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Invasive validation of the left ventricular global longitudinal strain for estimating left ventricular filling pressure

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Abstract

Purpose: An elevated left ventricular (LV) filling pressure is the main finding in heart failure patients with preserved ejection fraction, which is estimated with an algorithm using echocardiographic parameters recommended by the recent American Society of Echocardiography (ASE)/European Association of Cardiovascular Imaging (EACVI) guidelines. In this study, we sought to determine the efficacy of the LV global longitudinal strain (GLS) in predicting an elevated LV filling pressure.

Methods and Results: A total of 73 prospectively selected patients undergoing LV catheterization (mean age 63.19 ± 9.64, 69% male) participated in this study. Using the algorithm, the LV filling pressure was estimated using the echocardiographic parameters obtained within 24 hours before catheterization. The LV GLS was measured using an automated functional imaging system (GE, Vivid E9 USA). Invasive LV pre-A pressure corresponding to the mean left atrial pressure (LAP) was used as a reference, and a LAP of >12 mm Hg was defined as elevated.

Invasive LV filling pressure was elevated in 43 patients (59%) and normal in 30 patients (41%). Nine of 73 (12%) patients were defined as indeterminate based on the 2016 algorithm. Using the ROC method, −18.1% of LV GLS determined the elevated LAP (AUC =0.79; specificity, 73%; sensitivity, 84%) with better sensitivity compared to that by the algorithm (AUC =0.76; specificity, 77%; sensitivity, 72%).

Conclusions: We demonstrated that LV GLS was an independent predictor of elevated LAP as the E/e' ratio and TR jet velocity and may be used as a major criterion for the diagnosis of HFpEF.

KEYWORDS

diastolic dysfunction, echocardiography, heart failure, left ventricular ejection fraction, left ventricular filling pressure, myocardial strain

1 | INTRODUCTION

Heart failure (HF) is a common public health problem; 6.2 million adults had heart failure (HF) in the United States alone.[1] The description of HF mainly includes HF symptoms and left ventricular ejection fraction (LVEF), which is established by HF guidelines.[2] HF with preserved ejection fraction (HFpEF) considered as ≥50% LV EF[2–5] has complex pathophysiological mechanisms with challenging diagnostic features.[2,3,6,7] The prevalence of HFpEF continues to rise owing to the aging population, obesity, and certain diseases, including diabetes, hypertension, and atrial fibrillation.[6,7] In reality, up to 50% of patients with HF have HFpEF in developed countries.[1,2]

Patients with HFpEF commonly have normal LV systolic function with a normal systolic and diastolic diameter but an increased LV wall thickness and left atrial (LA) dilatation. Moreover, an increased LV filling pressure is an essential finding in patients with HFpEF.[3] Although cardiac catheterization is the gold standard method to demonstrate an elevated LV filling pressure, it is not practical.[2] Therefore, estimating the LV filling pressure using transthoracic echocardiography (TTE) has become a standard method because of its feasibility and reproducibility. Conventional Doppler methods, such as diastolic mitral inflow measurement from the tip of mitral leaflets with pulse wave Doppler (PW) and tissue Doppler imaging, have been used to define diastolic dysfunction.[2,8–10] To simplify the estimation of the LV filling pressure, the 2016 EACVI/ASE guidelines demonstrated a new algorithm[11] using similar echocardiographic parameters such as E/e' and left atrium volume index (LAVi).

Contrary to general belief, LV systolic function is often impaired and established as one of the main mechanisms of HFpEF with diastolic dysfunction. Irrespective of reduced EF, LV systolic dysfunction can be easily identified using the LV global longitudinal strain (GLS) method.[4] Furthermore, the Heart Failure Association of the European Society of Cardiology (HFA-ESC) published a consensus recommendation including a diagnostic algorithm of HFpEF (HFA-PEFF) in 2019, and GLS <16 was established as a minor functional criterion for the HFA-PEFF algorithm.[5] In this study, we sought to determine the relationship between the LV GLS and the elevated LV filling pressure in patients with preserved EF.

