

Original Research



Strain-Volume Loop Dynamics: A Novel Perspective on Left Ventricular Dysfunction

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AUTHOR'S SUMMARY

Strain-volume loop (SVL) analysis, which captures myocardial strain and left ventricular (LV) volume changes simultaneously, offers a novel approach to evaluating both systolic and diastolic function and LV remodeling. SVL revealed distinct differences among no cardiac disease, heart failure (HF) with preserved ejection fraction (EF), and HF with reduced EF, with parameters demonstrating sequential changes across disease states. These findings suggest that SVL may reflect functional transitions across HF phenotypes. By providing dynamic insight into remodeling and function, SVL may help support clinical assessment and has the potential to contribute to future evaluation of treatment response.

ABSTRACT

Background and Objectives: Strain-volume loop (SVL) dynamics demonstrate the relationship between myocardial strain and left ventricular (LV) volume throughout the cardiac cycle, offering insights into both systolic and diastolic function. This study aimed to identify SVL characteristics that differentiate heart failure (HF) patients from those without cardiac disease.

Methods: This retrospective analysis included 352 individuals who underwent 3-dimensional (3D) echocardiography at tertiary care hospitals. Participants were classified into no cardiac disease, HF with preserved ejection fraction (HFpEF), and HF with reduced ejection fraction (HFrEF) groups. Temporal 3D strain and LV volume data from each frame were used to construct SVLs. Key parameters—systolic, early and late diastolic slopes, area between curves, and peak strain—were analyzed.

Results: Patients with HFpEF exhibited lower systolic slopes compared to those without cardiac disease, while patients with HFrEF had the lowest values ($p < 0.001$). During early diastole, individuals without cardiac disease exhibited a sharp strain change relative to volume, whereas the HFpEF and HFrEF groups showed diminished changes. Differences in early and late diastolic slopes and the area between the systolic and diastolic curves progressively decreased from individuals without cardiac disease to those with HFpEF and

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Conflict of Interest

The authors have no financial conflicts of interest.

Data Sharing Statement

The data generated in this study is available from the corresponding author upon reasonable request.

Author Contributions

Conceptualization: Cho GY; Data curation: Kim HM, Lee H, Lim Y, Cho GY; Formal analysis: Kim HM, Lee H, Lim Y; Funding acquisition: Cho GY; Investigation: Kim HM, Cho GY; Methodology: Kim HM, Lee H, Lim Y, Cho GY; Project administration: Kim HM, Cho GY; Resources: Kim HM, Lee H, Lim Y, Cho GY; Software: Lee H, Lim Y, Cho GY; Supervision: Kim HM, Cho GY; Validation: Kim HM, Lim Y; Visualization: Kim HM, Lee H, Lim Y; Writing - original draft: Kim HM; Writing - review & editing: Kim HM, Lee H, Lim Y, Cho GY.

HF_{rEF}. Support vector machine analysis using SVL parameters showed strong discrimination, with 0.878 overall accuracy in classifying the 3 groups.

Conclusions: SVL analysis comprehensively represents the strain-volume relationship, distinguishing HF patients from those without cardiac disease. It may serve as a non-invasive tool for evaluating cardiac function, providing insights into functional transitions across HF phenotypes.

Keywords: Echocardiography, three-dimensional; Heart failure; Ventricular function, left; Ventricular dysfunction, diastolic; Ventricular remodeling

INTRODUCTION

Assessing myocardial performance is crucial for diagnosing and managing cardiac diseases. Left ventricular (LV) ejection fraction (EF) is a powerful prognostic indicator used most commonly. However, it does not reflect myocardial properties and is calculated based on the estimated volume change with geometric assumptions.¹⁻³⁾ Myocardial strain, another well-established approach, measures relative deformation of the myocardial tissue.⁴⁾⁵⁾ This method offers a more direct evaluation of myocardial contractile function, and is a strong independent prognostic factor for cardiac outcomes regardless of the LVEF.⁶⁾ However, myocardial strain is influenced by loading conditions, which can affect its accuracy.⁴⁾ Recently, the strain-volume loop (SVL) was introduced as a novel tool for assessing myocardial performance throughout the cardiac cycle.⁷⁾ The SVL captures dynamic changes in systolic and diastolic function and responds sensitively to altered loading conditions.⁸⁾

Heart failure (HF) is the final stage of various cardiac diseases and requires a comprehensive evaluation of systolic and diastolic functions, along with cardiac remodeling.³⁾ LV remodeling is pivotal in HF progression and prognosis. Studies highlight the importance of reverse remodeling as a prognostic marker and a potential therapeutic target.⁹⁾¹⁰⁾ Despite its significance, LV remodeling is often described only through volume and shape changes. Beyond remodeling, a thorough assessment of diastolic function is essential. However, Doppler-derived parameters are highly sensitive to loading conditions and may only provide a momentary evaluation.¹¹⁾ Given these limitations, SVL, which simultaneously captures myocardial strain and volume changes, has the potential to be a novel marker for evaluating systolic and diastolic dysfunction, as well as LV remodeling. However, research on SVL is still in its early stages, and most studies have focused on specific diseases.⁷⁾¹²⁻¹⁶⁾ Consequently, the differences between normal and diseased conditions remain unclear. Therefore, we aimed to characterize the normal function and diastolic and systolic dysfunction using SVL and investigate the serial mechanical changes associated with different HF phenotypes.

METHODS

Ethical statement

This study was conducted in accordance with the latest version of the Declaration of Helsinki and approved by each hospital's Institutional Review Board (Seoul National University Bundang Hospital, No. B-2204-751-10; Chung-Ang University Hospital, No. 2308-019-19485). The informed consent requirement was waived due to the study's retrospective design and minimal expected risk to the participants.

