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Clinical value of automated left atrial strain analysis based on deep learning algorithms in echocardiography for early diagnosis of heart failure with preserved ejection fraction

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Abstract

Background Heart failure with preserved ejection fraction (HFpEF) remains challenging to diagnose due to the absence of overt systolic dysfunction. Left atrial reservoir strain (LARS) has emerged as a sensitive marker of left atrial dysfunction, yet its clinical application is constrained by measurement variability and time demands. We investigated the diagnostic performance of automated deep learning (DL)-derived LARS for early HFpEF identification.

Methods This retrospective observational study enrolled 200 patients (107 HFpEF, 93 controls) who underwent transthoracic echocardiography. HFpEF was diagnosed per 2021 ESC guidelines. All echocardiographic datasets were analyzed using a validated DL-based automated platform (EchoGo Pro, Ultromics). Agreement between DL-derived and manually measured parameters was evaluated by Pearson correlation and Bland–Altman analysis. Diagnostic performance was assessed by receiver operating characteristic (ROC) curve analysis, and independent predictors of HFpEF were identified via multivariate logistic regression.

Results DL-derived LARS was significantly lower in HFpEF patients compared to controls (19.3 ± 5.7% vs. 30.8 ± 6.4%, $P < 0.001$). Strong agreement was demonstrated between DL-derived and manually measured LARS (r = 0.911; mean bias − 0.67 ± 2.34%), with superior reproducibility of the automated approach (ICC = 0.974). DL-derived LARS achieved an AUC of 0.806 (95% CI 0.748–0.864), sensitivity of 81.3%, and specificity of 83.9% at a cutoff of 24.2%, comparable to manually derived LARS (AUC = 0.818, $P = 0.631$) and numerically higher than LAVI and E/e' ratio, although these pairwise differences did not reach statistical significance. On multivariate analysis, DL-derived LARS was the strongest independent echocardiographic predictor of HFpEF (adjusted OR = 0.74, 95% CI 0.65–0.84, $P < 0.001$).

Conclusions Automated DL-based LARS analysis provides accurate, reproducible, and time-efficient quantification comparable to expert manual measurement, demonstrating robust diagnostic value for early HFpEF identification.

Keywords Heart failure with preserved ejection fraction, Left atrial strain, Deep learning, Echocardiography, Diastolic dysfunction, Speckle-tracking echocardiography

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Introduction

Heart failure with preserved ejection fraction (HFpEF) now accounts for approximately 50% of all heart failure cases worldwide, affecting an estimated 64 million patients globally, and its prevalence continues to rise in parallel with the increasing burden of aging, obesity, hypertension, and type 2 diabetes mellitus [1, 2]. Despite substantial morbidity and mortality, HFpEF remains a clinically challenging diagnosis owing to its heterogeneous pathophysiology and the absence of overt systolic dysfunction on standard echocardiography [3, 4].

Current diagnostic approaches rely on the integration of clinical symptoms, natriuretic peptide levels, and echocardiographic evidence of diastolic dysfunction, as outlined in the 2021 European Society of Cardiology (ESC) guidelines and the Heart Failure Association Pre-test assessment, Echocardiography and natriuretic peptide, Functional testing, Final etiology (HFA-PEFF) diagnostic algorithm [5]. However, conventional echocardiographic parameters, including E/e' ratio, left atrial volume index (LAVI), and left ventricular mass index, demonstrate limited sensitivity for early HFpEF identification, particularly when left ventricular filling pressures are only mildly elevated at rest [6, 7]. These limitations have prompted growing interest in more sensitive myocardial deformation imaging biomarkers.

Left atrial (LA) longitudinal strain assessed by two-dimensional speckle-tracking echocardiography has emerged as a robust imaging biomarker reflecting LA reservoir function and cumulative left ventricular filling pressure burden [8, 9]. LA reservoir strain (LARS) is less angle-dependent and less influenced by loading conditions than conventional Doppler parameters, offering superior diagnostic and prognostic information in HFpEF [10, 11]. Multiple studies have confirmed that LARS is significantly impaired in HFpEF and provides incremental diagnostic value beyond standard echocardiographic parameters, with a recent meta-analysis further validating the prognostic significance of peak atrial longitudinal strain across varying ejection fraction categories [12, 13]. Nevertheless, the widespread clinical adoption of LA strain analysis has been hampered by time-consuming manual measurements, considerable intervendor variability, and the requirement for specialized operator expertise [14].