2 | MATERIALS AND METHODS

2.1 | Patient data

A total of 87 consecutive adult patients who underwent clinically indicated coronary angiography and left heart catheterization between March 2018 and October 2019 were prospectively selected. TTE was performed immediately before catheterization; patients with ST-elevation and non-ST-elevation myocardial infarction (MI), EF <50%, moderate to severe aortic and mitral regurgitation, and moderate to severe aortic and mitral stenosis were excluded, and 73 patients remained in our study. The medical histories, including all clinical and demographic data, were obtained from the electronic medical records. Laboratory results that were received within 24 hours before catheterization were obtained. The study protocol was reviewed and approved by the ethics committee.

2.2 | Transthoracic echocardiography

Two-dimensional echocardiographic imaging was performed in 73 patients who met the clinical criteria for study inclusion at the Cardiology Department of Ankara University. Two-dimensional color flow, continuous pulse wave, and tissue Doppler TTE were performed by two experienced physicians using a Vivid E9 imaging system (with an M5Sc-D transducer; GE Medical Systems) within 24 hours before left heart catheterization, and measurements were obtained in a standard manner as recommended by the ASE. LV dimensions were measured in the parasternal long-axis view at end-systole and end-diastole. LV ejection fraction was calculated from the four-chamber view using the modified Simpson method.[6]

2.2.1 | TTE parameters assessed LV diastolic function

Diastolic filling periods, including rapid filling, diastasis, and atrial contraction, were assessed using pulsed-wave (PW) Doppler. Mitral inflow at the level of mitral valve leaflet tips was used to measure the peak early (E-wave) and late (A-wave) diastolic flow velocities and calculate the E/A ratio. Furthermore, tissue Doppler imaging (TDI) using PW was performed with the sample volume at the lateral and septal mitral annulus to obtain lateral and medial e' velocities. The arithmetic mean of lateral and medial e' was defined as the average e', which was used to calculate the E/e' ratio. The peak velocity of the tricuspid regurgitation (TR) jet was measured using continuous-wave Doppler. Left atrial volume was measured using a four-chamber view and divided by body surface area (BSA) to calculate the LAVi.[6]

2.2.2 | Speckle tracking 2D LV longitudinal strain

Speckle tracking of the 2D LV longitudinal average and regional strain was performed using automated functional imaging (AFI). AFI was performed in 73 patients using an E9 imaging system (with a 4V-D transducer; GE Medical Systems) and transferred to an EchoPAC imaging workstation (EchoPAC imaging system). The LV longitudinal strain was determined according to standardized measurements recommended by the 2015 ASE Cardiac Chamber Quantification guidelines.[6]

2.3 | LV catheterization

Left heart catheterization was performed according to the standard procedure by an interventional cardiologist blinded to the echocardiographic data. Invasive LV systolic and diastolic pressure measurements were performed using a 6 Fr pigtail catheter (Boston Scientific) placed in the left ventricle through the femoral or radial artery before the evaluation of coronary artery visualization. The measurements were obtained after the fluid-filled transducer was balanced with the zero level at the mid-axillary line. Continuous pressure tracings were acquired over at least three consecutive respiratory cycles. The LV pre-A pressure, which corresponds to the mean left atrial pressure (LAP), was used as the LV filling pressure, as recommended in the 2016 ASE/EACVI algorithm, and a pre-A pressure of >12 mm Hg was confirmed as an elevated LV filling pressure.

2.4 | Statistical analysis

Baseline characteristics were presented as mean ± SD for continuous variables and compared using the Student *t* test, or percentages for categorical variable differences were compared using the chi-square test. Statistical significance was set at $P < .05$. Univariate and multivariate analyses based on the logistic regression model were performed to determine the TTE parameters to estimate the elevated LV filling pressure. Only variables with $P < .05$ in univariate analysis were entered into multivariate analysis. The correlation between the LV GLS and diastolic parameters was analyzed using the Pearson correlation method. The correlation of invasive LV filling pressure with the LV GLS and diastolic parameters was also analyzed using the Pearson correlation method. The sensitivity, specificity, positive predictive value, and negative predictive value of diastolic parameters and the LV GLS were analyzed using the receiver operating characteristic (ROC) analysis based on the logistic regression method. The LV GLS cutoff value was determined using an ROC analysis. All data were analyzed using JMP version 14.0 (SAS Institute Inc).