Study population

We conducted a retrospective analysis of echocardiograms obtained from the echocardiography laboratory databases at Seoul National University Bundang Hospital and Chung-Ang University Hospital between January 2015 and June 2024. We included patients aged ≥ 18 years with 2- and 3-dimensional (2D and 3D) echocardiographic images having adequate 3D image quality for strain and volume analysis. In order to evaluate systolic and diastolic function as well as LV remodeling using the SVL, we included patients with HF with preserved EF (HFpEF), HF with reduced EF (HFrEF), classified as stage C or higher according to the universal definition and classification of HF.¹⁷⁾ HFrEF was defined as an LVEF of $\leq 40\%$, while HFpEF was defined as an LVEF of $\geq 50\%$.¹⁷⁾ In addition, patients with normal systolic and diastolic functions were categorized into the group without cardiac disease. Patients with atrial fibrillation, significant valvular disease, or hypertrophic cardiomyopathy were excluded.

Transthoracic echocardiography

As a part of clinical practice, all patients underwent 2D transthoracic echocardiography using commercially available equipment (Vivid E9; GE Medical Systems, Chicago, IL, USA). Imaging included conventional 2D, M-mode, and color Doppler ultrasonography conducted by experienced sonographers according to the recommendations of the American Society of Echocardiography, the European Association of Cardiovascular Imaging, and relevant expert consensus documents.¹⁸⁾

We performed real-time 3D echocardiography using a 4V-D probe (1.5–4.0 MHz; GE Healthcare, Chicago, IL, USA). Volumetric data were captured from an apical 4-chamber view in full-volume mode, with sequential subvolumes acquired over 6 consecutive cardiac cycles during breath-holding. These sub-volumes were combined to produce a complete 3D dataset. The frame rate was maintained at a minimum of 40% of the patient's heart rate.

Strain-volume loop analysis

For 3D analysis, we used the 4D LV Analysis software package (EchoPAC; GE Healthcare), a dedicated tool for quantitative 3D echocardiographic assessment. The software automatically traced the LV endocardium and manual adjustments were made when necessary, in the end-diastolic and end-systolic frames. After generating the 3D LV model, the software provided peak 3D strain values, as well as twist, torsion, and key volumetric parameters, including 3D LV end-diastolic volume (EDV), end-systolic volume, and EF. The reproducibility of 3D echocardiographic measurements in our laboratory has been demonstrated in previous studies. LV volume and strain were derived from the same 3D dataset using an identical tracking algorithm, and intra- and inter-observer intraclass correlation coefficients ranged from 0.936 to 0.991 in our prior validation studies.¹⁹⁾

The software measured the strain and volume values for each frame throughout the cardiac cycle, allowing for detailed frame-by-frame data extraction (**Supplementary Figure 1**). The SVL was derived by plotting the 3D strain values against the corresponding volume values for each frame, with strain on the y-axis and volume on the x-axis. We derived the following parameters from the SVL plot: 1) systolic slope, defined as the slope from the start to the end of systole; 2) early diastolic slope, calculated over the first third of diastole; 3) late diastolic slope, covering the last two-thirds of diastole; 4) area between curves, representing the enclosed area between the systolic and diastolic curves; and 5) peak strain, defined as the peak global longitudinal strain (**Figure 1**). Because the number of frames per cardiac cycle varied among subjects, each cardiac cycle was analyzed on a time-proportion basis. Diastole

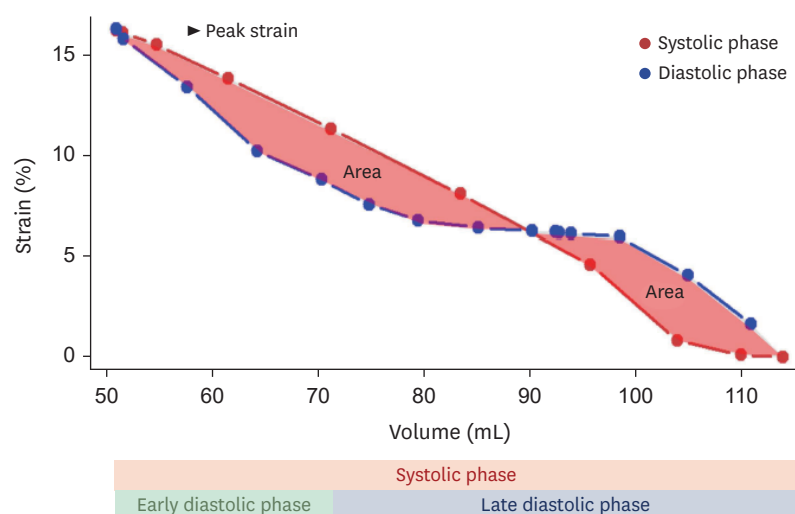


Figure 1. Graphical representation of the strain-volume loop and its derived parameters. Each dot represents a single frame of the cardiac cycle, with the x-axis indicating left ventricular volume and the y-axis indicating strain. The systolic (red) and diastolic (blue) phases are color-coded, and the diastolic phase is divided into an early (first one-third) and a late (remaining two-thirds) phase on a time-proportion basis. Slopes for systolic, early diastolic, and late diastolic phases were calculated as $\Delta\text{strain}/\Delta\text{volume}$ between the start and end points of each segment.

was divided into proportional segments corresponding to its early (first one-third) and late (remaining two-thirds) phases. This proportional division is consistent with physiological observations that rapid ventricular filling predominantly occurs during the early one-third of diastole.²⁰⁾ Each slope parameter was calculated as $\Delta\text{strain}/\Delta\text{volume}$ between the start and end points of the systolic, early diastolic, and late diastolic phases. The strain and slope values were expressed as absolute values ($|x|$) for clarity.

Statistical analysis

Categorical variables are presented as frequencies and percentages, while continuous variables are expressed as mean $\pm$ standard deviation. For continuous data, comparisons between groups were conducted using one-way analysis of variance or the Kruskal-Wallis test, depending on the data distribution. Categorical variables were analyzed using Pearson's χ^2 test. The relationship between the LVEDV and systolic slope was assessed using a quadratic regression model, as the data demonstrated a non-linear correlation. Correlations between conventional echocardiographic measures and SVL parameters were assessed using Pearson's correlation coefficient.

Mathematically, the slope variables were calculated as follows: the start and end points of the curve were selected, and the slope was calculated as the ratio of the difference in the y-axis to the difference in the x-axis. We used Gauss's area formula,²¹⁾ implemented by the R function "polyarea" in the package "pracma" to find the area between 2 curves. If the curves intersected, the areas of each section were computed and summed to obtain the total area.

