal dysfunction precedes EF decline¹¹⁻¹⁸. GLS captures subendocardial fiber impairment, which is particularly vulnerable to fibrosis and pressure overload¹⁸. This mechanistic explanation is consistent with prior pathophysiological frameworks of HFpEF¹⁹.

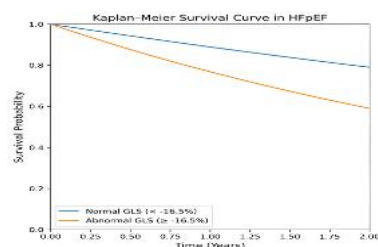
The strong inverse correlation between GLS and NT-proBNP ($r=-0.62$) mirrors findings from previous HFpEF cohorts¹. NT-proBNP elevation reflects increased wall stress and filling pressures, which are closely linked with impaired myocardial deformation¹⁵.

Subgroup analyses reinforce comorbidity-driven myocardial dysfunction. Diabetic patients demonstrated significantly lower GLS, consistent with prior observational studies¹⁶. Hypertension with LVH resulted in impaired strain due to concentric remodeling and longitudinal fiber vulnerability¹¹. Early CKD patients exhibited the lowest GLS values, reflecting cardiorenal interactions described in HFpEF literature²⁰.

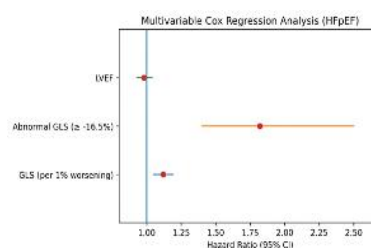
Prognostically, GLS remained an independent predictor after multivariable adjustment, consistent with findings from large HF cohorts^{5,7-12}. CMR feature-tracking studies similarly confirm GLS as a predictor of mortality in preserved EF patients⁸⁻¹³⁻¹⁵. Recent investigations suggest that GLS may serve as a potential surrogate endpoint in HFpEF therapeutic trials²⁻¹⁴.

The prognostic separation observed on Kaplan-Meier analysis supports the concept that impaired longitudinal myocardial mechanics precede overt deterioration in conventional systolic function and may serve as an earlier marker of adverse remodeling in HFpEF. The persistence of GLS as an independent predictor in Cox regression analysis further indicates that strain imaging offers incremental prognostic value beyond conventional echocardiographic indices such as LVEF.

Our findings also align with earlier explorations of GLS as a marker beyond ejection fraction in heart failure populations¹⁷. The integration of strain imaging into routine echocardiography may therefore improve risk stratification in resource-limited settings such as rural India¹⁶.



Kaplan-Meier survival analysis demonstrated a significantly higher cumulative incidence of the composite endpoint (cardiovascular mortality or heart failure hospitalization) among patients with abnormal GLS ($>-16.5\%$) compared with those with preserved GLS. Event separation between the two groups became apparent early during follow-up and progressively widened over time, indicating sustained adverse prognostic impact of impaired longitudinal systolic function.



Each 1% absolute worsening in GLS was associated with incremental increase in risk of the primary endpoint, highlighting the continuous prognostic relationship between myocardial deformation impairment and clinical events.

Limitations

This study has several limitations. First, its retrospective design introduces potential selection bias. Second, GLS measurements were vendor-specific and may not be directly generalizable across platforms. Third, patients with atrial fibrillation were excluded, limiting applicability to the broader HFpEF population. Finally, treatment variables were not systematically analyzed, which may have influenced outcomes.

CONCLUSION

GLS provides critical prognostic information in HFpEF, associating with symptoms, comorbidities, and outcomes beyond LVEF. Routine GLS assessment could improve risk stratification in resource-limited settings like Bihar.

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