2.4.1 | Inter-observer and intra-observer variabilities

Images from 10 patients were randomly selected, and a second independent blinded observer measured the images to assess the inter-observer variability. The first observer, who measured all patients' views, remeasured the same randomly selected 10 patients' views at least 6 weeks apart from the first measurement. Inter-observer and intra-observer variabilities were assessed using the intra-class correlation coefficient (ICC) method.

3 | RESULTS

3.1 | Baseline characteristics

A total of 73 patients (mean age 63.19 ± 9.64, 69% male) who underwent left heart catheterization comprised the study population. The patients were divided into two groups based on their invasive LV pre-A pressure values. The group with a pre-A pressure of >12 mm Hg (43 patients, 59%; LV pre-A pressure =17.2 ± 3.05) was defined as the elevated LAP group, and the group with a pre-A pressure of ≤12 mm Hg (30 patients, 40%; LV pre-A pressure =7.5 ± 2.19) was defined as the normal LAP group. Demographics, clinical characteristics, laboratory results, medications used, and TTE results were compared between the groups (Table 1). There were no differences in age, sex, medication use, or comorbidities. Laboratory results (obtained within 24 hours prior to LV catheterization), including hemoglobin, platelet, ALT, and AST levels, were also similar between the groups. In addition, baseline SBP and SBP during catheterization did not differ between the groups.

3.1.1 | Echocardiographic measurements

Although the E value, E/e', and E/A ratios were significantly higher in patients in the elevated LAP group, there were no differences in the A value between the groups. The TR jet velocity was measured in 50 of 73 patients and was observed to be significantly higher in the elevated LAP group. However, the LAVi was similar between the groups.

3.1.2 | LV global longitudinal strain

The LV longitudinal strain was determined in all patients within 24 hours. Notably, prior LV global longitudinal strain was significantly impaired in patients in the elevated LAP group (LV strain, −15.4 ± 2.83 vs −18.9 ± 2.14; $P < .0001$). The intra-observer (ICC: 0.97; 95% CI, 0.91–0.99) and inter-observer (ICC: 0.94; 95% CI, 0.78–0.98) agreement of strain measurements were excellent.

3.1.3 | Univariate and multivariate predictors of the elevated LV filling pressure

Echocardiographic parameters using the algorithm recommended in the 2016 ASE/EACVI guideline and LV GLS were entered into the univariate and multivariate logistic regression models to identify the independent predictors of the elevated LV filling pressure. In univariate modeling (Table 2), a higher E/e'ratio and TR jet velocity were the univariate predictors of the elevated LAP. In addition, the LV GLS was significantly associated with the elevated LV filling pressure.

In multivariate analysis (Table 2), the E/e' ratio and TR jet velocity were the independent predictors of the elevated LAP. Furthermore, an impaired LV GLS was an independent predictor of the elevated LV filling pressure.

3.2 | ROC analysis

The estimated LAP was determined using the algorithm recommended in the 2016 ASE/EACVI guidelines. Nine of 73 (12%)