The emergence of deep learning (DL)-based automated echocardiographic analysis platforms offers a compelling solution to these barriers, enabling rapid, reproducible, and operator-independent quantification of myocardial deformation parameters directly from standard echocardiographic cine loops [15]. More broadly, machine learning and artificial intelligence-based approaches have been increasingly integrated into cardiovascular imaging and clinical decision-making, demonstrating promising performance in automated image interpretation, risk stratification, and outcome prediction across various cardiovascular conditions [31–33]. However, the application of DL-based automation specifically to LA strain quantification and its clinical diagnostic value for HFpEF identification remain incompletely characterized. Therefore, the present study aimed to evaluate the diagnostic performance of automated DL-derived LARS for early HFpEF identification and to compare its accuracy and reproducibility with conventional manually derived echocardiographic parameters.

Materials and methods

Study design and patient population

This retrospective observational study was conducted at our institution and enrolled 200 patients who underwent transthoracic echocardiography (TTE) between December 2022 and December 2024. The primary objective of this study was to evaluate the diagnostic performance of automated DL-derived LARS for HFpEF identification. The secondary objectives were to assess the agreement and reproducibility between DL-derived and manually measured echocardiographic parameters and to identify independent echocardiographic predictors of HFpEF. Patients were allocated into two groups based on comprehensive clinical and echocardiographic evaluation: an HFpEF group ($n = 107$) and a control group ($n = 93$). The diagnosis of HFpEF was established in accordance with the 2021 European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of acute and chronic heart failure, requiring the presence of symptoms and/or signs of heart failure, a left ventricular ejection fraction (LVEF) $\geq 50\%$, objective evidence of elevated left ventricular filling pressures or structural/functional cardiac abnormalities, and elevated natriuretic peptide levels (NT-proBNP > 125 pg/mL in non-acute settings). The control group consisted of individuals with comparable age and sex distribution referred to our echocardiography laboratory for routine cardiac evaluation during the same enrollment period who demonstrated no clinical evidence of heart failure, normal LVEF, and no significant structural cardiac abnormalities on comprehensive echocardiographic assessment. All control subjects underwent NT-proBNP measurement (required to be within normal limits) and comprehensive diastolic function assessment to exclude subclinical diastolic dysfunction according to ASE/EACVI criteria. The study protocol was approved by the Institutional Review Board of our hospital, and the requirement for informed consent was waived given the retrospective nature of the study. All procedures were conducted in accordance with the Declaration of Helsinki.

Inclusion criteria for the HFpEF group were as follows: age ≥ 18 years, LVEF ≥ 50% confirmed by echocardiography, clinically established heart failure diagnosis supported by natriuretic peptide elevation and echocardiographic diastolic dysfunction criteria, and availability of complete echocardiographic data of adequate image quality for both conventional parameter measurement and speckle-tracking analysis. Inclusion criteria for the control group required age ≥ 18 years, absence of cardiac symptoms, normal LVEF, and absence of significant valvular, structural, or functional cardiac abnormalities. Exclusion criteria applied to both groups included: atrial fibrillation or other significant cardiac arrhythmias at the time of echocardiographic examination (patients with a documented history of paroxysmal atrial fibrillation were not excluded provided they were in sinus rhythm during the index echocardiographic study), more than mild mitral or aortic valvular disease, hypertrophic cardiomyopathy, constrictive pericarditis, prior cardiac surgery, inadequate acoustic windows resulting in suboptimal image quality precluding reliable strain analysis, and LVEF < 50%. Patients with incomplete clinical records or missing laboratory data essential for HFpEF classification were also excluded.

Conventional echocardiographic assessment

All transthoracic echocardiographic examinations were performed using a commercially available ultrasound system (Vivid E95, GE HealthCare, Horten, Norway) equipped with a 1.5–4.0 MHz phased-array transducer, following the recommendations of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI). Standard two-dimensional (2D) grayscale images were acquired across parasternal long-axis, parasternal short-axis, apical four-chamber, apical two-chamber, and apical three-chamber views at a frame rate of ≥ 50 frames per second to ensure adequate temporal resolution for subsequent speckle-tracking analysis. At least three consecutive cardiac cycles were recorded per view, and image loops were stored in Digital Imaging and Communications in Medicine (DICOM) format for offline analysis.