To identify relevant variables for group discrimination, stepwise logistic regression was applied as an initial screening step to evaluate pairwise discrimination (HFpEF vs. normal and HFpEF vs. HFrEF). The selected variables were subsequently used to construct and compare multiple support vector machine (SVM) models, and the final variable set was determined based on the model with the best classification performance. SVM analysis was

used to classify 3 groups, and the SVM parameters were selected through cross-validation. We also examined the performance of the SVM models under various cost parameters.²²⁾ Model discrimination was further evaluated using receiver operating characteristic (ROC) analysis, and the multi-class area under the ROC curve was calculated for each SVM model. All statistical analyses were conducted using SPSS software (version 22.0; SPSS Inc., Chicago, IL, USA) and R software version 3.6.1 (The R Foundation for Statistical Computing, Vienna, Austria). A p value of less than 0.05 was considered statistically significant.

RESULTS

Study population and baseline characteristics

We analyzed 352 patients (100 no cardiac disease, 148 with HFpEF, and 104 with HFrEF).

Table 1 summarizes the patients' baseline characteristics. The mean age of the study population was 65.2±15.7 years, with the no cardiac disease group being the youngest, followed by the HFrEF group, and the HFpEF group being the oldest. Of the total study population, 46.0% were male; women were more prevalent in the HFpEF group, and men

Table 1. Baseline characteristics according to the groups

Characteristics	No cardiac disease	HFpEF	HFrEF	p value
Number	100	148	104	
Demographics				
Age (years)	50.8±13.6	74.7±9.0	65.6±14.6	<0.001
Male	44 (44.0)	49 (33.1)	69 (66.3)	<0.001
Height (cm)	164.5±9.3	156.5±9.7	163.7±10.6	<0.001
Weight (kg)	64.2±13.6	60.9±11.6	64.3±13.4	0.051
BSA (m ²)	1.7±0.2	1.6±0.2	1.7±0.2	0.001
Underlying diseases				
Hypertension	25 (25.0)	75 (50.7)	51 (49.0)	0.001
Diabetes mellitus	13 (13.0)	52 (35.1)	38 (36.5)	<0.001
Laboratory exam				
Glucose	102.8±21.6	109.3±29.7	114.9±36.7	0.024
BUN	13.6±3.8	24.7±18.1	23.6±15.6	<0.001
Creatinine	0.8±0.2	1.8±2.2	1.2±0.9	<0.001
EGFR	99.2±16.5	61.2±30.8	73.7±29.5	<0.001
HbA1c	5.7±0.8	5.7±0.7	6.3±1.1	<0.001
NT-proBNP	65.1±46.1	2,676.4±4,113.7	19,144.9±76,312.7	0.06
Echocardiography				
LVEDD	46.2±3.9	47.3±5.3	61.2±8.0	<0.001
LVESD	29.2±3.6	30.4±5.7	51.8±9.1	<0.001
LVEDV	82.0±18.7	80.4±26.8	170.0±60.7	<0.001
LVESV	28.6±7.6	30.4±12.5	124.1±54.3	<0.001
LVEF	64.5±3.5	62.6±6.3	28.3±7.0	<0.001
LVMi	75.9±14.0	112.1±31.7	145.6±40.3	<0.001
E/A ratio	1.1±0.4	1.3±0.7	1.0±0.7	0.002
e'	9.1±2.3	5.1±1.4	4.3±1.6	<0.001
a'	8.8±1.7	6.8±2.2	6.8±2.3	<0.001
E/e'	8.2±2.0	19.6±7.5	17.8±0.8	<0.001
LAVI	27.4±5.8	56.5±19.3	52.8±21.7	<0.001
RVSP	25.9±4.4	41.2±15.5	34.1±14.4	<0.001

Values are shown as mean ± standard deviation or number (%).

BSA = body surface area; BUN = blood urea nitrogen; EGFR = estimated glomerular filtration rate; HbA1c = hemoglobin A1c; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LAVI = left atrial volume index; LVEDD = left ventricular end-diastolic dimension; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic dimension; LVESV = left ventricular end-systolic volume; NT-proBNP = N-terminal pro-B-type natriuretic peptide; RVSP = right ventricular systolic pressure.

were more common in the HFrEF group. The LV end-diastolic dimension and LVEDV were not significantly different between the no cardiac disease and HFpEF groups but were notably higher in the HFrEF group. LVEF was >60% on average in the no cardiac disease and HFpEF groups. Diastolic function was normal in all patients in the no cardiac disease group. In contrast, 19.6%, 67.6%, and 12.8% of the patients in the HFpEF group had grades 1, 2, and 3 dysfunctions, respectively. In the HFrEF group, 31.7%, 38.5%, and 7.7% had grades 1, 2, and 3 dysfunctions, respectively, excluding 23 indeterminate cases (22.1%).

Representative strain volume loops for each group

Figure 2 shows the representative SVL for each patient group. The group without cardiac disease exhibited a steep slope during the systolic phase. In contrast, the HFpEF and HFrEF groups showed a rightward shift in the graph. The shift became more pronounced from HFpEF to HFrEF, accompanied by decreased steepness of the systolic phase compared with the no cardiac disease group. During diastole, those without cardiac disease initially displayed a steep slope, indicating a rapid change in strain relative to the volume change. However, this response was less pronounced in the HFpEF and HFrEF groups. The quantitative data confirms this visual assessment (**Table 2**).

Assessment of remodeling and left ventricular systolic function using strain-volume loops

Progressive remodeling is indicated by a decrease in the systolic slope along with simultaneous chamber dilation and a gradual reduction in strain, occurring in the order of no cardiac disease, HFpEF, and HFrEF groups. **Supplementary Figure 2** shows the correlation between 3D LVEDV, a measure commonly used to evaluate LV remodeling, and the systolic slope derived from the SVL. The 3D LVEDV exhibited a non-linear correlation ($r^2=0.673$, $p<0.001$) with a strong association using a quadratic model. The peak strain values decreased in the order of no cardiac disease, HFpEF, and HFrEF groups (**Table 2**).