TABLE 1 Baseline characteristics divided by invasive left atrial pressure

Characteristics	Elevated LAP Group (n = 43)	Normal LAP Group (n = 30)	*P* value
Age	63.3 ± 10.10	63.03 ± 9.11	.90
Gender			
Male	63%	77%	.20
Female	37%	23%	.20
BSA m^2	1.88 ± 0.16	1.89 ± 0.15	.82
SBP mm Hg	120.3 ± 10.3	120.1 ± 11.8	.93
SBP-Catheter mm Hg	129.6 ± 10.58	128.06 ± 10.07	.52
HT%	81.4	76.7	.62
DM%	32.6	43.3	.34
HL%	34.9	36.7	.87
Medication			
ACE inhibitors%	39.5	36.7	.80
ARB%	42	40	.87
Beta blocker%	46.5	46.7	.99
Aldosterone inhibitors%	11.6	6.7	.69
Diuretic%[a]	39.5	33.3	.59
Statin%	21	30	.38
Laboratory result			
Hemoglobin, g/dL	13.6 ± 1.55	14.4 ± 2.49	.14
Platelet	248 ± 75.4	246.7 ± 64.2	.94
Creatinine (mg/dL)	0.83 ± 0.12	0.84 ± 0.14	.82
ALT U/L	21.5 ± 3.56	21.2 ± 3.96	.76
AST U/L	21.4 ± 2.35	21.4 ± 2.96	.99
Echocardiography			
LVEDD mm	48.04 ± 4.68	48.93 ± 5.38	.46
LVESD mm	27.02 ± 3.04	28.6 ± 4.84	.11
EF%	58.8 ± 4.23	57.56 ± 3.46	.17
E m/sec	0.71 ± 0.19	0.62 ± 0.11	.0093
A m/sec	0.78 ± 0.19	0.81 ± 0.13	.34
E/A ratio	0.95 ± 0.32	0.73 ± 0.16	.0002
E/e' ratio	13.5 ± 5.56	8.65 ± 2.51	<.0001
TR velocity	2.75 ± 0.48	2.28 ± 057	.004
LAVI mL/m^2[b]	33.3 ± 6.49	31.08 ± 4.78	.093
LV GLS %	−15.4 ± 2.83	−18.9 ± 2.14	<.0001

Note: Data are expressed as mean ± SD or as (%).

Abbreviations: ACE = angiotensin-converting enzyme; ALT = alanine amino transferase; ARB = Aldosterone receptor antagonist; AST = aspartate amino transferase; BSA = body surface area; EF = ejection fraction; LAVI = left atrial volume index; LV = left ventricular; LVEDD = left ventricular end-diastolic diameter; LVESS = left ventricular end systolic diameter; LV GLS= left ventricular global longitudinal strain; *P* = probability; SBP = systolic blood pressure; TR = tricuspid regurgitation.

[a]Including furosemide and torasemide.

[b]Calculation of left atrial volume ratio body surface area.

patients were defined as indeterminate based on the algorithm. Among those, six patients had an elevated pre-A pressure, and three patients had a normal pre-A pressure. According to the algorithm, 29 (40%) patients were defined as having an elevated LAP, and 35 (48%) patients were defined as having a normal LAP. An ROC analysis based on the logistic regression model was used to analyze the accuracy of the algorithm for predicting the elevated LAP. In addition, the individual effects of the parameters were analyzed using

TABLE 2 Univariate and multivariate analysis of echocardiographic predictors of elevated LV filling pressure in all patients

	Univariate		Multivariate	
Variable	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
E/e'(1 unit increase)	1.32 (1.12–1.55)	<.0001	1.45 (1.07–1.95)	.002
LAVi mL/m^2 (1unit increase)	1.07 (0.98–1.16)	.10		
TR jet velocity m/sn (0.1 m/sn increase)	1.20 (1.04–1.37)	.002	1.25 (1.01–1.55)	.010
LV GLS (1unit increase)	1.67 (1.31–2.14)	<.0001	1.76 (1.14–2.71)	.002

Abbreviation: CI =confidence interval, other abbreviations as in Tables 1 and 2.

the algorithm. The AUC of LAVi was lower (AUC, 0.61; specificity, 73.40%; sensitivity, 65%) than that of TR velocity (AUC, 0.77; specificity, 81%; sensitivity, 75.80%) and E/e' (AUC, 0.75; specificity, 87%; sensitivity, 65%) to estimate the elevated LAP (Figure 1, Table 3). Furthermore, the LV GLS better identified patients with elevated invasive LAP (AUC, 0.83; specificity, 73.4%; sensitivity, 86%) compared to echocardiographic parameters using the algorithm. The LV longitudinal strain cutoff value was −18.1%, based on the ROC curve, and a value >−18.1% of GLS was defined as an elevated LAP. A GLS of −18.1% had higher sensitivity to predict LAP (AUC, 0.79; specificity, 73%; sensitivity, 84%) compared to the algorithm (AUC, 0.76; specificity, 77%; sensitivity, 72%) (Figure 2).