Conventional diastolic parameters were measured according to current ASE/EACVI guidelines. Mitral inflow peak early diastolic velocity (E wave) and late diastolic velocity (A wave) were obtained by pulsed-wave Doppler with the sample volume positioned at the mitral leaflet tips in the apical four-chamber view, and the E/A ratio was subsequently calculated. Tissue Doppler imaging (TDI) was performed to obtain septal and lateral mitral annular early diastolic velocities (e' septal and e' lateral), and the average E/e' ratio was derived as an estimate of left ventricular filling pressure. The peak tricuspid regurgitation velocity was measured using continuous-wave Doppler for estimation of right ventricular systolic pressure. Left atrial volume index (LAVI) was calculated using the biplane area-length method from apical four-chamber and two-chamber views and indexed to body surface area. LVEF was determined using the modified biplane Simpson's method. Manual LARS measurement was performed offline using dedicated speckle-tracking software (EchoPAC version 204, GE HealthCare) on the same DICOM cine loops used for automated analysis. The left atrial endocardial border was manually traced at end-systole in the apical four-chamber and two-chamber views, and the software automatically generated LA strain–time curves using a speckle-tracking algorithm. LARS was defined as peak positive longitudinal strain measured relative to the QRS onset as the zero-reference point, consistent with the convention used by the DL platform. Manual adjustment of the endocardial tracing was required in approximately 15% of cases to achieve adequate tracking quality. All measurements were averaged over three consecutive cardiac cycles and performed by two experienced echocardiographers with more than five years of dedicated echocardiographic experience, who were blinded to clinical diagnoses and group assignments. Inter-observer and intra-observer variability were assessed in a randomly selected subset of 40 patients.

Deep learning-based automated left atrial strain analysis

All stored DICOM echocardiographic datasets identical to those used for manual analysis were processed using a validated commercial deep learning-based automated analysis platform (EchoGo Pro, Ultromics Ltd., Oxford, United Kingdom). This platform employs convolutional neural networks (CNNs) to automatically classify and identify standard echocardiographic views from 2D cine loops, followed by automated segmentation of cardiac chambers and quantification of both conventional parameters and speckle-tracking-derived strain measurements without manual user input. The algorithm automatically delineated the left atrial endocardial border throughout the cardiac cycle in the apical four-chamber and two-chamber views, tracking myocardial speckles frame by frame to generate LA strain–time curves. Consistent with the manual measurement protocol, the zero-reference for strain quantification was set at QRS onset. Left atrial reservoir strain (LARS), defined as the peak positive longitudinal strain occurring at end-systole relative to QRS onset, was automatically extracted as the primary study endpoint. LARS was selected as the primary DL endpoint because reservoir strain has the most robust evidence base as a diagnostic and prognostic marker in HFpEF and demonstrates the highest reproducibility

among the three phasic LA strain components; LA conduit strain and LA contractile strain were also generated by the platform but were not analyzed as primary endpoints in the present study, as their independent diagnostic contribution in HFpEF remains less well established and was considered beyond the predefined scope of this work. In addition, the DL platform simultaneously derived conventional parameters including LAVI, E/A ratio, e' velocity, E/e' ratio, and LVEF, enabling direct comparison with manually obtained measurements. All 200 echocardiographic datasets were successfully processed by the automated platform without processing failure or the need for manual preprocessing, quality screening, or resubmission. The mean automated processing time per study was recorded.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD) or median with interquartile range (IQR) depending on the normality of distribution, as assessed by the Shapiro–Wilk test and confirmed by the Kolmogorov–Smirnov test. Categorical variables are presented as frequencies and percentages. Between-group comparisons of continuous variables were performed using the independent samples t-test or Mann–Whitney U test as appropriate, while categorical variables were compared using the chi-square test or Fisher's exact test. Agreement between DL-derived and manually measured parameters was evaluated using Pearson correlation coefficients and Bland–Altman analysis, with calculation of mean bias and 95% limits of agreement. Inter-observer and intra-observer reproducibility was assessed using the intraclass correlation coefficient (ICC) with 95% confidence intervals. Diagnostic performance of DL-derived LARS and conventional diastolic parameters for HFpEF identification was evaluated using receiver operating characteristic (ROC) curve analysis, with comparison of areas under the curve (AUC) performed using the DeLong method. Optimal diagnostic cutoff values were determined by maximizing the Youden index. Univariate and multivariate binary logistic regression analyses were conducted to identify independent echocardiographic predictors of HFpEF, with variables achieving $P < 0.10$ on univariate analysis entered into the multivariate model. LVEF was not included as a covariate in the multivariate model because both groups had preserved ejection fraction by study design (all participants had LVEF ≥ 50%), and the observed between-group difference (58.7% vs. 61.2%) was not considered clinically meaningful in the context of HFpEF classification; inclusion of LVEF would have introduced redundancy with the diagnostic definition rather than serving as a meaningful confounder. Variance inflation factors (VIFs) were calculated to assess multicollinearity among predictor variables included in the multivariate model; all VIFs were below 3.0, indicating acceptable collinearity levels. All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and MedCalc version 20.0 (MedCalc Software, Ostend, Belgium). A two-tailed P value of < 0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 200 patients were enrolled in the final analysis, comprising 107 patients in the HFpEF group and 93 patients in the control group. The baseline demographic and clinical characteristics of both groups are summarized in Table 1. The mean age of the HFpEF group was 67.4 ± 9.8 years, compared with 63.1 ± 10.3 years in the control group ($P = 0.003$). The proportion of female patients was higher in the HFpEF group (58.9% vs. 44.1%, $P = 0.041$). Body mass index (BMI) was significantly greater in the HFpEF group (27.6 ± 3.9 kg/m^2 vs. 25.1 ± 3.4 kg/m^2, $P < 0.001$). The prevalence of hypertension (72.9% vs. 38.7%, $P < 0.001$), type 2 diabetes mellitus (41.1% vs. 19.4%, $P = 0.002$), and atrial fibrillation history prior to enrollment (excluded at time of echocardiography) was all significantly higher in the HFpEF group. NT-proBNP levels were markedly elevated in the HFpEF group compared to controls (387.4 ± 214.6 pg/mL vs. 68.3 ± 41.2 pg/mL, $P < 0.001$). No significant between-group differences were observed in smoking history, coronary artery disease prevalence, or renal function indices.