Evaluation of left ventricular diastolic dysfunction with strain-volume loops

In the no cardiac disease group, a sharp change in strain relative to volume was observed during the early diastolic phase compared with the systolic phase (**Figure 2A**). However, in patients with HFpEF and HFrEF, this sharp strain change during early diastole diminished progressively (**Figures 2B and C, Figure 3B**). In contrast, the late diastolic slope did not differ between the no cardiac disease and HFpEF groups but decreased only in the HFrEF group. Consequently, the difference between the early and late diastolic slopes observed in the no cardiac disease group narrowed in HFpEF and HFrEF groups, with the slopes becoming nearly similar in HFrEF. To further investigate this trend, we analyzed the area between the systolic and diastolic curves and discovered that it was largest in subjects without cardiac disease (88.74 ± 51.01), progressively decreasing in HFpEF (65.57 ± 47.50) and HFrEF (45.63 ± 38.89) (**Figure 3D**).

Table 2. Strain-volume loop parameters according to the groups

Parameters	No cardiac disease	HFpEF	HFrEF	p value	p value*	p value†	p value‡
Systolic slope (%/mL)	0.33±0.08	0.28±0.10	0.14±0.06	<0.001	<0.001	<0.001	<0.001
Early diastolic slope (%/mL)	0.51±0.21	0.34±0.18	0.17±0.13	<0.001	<0.001	<0.001	<0.001
Late diastolic slope (%/mL)	0.25±0.09	0.22±0.08	0.14±0.07	<0.001	0.362	<0.001	<0.001
Area between curves	88.74±51.01	65.57±47.50	45.63±38.89	<0.001	0.001	<0.001	0.002
Peak strain (%)	17.10±3.00	13.30±6.90	6.90±2.70	<0.001	<0.001	<0.001	<0.001

Values are given as the mean with standard deviation. For ease of interpretation, we utilize the absolute value |x| for both peak strain and slopes.

HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction.

*Between no cardiac disease and HFpEF; †Between no cardiac disease and HFrEF; ‡Between HFpEF and HFrEF.

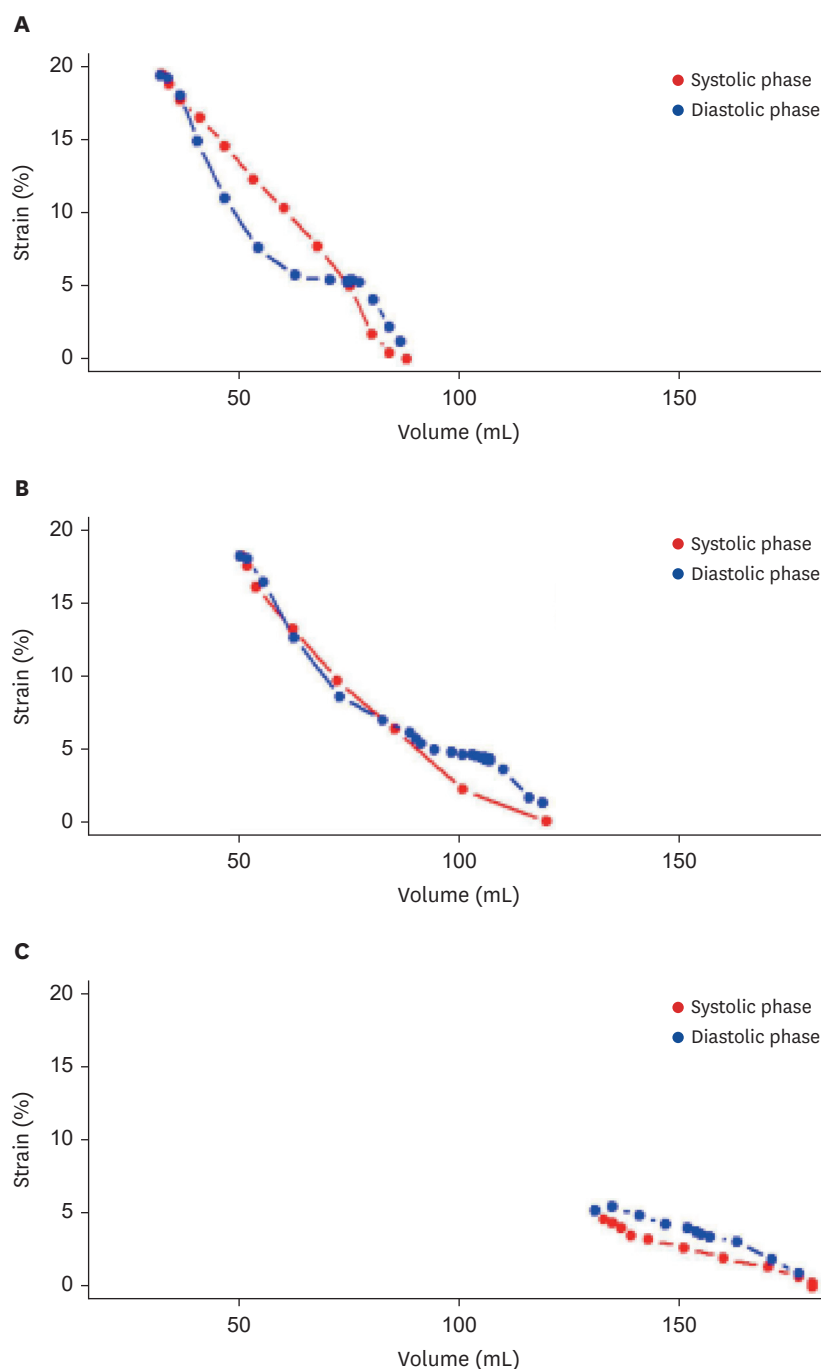


Figure 2. Representative strain-volume loops for each group. (A) No cardiac disease, (B) HFpEF, (C) HFrEF. HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction.