3.3 | Correlation analysis

The Pearson correlation method was used to assess the correlation between the pre-A pressure and echocardiographic parameters (Table 4). There was no good correlation between the pre-A and echocardiographic parameters. However, there was a moderate correlation between the LV GLS (r = .47) and the invasive pre-A pressure. Furthermore, there was no good correlation between the LV GLS and diastolic echocardiographic parameters, E/e' (r = .34, P = .003), LAVi (r = .04, P = .68), and TR velocity (r = .11, P = .13).

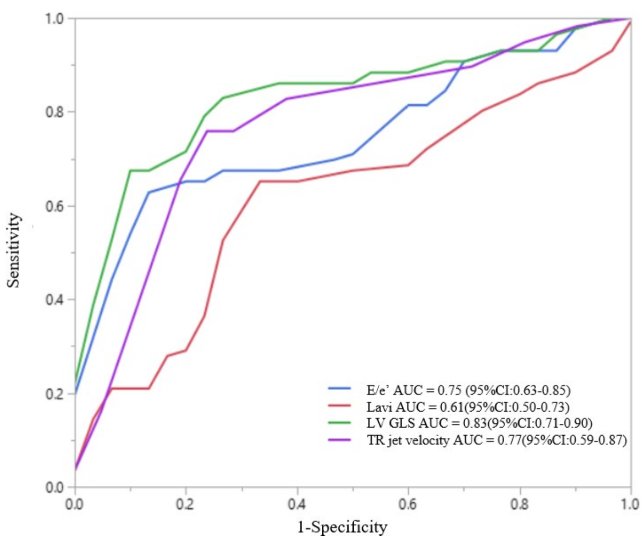

FIGURE 1 Receiver operating curves of estimated LV filling pressure. E/e' AUC = 0.75 (95% CI, 0.63–0.85), LAVi AUC = 0.61 (95% CI, 0.50–0.73), LV GLS AUC = 0.83 (95% CI, 0.71–0.90), and TR jet velocity AUC = 0.77 (95% CI, 0.59–0.87)

4 | DISCUSSION

In our study, we aimed to demonstrate the invasive validation of LV GLS in predicting elevated LV filling pressure. We confirmed that the LV GLS was significantly associated with the elevated LAP in patients with preserved EF, such as E/e' and TR jet velocity. We also demonstrated that −18.1% of LV GLS had higher sensitivity in identifying patients with elevated invasive LV filling pressure compared to the 2016 ASE/EACVI algorithm.[3]

Notably, increased myocardial stiffness and the prolongation of active myocardial relaxation are the main reasons for HFpEF, which leads to an elevated LV filling pressure. Thus, the invasive evaluation of the elevated LV filling pressure is the gold standard method for defining diastolic dysfunction in patients with HF symptoms. However, invasive assessment is not practical and reproducible for all patients with HF symptoms. Therefore, the 2009 ASE and EACVI[7] guidelines were simplified, and a practical algorithm was developed in 2016 guidelines[3] to estimate the LV filling pressure. However, the studies designed to validate the 2016 ASE/EACVI algorithm with invasive LV filling pressure have provided conflicting results. Some demonstrated good agreement with the invasive LV pressure.[2,8]

Furthermore, the Euro-Filling study demonstrated a substantial sensitivity in diagnosing elevated LV filling pressures, with the 2016 recommendations, in patients undergoing invasive LV end-diastolic pressure measurement. However, they concluded that the algorithm was suboptimal in patients with preserved ejection fraction.[9] In contrast, Obokata et al[10] reported that the new algorithm was specific, but poorly sensitive, and identified only 34% of individuals with HFpEF diagnosis. Our study also showed that the new algorithm had good specificity but lower sensitivity in predicting the LV filling pressure.