Conventional echocardiographic parameters

Conventional echocardiographic measurements are presented in Table 2. LVEF was significantly higher in the control group than in the HFpEF group (61.2 ± 5.8% vs. 58.7 ± 6.4%, $P = 0.007$); however, both group means were well above the 50% threshold defining preserved ejection fraction.

Agreement between deep learning-derived and manual measurements

The DL-based automated platform successfully analyzed all 200 echocardiographic studies without processing failure, with a mean automated analysis time of 8.3 ± 1.4 min per study, compared with 24.7 ± 5.6 min for complete manual analysis ($P < 0.001$). Agreement between DL-derived and manually measured parameters is detailed in Table 3. Pearson correlation coefficients between DL-derived and manual measurements were strong across all parameters, ranging from r = 0.847 for the E/e' ratio to r = 0.941 for LVEF. Importantly, DL-derived LARS demonstrated strong

Table 1 Baseline demographic and clinical characteristics

Variable	HFpEF group ($n = 107$)	Control group ($n = 93$)	*P* value
Age (years)	67.4 ± 9.8	63.1 ± 10.3	0.003
Female sex, n (%)	63 (58.9%)	41 (44.1%)	0.041
BMI (kg/m^2)	27.6 ± 3.9	25.1 ± 3.4	< 0.001
Hypertension, n (%)	78 (72.9%)	36 (38.7%)	< 0.001
Type 2 diabetes, n (%)	44 (41.1%)	18 (19.4%)	0.002
Coronary artery disease, n (%)	29 (27.1%)	19 (20.4%)	0.271
Dyslipidemia, n (%)	51 (47.7%)	37 (39.8%)	0.267
Current/former smoker, n (%)	33 (30.8%)	26 (28.0%)	0.669
Heart rate (bpm)	74.3 ± 12.6	70.8 ± 11.4	0.038
Systolic BP (mmHg)	138.7 ± 18.4	126.3 ± 15.9	< 0.001
Diastolic BP (mmHg)	82.4 ± 11.7	78.1 ± 10.3	0.006
NT-proBNP (pg/mL)	387.4 ± 214.6	68.3 ± 41.2	< 0.001
eGFR (mL/min/1.73m^2)	71.3 ± 18.7	76.8 ± 16.4	0.027
Hemoglobin (g/dL)	12.8 ± 1.7	13.4 ± 1.5	0.011
NYHA class I/II/III, n (%)	0/61/46	93/0/0	< 0.001

BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association

Table 2 Conventional echocardiographic parameters

Parameter	HFpEF group ($n = 107$)	Control group ($n = 93$)	*P* value
LVEF (%)	58.7 ± 6.4	61.2 ± 5.8	0.007
LVEDd (mm)	49.3 ± 6.2	47.1 ± 5.4	0.014
IVSd (mm)	11.4 ± 1.8	9.6 ± 1.5	< 0.001
PWd (mm)	10.8 ± 1.6	9.1 ± 1.4	< 0.001
LAVI (mL/m^2)	38.7 ± 9.3	26.4 ± 6.1	< 0.001
E wave (cm/s)	84.6 ± 22.3	71.3 ± 18.7	< 0.001
A wave (cm/s)	76.4 ± 19.8	81.2 ± 17.4	0.073
E/A ratio	1.18 ± 0.41	0.89 ± 0.27	< 0.001
Septal e′ (cm/s)	6.2 ± 1.9	9.4 ± 2.3	< 0.001
Lateral e′ (cm/s)	7.8 ± 2.4	11.6 ± 2.7	< 0.001
Average E/e′ ratio	14.6 ± 4.7	8.3 ± 2.4	< 0.001
Peak TR velocity (m/s)	2.74 ± 0.38	2.21 ± 0.31	< 0.001
LV mass index (g/m^2)	118.4 ± 27.6	88.3 ± 19.4	< 0.001
LVGLS (%)	− 17.3 ± 3.1	− 19.8 ± 2.6	< 0.001
RWT	0.46 ± 0.09	0.38 ± 0.07	< 0.001

IVSd, interventricular septal thickness at diastole; LAVI, left atrial volume index; LVEDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain; PWd, posterior wall thickness at diastole; RWT, relative wall thickness; TR, tricuspid regurgitation

correlation with manually measured LARS (r = 0.911, $P < 0.001$), with Bland–Altman analysis revealing a mean bias of − 0.67 ± 2.34% and 95% limits of agreement of − 5.26% to 3.92%, indicating acceptable agreement without systematic over- or underestimation. ICC values for intra-observer and inter-observer reproducibility of manual LARS measurements were 0.883 (95% CI 0.841–0.916) and 0.847 (95% CI 0.798–0.889), respectively, while DL-derived LARS demonstrated near-perfect reproducibility (ICC = 0.974, 95% CI 0.961–0.983) (see Fig. 1).

Diagnostic performance of DL-derived LARS for HFpEF

DL-derived LARS was significantly lower in the HFpEF group compared to controls (19.3 ± 5.7% vs. 30.8 ± 6.4%, $P < 0.001$). ROC curve analyses for the diagnostic performance of DL-derived LARS and key conventional parameters are presented in Fig. 2 and summarized in Table 4.

Table 3 Agreement between deep learning-derived and manual echocardiographic measurements

Parameter	Pearson r	*P* value	Mean bias	95% LoA	ICC (DL)	ICC (Manual inter-observer)
LARS (%)	0.911	< 0.001	− 0.67 ± 2.34	− 5.26 to 3.92	0.974	0.847
LAVI (mL/m^2)	0.893	< 0.001	1.23 ± 3.47	− 5.55 to 8.01	0.961	0.832
LVEF (%)	0.941	< 0.001	0.84 ± 2.18	− 3.43 to 5.11	0.978	0.891
E/e' ratio	0.847	< 0.001	0.51 ± 1.86	− 3.14 to 4.16	0.934	0.803
Septal e' (cm/s)	0.876	< 0.001	− 0.19 ± 0.94	− 2.03 to 1.65	0.952	0.821
LVGLS (%)	0.902	< 0.001	0.38 ± 1.67	− 2.89 to 3.65	0.963	0.857

DL, deep learning; ICC, intraclass correlation coefficient; LARS, left atrial reservoir strain; LAVI, left atrial volume index; LoA, limits of agreement; LVEF, left ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain

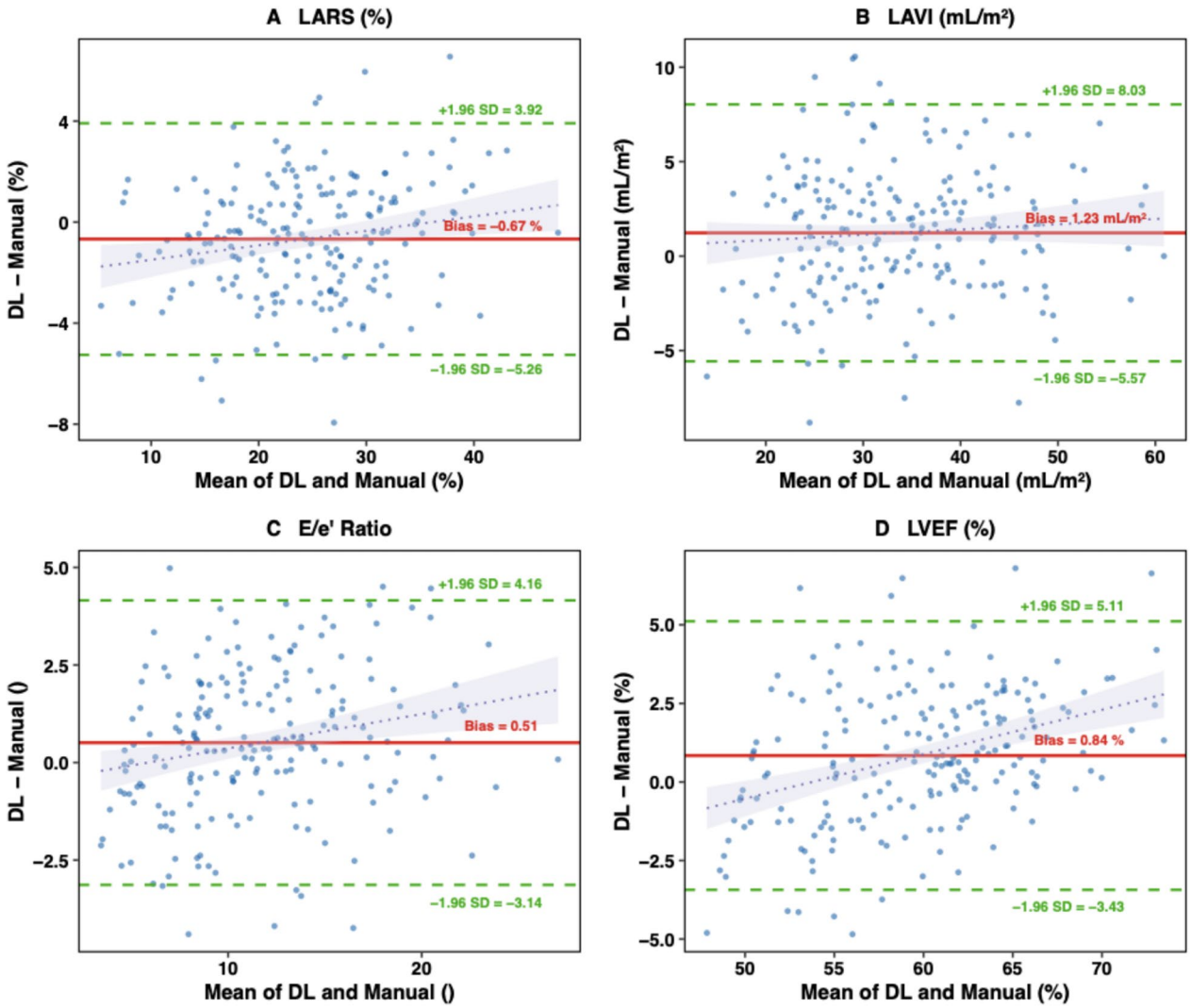


Fig. 1 Bland–Altman plots illustrating agreement between DL-derived and manually measured LARS, LAVI, E/e' ratio, and LVEF

DL-derived LARS achieved an AUC of 0.806 (95% CI 0.748–0.864) for the diagnosis of HFpEF, with an optimal cutoff of 24.2% yielding a sensitivity of 81.3% and specificity of 83.9%. The AUC of DL-derived LARS was numerically higher than that of LAVI (AUC = 0.799, 95% CI 0.739–0.859, $P = 0.724$), E/e' ratio (AUC = 0.781, 95%