Disease differentiation performance of strain-volume loop parameters

We analyzed the SVL parameters using an SVM to assess their ability to differentiate between no cardiac disease, HFpEF, and HFrEF. The accuracy was high when LVEF (a standard parameter) was used to predict HFrEF. However, distinguishing between no cardiac disease and HFpEF was challenging (accuracy: 0.706 and 0.747 for no cardiac disease and HFpEF, respectively, **Table 3**). The peak strain showed similar trends to LVEF (overall accuracy: 0.735). However, the overall accuracy improved to 0.818 when HFrEF was predicted using

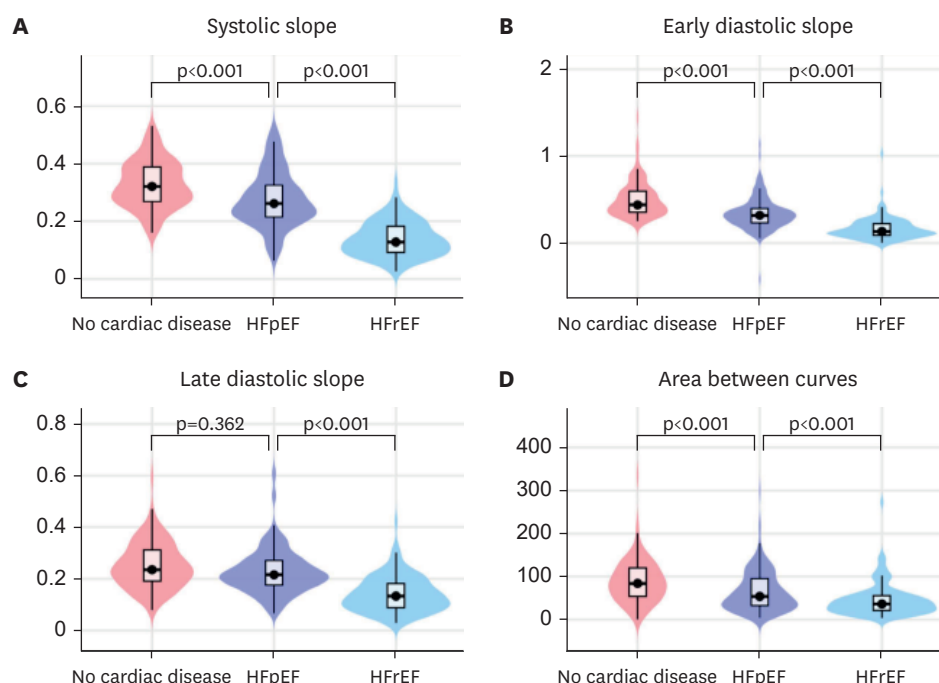


Figure 3. Differences in strain-volume loop parameters for each group. Violin plots illustrating the distribution of each parameter by group. (A) Systolic slope, (B) Early diastolic slope, (C) Late diastolic slope, and (D) Area between the curves.

HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction.

5 graph-based indicators (systolic slope, early diastolic slope, late diastolic slope, area between curves, and peak strain). We identified 3 highly relevant indicators, systolic slope, early diastolic slope, and peak strain, through stepwise selection, which further increased the overall accuracy to 0.878. We also examined the performance of the models under various cost parameters in the SVM (**Figure 4**). The results demonstrated that the SVM model with the selected indicators performed best across all cases.

Table 3. Performance evaluation of support vector machine using strain-volume loop parameters

Variables	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy	Overall accuracy (95% CI)	Multi-class AUC
LVEF						0.755 (0.707–0.800)	0.897
No cardiac disease vs. others	0.586	0.826	0.569	0.836	0.706		
HFpEF vs. others	0.696	0.798	0.715	0.783	0.747		
HFrEF vs. others	1.000	0.996	0.991	1.000	0.998		
Peak strain						0.735 (0.686–0.781)	0.866
No cardiac disease vs. others	0.606	0.925	0.760	0.857	0.765		
HFpEF vs. others	0.723	0.754	0.682	0.789	0.738		
HFrEF vs. others	0.875	0.903	0.792	0.945	0.889		
Systolic slope + early diastolic slope + late diastolic slope + area between curves + peak strain						0.818 (0.773–0.857)	0.941
No cardiac disease vs. others	0.707	0.972	0.909	0.894	0.901		
HFpEF vs. others	0.831	0.813	0.764	0.867	0.822		
HFrEF vs. others	0.904	0.923	0.832	0.958	0.914		
Systolic slope + early diastolic slope + peak strain						0.878 (0.839–0.910)	0.965
No cardiac disease vs. others	0.839	0.964	0.902	0.938	0.901		
HFpEF vs. others	0.885	0.872	0.834	0.912	0.878		
HFrEF vs. others	0.904	0.968	0.922	0.960	0.936		

AUC = area under the curve; CI = confidence interval; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction.

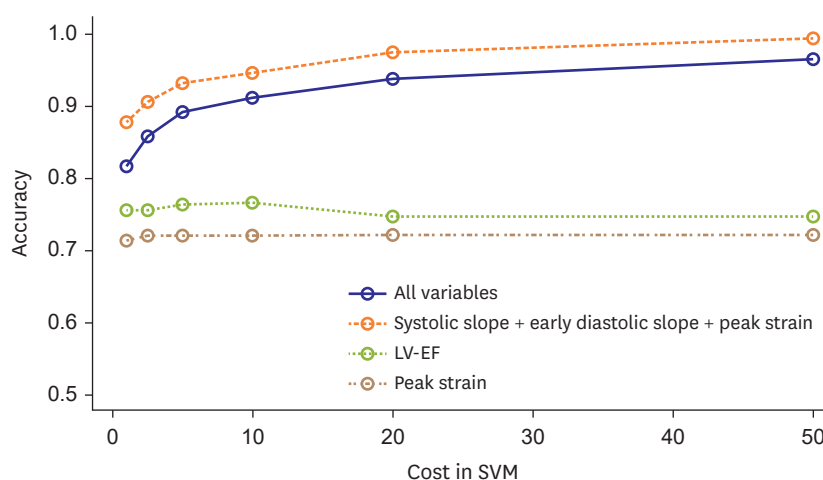


Figure 4. Performance evaluation of SVM using strain-volume loop parameters. Graph showing the accuracy of each variable as the cost parameter of the SVM changes.

LVEF = left ventricular ejection fraction; SVM = support vector machine.