Although TTE is practical and reproducible for determining diastolic dysfunction, it is not feasible in certain instances, including atrial fibrillation, mitral annular calcification, and indeterminate groups defined in the guidelines. Almedia et al demonstrated an increase in indeterminate cases using the 2016 algorithm compared to using the 2009 guidelines.[7] The inclusion of TR velocity in the

TABLE 3 Receiver operating characteristic of echo parameters

Variable	Specificity %	Sensitivity %	PPV	NPV	AUC (95% CI)	*P*
E/e' ratio	87%	65%	88%	63%	0.75 (0.63–0.85)	<.0001
TR jet velocity	81%	75.8%	84.6%	70.8%	0.77 (0.59–0.87)	.002
LAVI mL/m²	73.4%	65%	87.5%	59.4%	0.61 (0.50–0.73)	.1
LV GLS %	73.4%	86.%	82%	78.5%	0.83 (0.71–0.90)	<.0001
Estimated LAP mm Hg	77%	72%	81.6%	65.7%	0.76 (0.64–0.84)	<.0001

Abbreviations: AUC = area under curve; GLS = global longitudinal strain; NPV = negative predictive value; PPV = positive predictive value; Other abbreviations as in Table 1.

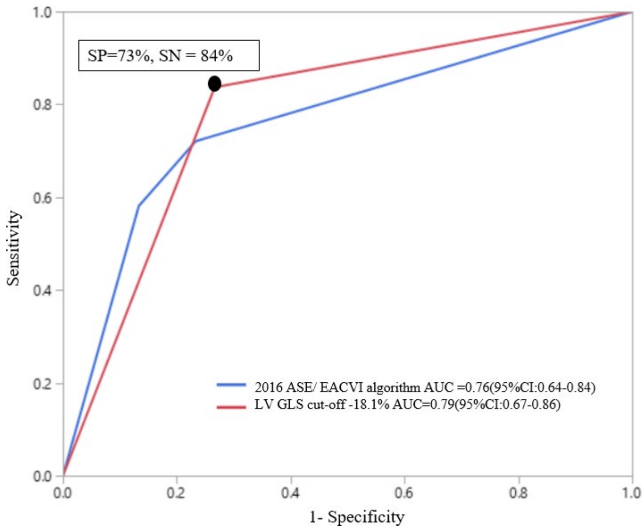

FIGURE 2 Receiver operating curves of estimated LV filling pressure. Cutoff point of −18.1% of LV GLS AUC = 0.79 (95% CI, 0.67–0.86; *P* < .0001) and the 2016 ASE/EACVI algorithm AUC =0.76 (95% CI, 0.64–0.84; *P* < .0001) alone

TABLE 4 Correlation of invasive LAP and echo parameters

Variable	*r*	*P* value
E m/sec	.18	.11
A m/sec	−.07	.54
E/A ratio	.27	.02
E/e' ratio	.36	.002
LAVi	.19	.1
TR velocity	.36	.003
LV GLS	.47	<.0001

Abbreviations: *r* = correlation coefficient; Other abbreviations as in Table 1.

new algorithm might be an essential reason for the increased number of indeterminate cases. TR velocity generally reflects severe HFpEF; therefore, the early stage of the disease may not be evaluated. Moreover, 30% of patients show normal resting diastolic function according to standard echocardiographic assessments.[11,12] Although the cumulative effect of the parameters using the algorithm provides substantial information about the LV filling pressure, individual parameters have certain limitations. In particular, E/e' is load-dependent and might be affected from angle intonation and also has poor predictability to detect the elevation of LV filling pressures with 37% estimation.[13]

Nevertheless, the LAVi is an adequate parameter for estimating the cumulative effect of increased LV filling pressures.[3,14,15] It might be inadequate to detect early LV diastolic dysfunction because this volumetric parameter essentially reflects the chronic effect of elevated LV filling pressure.[16] Our study observed a weak correlation among the TR jet velocity, E/e', and invasive pre-A pressure and no correlation between the LAVi and the invasive pre-A pressure. Additionally, the LAVi had lower sensitivity (specificity, 73.40%; sensitivity, 65%) compared to E/e' and TR jet velocity.