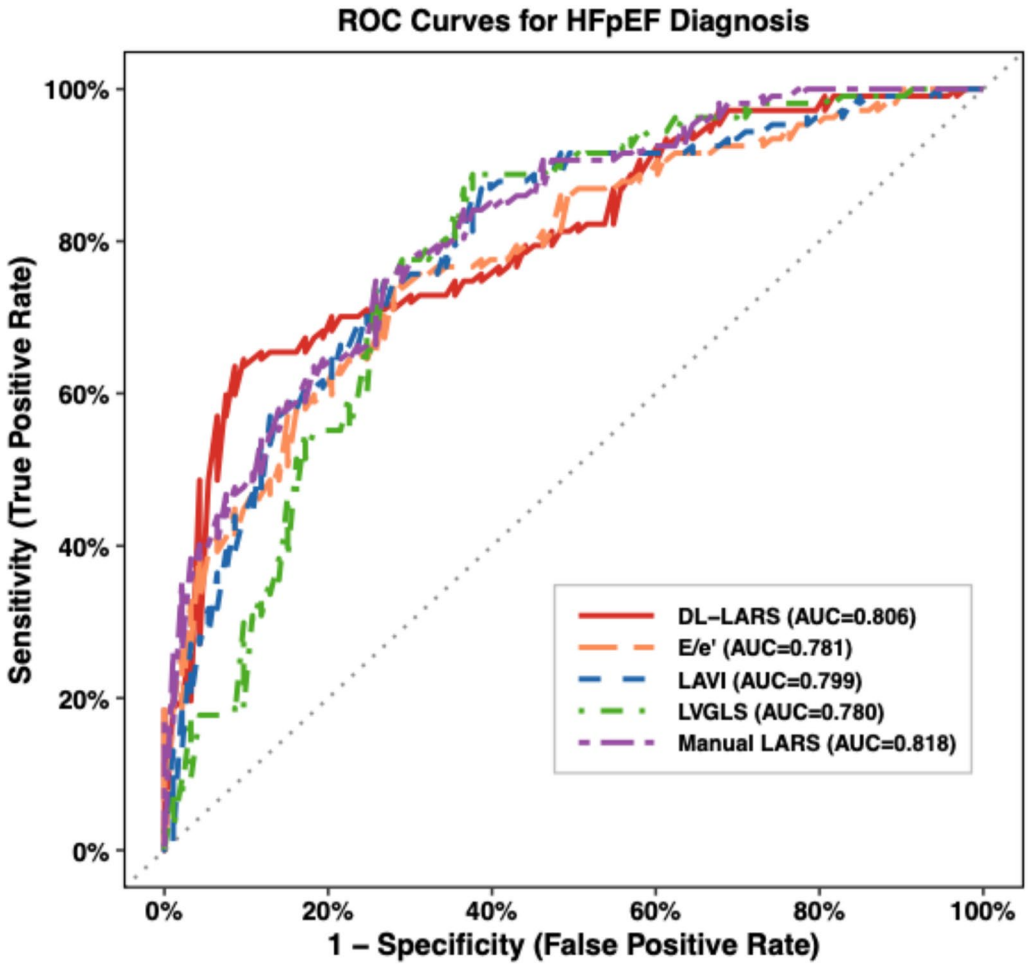


Fig. 2 ROC curves comparing diagnostic performance of DL-derived LARS, manually derived LARS, LAVI, E/e' ratio, and LVGLS for HFpEF diagnosis

Table 4 Diagnostic performance of echocardiographic parameters for HFpEF identification

Parameter	AUC (95% CI)	Optimal Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	*P* vs. DL-LARS
DL-derived LARS	0.806 (0.748–0.864)	< 24.2%	81.3	83.9	85.1	79.8	–
Manual LARS	0.818 (0.761–0.875)	< 23.8%	79.4	82.8	84.0	77.9	0.631
LAVI	0.799 (0.739–0.859)	> 32.5 mL/m^2	70.1	77.4	79.3	67.6	0.724
E/e' ratio	0.781 (0.719–0.843)	> 11.4	72.9	73.1	75.4	70.3	0.512
LVGLS	0.780 (0.717–0.843)	≥ 18.4%	67.3	71.0	72.6	65.5	0.483
E/A ratio	0.714 (0.645–0.783)	> 1.03	62.6	69.9	71.2	61.1	0.201

AUC, area under the curve; DL, deep learning; LARS, left atrial reservoir strain; LAVI, left atrial volume index; LVGLS, left ventricular global longitudinal strain; NPV, negative predictive value; PPV, positive predictive value

CI 0.719–0.843, $P=0.512$), and LVGLS (AUC = 0.780, 95% CI 0.717–0.843, $P=0.483$), although none of these pairwise differences reached statistical significance by DeLong test. The AUC of manually derived LARS (0.818, 95% CI 0.761–0.875) was not significantly different from that of DL-derived LARS ($P=0.631$), confirming comparable diagnostic accuracy between the two approaches.

Independent predictors of HFpEF

Multivariate binary logistic regression analysis identified DL-derived LARS, LAVI, average E/e' ratio, and hypertension as independent predictors of HFpEF (Table 5). After adjusting for age, sex, BMI, hypertension, diabetes, and conventional diastolic parameters, DL-derived LARS remained the strongest independent

Table 5 Univariate and Multivariate Logistic Regression Analysis for Independent Predictors of HFpEF

Variable	Univariate OR (95% CI)	*P* value	Multivariate OR (95% CI)	*P* value
Age (per year)	1.04 (1.01–1.07)	0.004	1.02 (0.99–1.06)	0.184
Female sex	1.81 (1.02–3.21)	0.042	1.43 (0.76–2.69)	0.271
BMI (per kg/m^2)	1.19 (1.09–1.30)	< 0.001	1.08 (0.97–1.20)	0.143
Hypertension	4.38 (2.36–8.13)	< 0.001	2.61 (1.31–5.21)	0.006
Type 2 diabetes	2.88 (1.49–5.56)	0.002	1.64 (0.79–3.40)	0.183
LAVI (per mL/m^2)	1.11 (1.07–1.16)	< 0.001	1.07 (1.02–1.13)	0.008
Average E/e' ratio	1.34 (1.22–1.47)	< 0.001	1.16 (1.04–1.29)	0.008
DL-derived LARS (per 1%)	0.69 (0.62–0.77)	< 0.001	0.74 (0.65–0.84)	< 0.001
LVGLS (per 1%)	0.83 (0.74–0.93)	0.001	0.91 (0.80–1.03)	0.138
NT-proBNP (per 100 pg/mL)	1.47 (1.28–1.69)	< 0.001	1.18 (0.99–1.41)	0.067