Correlation between strain-volume loop parameters and conventional echocardiographic parameters

Figure 5 presents the correlation between conventional echocardiographic parameters and SVL measurements, illustrated using a correlation plot and heatmap. The systolic slope exhibited the strongest correlation with the conventional parameters LVEF and LVEDV. Early and late diastolic slopes were significantly correlated with LVEF, and the early diastolic slope demonstrated the strongest association with the traditional diastolic parameter, e' , followed by E/e' . In addition, late diastolic slope and area under the curve, which characterize the diastolic phase, were significantly correlated with traditional diastolic parameters. Of the diastolic parameters outlined in the current guidelines,²³ e' , left atrial volume index, and E/e' showed a significant correlation with SVL parameters. In contrast, tricuspid regurgitation velocity demonstrated a relatively weak correlation.

DISCUSSION

In this study, we aimed to characterize the SVL in individuals without cardiac disease and patients with HF. Our key findings are as follows: 1) The systolic slope of the SVL progressively decreased from no cardiac disease to HFpEF and further decreased in HFrEF. 2) In individuals without cardiac disease, early diastole showed an abrupt strain change relative to volume, followed by a more gradual late diastolic slope. In the HFpEF and HFrEF groups, this early diastolic drop was absent, and the slope difference between early and late diastole progressively decreased from HFpEF to HFrEF. 3) The SVL parameters demonstrated strong discriminant performance in distinguishing between the no cardiac disease, HFpEF, and HFrEF groups. These patterns may reflect gradual changes in LV mechanics across HF phenotypes, suggesting a potential continuum of functional alterations among different HF subtypes. Furthermore, we anticipate that incorporating SVL along with absolute strain values will enhance the diagnostic accuracy. These findings underscore the potential of SVL as a noninvasive tool for enhanced cardiac function assessment.

LV remodeling, a critical aspect of HF, has traditionally been evaluated based on cavity size and wall thickness. However, the normal ranges can vary depending on patient size,

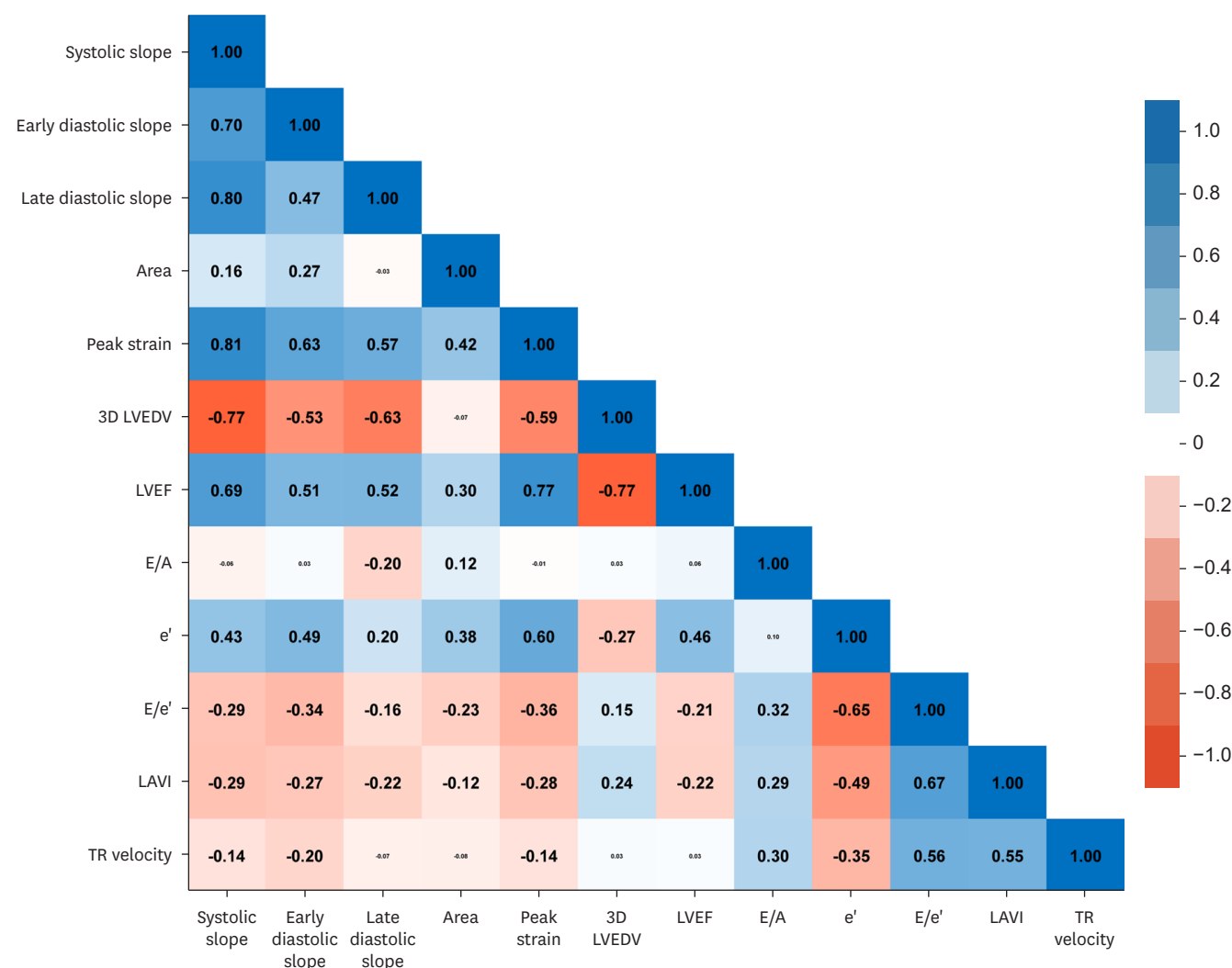


Figure 5. Relationship between conventional echocardiographic parameters and SVL parameters. Correlation matrix of conventional echocardiographic and SVL parameters. Spearman's ρ is color-coded, and significant ($p < 0.05$) coefficients are displayed in larger font. 3D = 3-dimensional; LAVI = left atrial volume index; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; SVL = strain-volume loop; TR = tricuspid regurgitation.

even when adjusted for body surface area. Moreover, simply measuring the cavity size and wall thickness may not accurately reflect the underlying condition because of the distinct mechanisms of pressure and volume overloads that lead to different forms of remodeling. The systolic slope derived from the SVL analysis offers a more integrated approach to assess remodeling by quantifying the relationship between strain and volume throughout the cardiac cycle. Previous pilot studies have demonstrated the potential utility of SVL for remodeling assessment,¹⁴⁾ and other studies have indicated that the systolic slope can be a useful marker, even in patients with different remodeling mechanisms but similar strain values.⁷⁾ In this study, we observed statistically significant differences in the systolic slope among the no cardiac disease, HFpEF, and HFrEF groups. The systolic slope showed a strong correlation with LVEDV, the most common indicator of remodeling. Future studies exploring its potential to reflect reverse remodeling in patients with HF may establish the systolic slope of the SVL as a new parameter that reflects LV remodeling.