The speckle-tracked LV GLS is a valuable parameter for assessing global and regional left ventricular systolic dysfunction. Moreover, the LV GLS reflects the longitudinally arranged sub-endocardial fiber function that is influenced early in disease pathogenesis, allowing the detection of even subtle impairments; in contrast, EF only detects overt systolic failure.[17] It is believed that a diastolic impairment of the LV is the main mechanism of HFpEF.[18,19] However, the pathophysiological features of HFpEF, including myocardial fibrosis and microvascular dysfunction, can impair both diastolic and systolic functions. Currently, there is a clear evidence of significant systolic impairment in patients with HFpEF, such as decreased contractility, which is associated with greater mortality.[20]

Furthermore, the PARAMOUNT study has demonstrated an independent association between NT-proBNP levels and LV GLS and impaired LV GLS has highly predicted adverse outcomes.[4,21] The 2016 ASE/ESC guidelines recommend assessing the LV GLS in patients with atrial fibrillation and severe mitral annular calcification. They also recommend the LV GLS to provide the discriminative diagnostic capacity in indeterminate groups.[3] Biering-Sørensen et al reported that the LV GLS for a noninvasive evaluation of LV filling pressure acquired good correlation with PCWP, both at rest and exertion.[22] In addition, a cutoff point of <16% for LV GLS was included in the HFA-PEFF algorithm as a minor criterion for diagnosing HFpEF as recommended by the HFA-ESC in 2019.[5] LV GLS is significantly altered in HFpEF patients, regardless of the loading conditions, as it is impaired due to the pathophysiologic mechanism of HFpEF. Additionally, LV GLS has been demonstrated to be the most accurate component of LV function for predicting the presence of significant myocardial fibrosis, which is the main cause of myocardial stiffness and most common pathophysiologic feature of HFpEF.[23,24]

LV GLS is a parameter used to assess systolic function, and it can also be used as a parameter to assess myocardial fibrosis which causes myocardial stiffness.[23] Therefore, we thought that this could detect the elevated LV filling pressure, not as a parameter to assess diastolic function but as a parameter to assess myocardial stiffness. Overall, we investigated whether the LV GLS was more sensitive in predicting the elevated LV filling pressure. We showed that LV GLS had better sensitivity than the 2016 echocardiography algorithm in determining elevated invasive LV filling pressure. We thought that LV GLS might be added to the echocardiography algorithm to improve the estimation of LAP. Moreover, deficiencies in the algorithm, including indeterminate group, atrial fibrillation, and mitral annulus calcification, might be evaluated using LV GLS. We also believe that LV GLS may be used as a major echocardiographic criterion for the HFA-PEFF algorithm and may be incremental value to HFpEF diagnosis.

5 | STUDY LIMITATIONS

Our study had several limitations, including a single center and a small patient group. Because of our small number of patients, the study included only nine indeterminate patients; therefore, we could not demonstrate whether the LV GLS was adequate to define diastolic dysfunction in those patient groups. In addition, all standard echocardiographic measurements and LV GLS were performed at rest; therefore, we could not assess the relationship between the LV GLS and the impaired functional capacity, which is a highly essential hallmark of HFpEF. Future multicenter studies with a larger study population will be essential to demonstrate the additional effects of GLS on the 2016 ASE/EACVI algorithm and on the HFA-PEFF algorithm.

6 | CONCLUSION

An early assessment of systolic impairment is crucial in patients with HFpEF because it is an independent risk factor for hospitalization and mortality. Our findings suggested that the LV GLS might significantly contribute to the conventional algorithm in predicting the elevated LAP and may be used as the diagnostic criteria in the detection of HFpEF and for an early decision of proper treatment.

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CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, TST, upon reasonable request.

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