LVEF and strain are widely used measures of systolic function; however, they have inherent limitations. In contrast, SVL considers the impact of loading conditions and provides a more comprehensive assessment of systolic function throughout the entire systolic phase.⁸⁾⁽²⁴⁾

Diastolic dysfunction, which leads to increased LV filling pressure, is the main component of HFpEF pathophysiology.²⁵⁾ Current methods, such as Doppler analysis, are complex, overlap with normal functions, and are sensitive to loading conditions. The LA strain has shown promise as an indirect tool for assessing diastolic function; however, it does not reliably reflect LV function or elevated filling pressures, particularly in patients with preserved systolic function.²⁶⁾ In contrast, SVL has the advantage of directly assessing LV relaxation capacity. In individuals without cardiac disease, the SVL demonstrates a rapid strain change during early diastole, corresponding to rapid filling, followed by a gradual slope during diastasis and late diastole. However, this early rapid strain change was absent in patients with HFpEF and HFrEF, and the slope difference between early and late diastole diminished, with a reduced area between the systolic and diastolic curves. Notably, individuals without cardiac disease, the systolic curve is positioned above the early diastolic curve, indicating that for a given volume, the strain values during systole are typically higher than those during early diastole. However, in some patients with diastolic dysfunction, the steep decline in the early diastolic phase is attenuated and positioned above the systolic curve. The early diastolic slope was closely related to the existing indicator e' , but in the case of e' , evaluation is limited in cases with regional wall motion or mitral annular calcification.²³⁾ The early diastolic slope may provide a more reliable assessment in such cases. The early diastolic slope showed significant differences between the groups, but the late diastolic slope remained similar between the no cardiac disease and HFpEF groups. Previous studies have shown that early diastolic slope is associated with patients with HFpEF, although the definitions were different.¹⁶⁾ Taken together, these results suggest that the reduced early diastolic slope of the SVL is a characteristic feature of diastolic dysfunction and could be further used to diagnose and predict the prognosis of patients with HF and diastolic dysfunction.

Echocardiography remains the most accessible modality for diagnosing and managing cardiac diseases, including evaluating systolic and diastolic functions. However, it has some limitations. First, the current methods that focus on heart size and wall thickness may not fully capture the complexity of cardiac remodeling. Second, evaluating the diastolic function, which plays a central role in HFpEF and has important prognostic implications for HFrEF²⁷⁾ may occasionally present challenges. SVL addresses these limitations by visualizing strain–volume relationships throughout the cardiac cycle and offers the potential for more precise tracking of LV remodeling and functional changes. Moreover, SVL may conceptually complement guideline-based assessments focused on left atrial pressure by providing direct insights into LV diastolic mechanics.

Previous SVL studies relied on 2D echocardiography using monoplane LV volumes⁷⁾⁽¹⁵⁾⁽¹⁶⁾⁽²³⁾; however, this is the first study to capture the entire cardiac cycle using 3D ultrasound. Notably, most previous studies have been pilot analyses with small patient groups focusing on diastolic dysfunction. We included 100 individuals without cardiac disease to establish a reference graph and compared it with the characteristics of patients with HFpEF and HFrEF to provide a more comprehensive understanding of SVL. Additionally, this study demonstrated a pattern of gradual change from the no cardiac disease group to HFpEF and HFrEF, suggesting that SVL parameters may represent functional transitions across the HF spectrum.

This study had some limitations. This was a proof-of-concept study, and patients were selected based on image quality, which may introduce some bias as it limits the generalizability. Second, we analyzed a virtual single cycle obtained by stitching 6 cardiac cycles together, which raises concerns about whether it adequately represents overall cardiac function. Patients with severe arrhythmia or atrial fibrillation were excluded; however, some variability due to factors such as respiration may remain. Third, this study did not include a clinical outcome analysis related to SVL characteristics. Lastly, differences in demographic and clinical characteristics such as age, sex, and comorbidities may have partially influenced the results; however, these variations are inherent to each HF phenotype and reflect real-world disease characteristics.

SVL analysis provides a comprehensive representation of the relationship between LV strain and volume throughout the cardiac cycle. Our findings highlight the potential of SVL parameters as a noninvasive tool for enhancing cardiac function evaluation. Conventional echocardiography remains the cornerstone of cardiac imaging. However, SVL addresses areas that are difficult to assess using current techniques, providing deeper insights into dynamic myocardial changes. Further studies integrating SVL into clinical practice may solidify its role in improving the diagnosis and therapeutic monitoring of various heart diseases.

SUPPLEMENTARY MATERIALS

Supplementary Figure 1

Steps for generating the strain-volume loop. (A) Selection of 3D image, (B) Selecting and adjusting the long axis of the ventricle in end-diastolic frame, (C) Selecting and adjusting the long axis of the ventricle in end-systolic frame, (D) Automatic calculation of LV volume and LVEF, (E) Tracking of the 3D region of interest throughout the cardiac cycle, (F) Extract CSV file from 3D dataset.

Supplementary Figure 2

Relationship between systolic slope and 3D LVEDV. Systolic slope and 3D LVEDV showed a strong correlation using a quadratic model.

REFERENCES

1. Vancheri F, Longo G, Henein MY. Left ventricular ejection fraction: clinical, pathophysiological, and technical limitations. *Front Cardiovasc Med* 2024;11:1340708. [PUBMED](#) | [CROSSREF](#)
2. Lenell J, Lindahl B, Karlsson P, et al. Reliability of estimating left ventricular ejection fraction in clinical routine: a validation study of the SWEDEHEART registry. *Clin Res Cardiol* 2023;112:68-74. [PUBMED](#) | [CROSSREF](#)
3. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021;42:3599-726. [PUBMED](#) | [CROSSREF](#)
4. Voigt JU, Cvijic M. 2- and 3-Dimensional myocardial strain in cardiac health and disease. *JACC Cardiovasc Imaging* 2019;12:1849-63. [PUBMED](#) | [CROSSREF](#)
5. Park JH. Two-dimensional echocardiographic assessment of myocardial strain: important echocardiographic parameter readily useful in clinical field. *Korean Circ J* 2019;49:908-31. [PUBMED](#) | [CROSSREF](#)
6. Park JJ, Park JB, Park JH, Cho GY. Global longitudinal strain to predict mortality in patients with acute heart failure. *J Am Coll Cardiol* 2018;71:1947-57. [PUBMED](#) | [CROSSREF](#)

7. Hulshof HG, van Dijk AP, George KP, Hopman MTE, Thijssen DHJ, Oxborough DL. Exploratory assessment of left ventricular strain-volume loops in severe aortic valve diseases. *J Physiol* 2017;595:3961-71. [PUBMED](#) | [CROSSREF](#)
8. Kleinnibbelink G, Hulshof HG, van Dijk APJ, et al. Effects of preload manipulation on right ventricular contractility: invasive pressure-area loop versus non-invasive strain-area loop. *J Am Soc Echocardiogr* 2021;34:447-9. [PUBMED](#) | [CROSSREF](#)
9. Cohn JN, Ferrari R, Sharpe N. Cardiac remodeling--concepts and clinical implications: a consensus paper from an international forum on cardiac remodeling. Behalf of an international forum on cardiac remodeling. *J Am Coll Cardiol* 2000;35:569-82. [PUBMED](#) | [CROSSREF](#)
10. Yu CM, Bleeker GB, Fung JW, et al. Left ventricular reverse remodeling but not clinical improvement predicts long-term survival after cardiac resynchronization therapy. *Circulation* 2005;112:1580-6. [PUBMED](#) | [CROSSREF](#)
11. Nagueh SF. Left ventricular diastolic function: understanding pathophysiology, diagnosis, and prognosis with echocardiography. *JACC Cardiovasc Imaging* 2020;13:228-44. [PUBMED](#) | [CROSSREF](#)
12. Hubert A, Le Rolle V, Galli E, Bidaud A, Hernandez A, Donal E. New expectations for diastolic function assessment in transthoracic echocardiography based on a semi-automated computing of strain-volume loops. *Eur Heart J Cardiovasc Imaging* 2020;21:1366-71. [PUBMED](#) | [CROSSREF](#)
13. Hulshof HG, van Dijk AP, George KP, et al. Echocardiographic-derived strain-area loop of the right ventricle is related to pulmonary vascular resistance in pulmonary arterial hypertension. *JACC Cardiovasc Imaging* 2017;10:1286-8. [PUBMED](#) | [CROSSREF](#)
14. Lilli A, Baratto MT, Del Meglio J, et al. Three-dimensional simultaneous strain-volume analysis describes left ventricular remodelling and its progression: a pilot study. *Eur J Echocardiogr* 2011;12:520-7. [PUBMED](#) | [CROSSREF](#)
15. Kerstens TP, Weerts J, van Dijk APJ, et al. Left ventricular strain-volume loops and diastolic dysfunction in suspected heart failure with preserved ejection fraction. *Int J Cardiol* 2023;378:144-50. [PUBMED](#) | [CROSSREF](#)
16. Kerstens TP, Weerts J, van Dijk APJ, et al. Association of left ventricular strain-volume loop characteristics with adverse events in patients with heart failure with preserved ejection fraction. *Eur Heart J Cardiovasc Imaging* 2023;24:1168-76. [PUBMED](#) | [CROSSREF](#)
17. Bozkurt B, Coats AJ, Tsutsui H, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the universal definition of heart failure. *J Card Fail* 2021;27:387-413. [PUBMED](#) | [CROSSREF](#)
18. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28:1-39.e14. [PUBMED](#) | [CROSSREF](#)
19. Kim HM, Hwang IC, Yoon YE, et al. Prediction of deterioration of left ventricular function using 3-dimensional speckle-tracking echocardiography in patients with left bundle-branch block. *J Am Heart Assoc* 2023;12:e026194. [PUBMED](#) | [CROSSREF](#)
20. Little WC, Cheng CP. Left ventricular-arterial coupling in conscious dogs. *Am J Physiol* 1991;261:H70-6. "https://pubmed.ncbi.nlm.nih.gov/36583438" [PUBMED](#) | [CROSSREF](#)
21. Bart B. The surveyor's area formula. *Coll Math J* 1986;17:326-37. [CROSSREF](#)
22. Suthaharan S. Support vector machine. In: Suthaharan S, editor. *Machine Learning Models and Algorithms for Big Data Classification: Thinking with Examples for Effective Learning*. New York (NY): Springer; 2016. p.207-235
23. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2016;29:277-314. [PUBMED](#) | [CROSSREF](#)
24. Hulshof HG, van Dijk AP, Hopman MTE, et al. Acute impact of changes to hemodynamic load on the left ventricular strain-volume relationship in young and older men. *Am J Physiol Regul Integr Comp Physiol* 2020;318:R743-50. [PUBMED](#) | [CROSSREF](#)
25. Youn JC, Ahn Y, Jung HO. Pathophysiology of heart failure with preserved ejection fraction. *Heart Fail Clin* 2021;17:327-35. [PUBMED](#) | [CROSSREF](#)
26. Nagueh SF, Khan SU. Left atrial strain for assessment of left ventricular diastolic function: focus on populations with normal LVEF. *JACC Cardiovasc Imaging* 2023;16:691-707. [PUBMED](#) | [CROSSREF](#)
27. Benfari G, Miller WL, Antoine C, et al. Diastolic determinants of excess mortality in heart failure with reduced ejection fraction. *JACC Heart Fail* 2019;7:808-17. [PUBMED](#) | [CROSSREF](#)