BMI, body mass index; DL, deep learning; LAVI, left atrial volume index; LARS, left atrial reservoir strain; LVGLS, left ventricular global longitudinal strain; NT-proBNP, N-terminal pro-B-type natriuretic peptide; OR, odds ratio

echocardiographic predictor of HFpEF (adjusted OR = 0.74, 95% CI 0.65–0.84, $P < 0.001$), indicating that each 1% decrease in DL-derived LARS was associated with a 26% increase in the odds of HFpEF. The correlation between DL-derived LARS values and ESC HFA-PEFF diagnostic score categories is illustrated in Fig. 3, demonstrating a stepwise reduction in LARS across increasing diagnostic score strata (P for trend < 0.001).

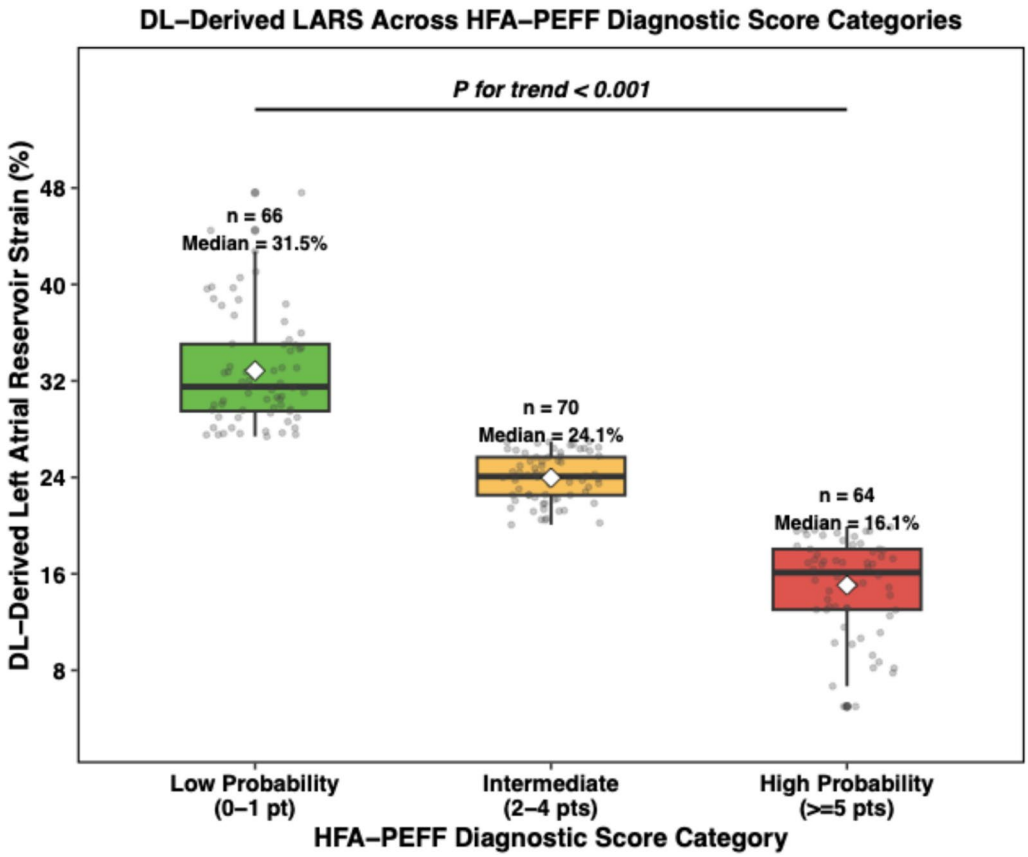


Fig. 3 Box plots depicting the distribution of DL-derived LARS values across HFA-PEFF diagnostic score categories (low probability, intermediate, and high probability of HFpEF)

Discussion

Heart failure with preserved ejection fraction represents the predominant and fastest-growing form of heart failure globally, yet its diagnosis remains a persistent clinical challenge. Unlike heart failure with reduced ejection fraction, HFpEF lacks a single pathognomonic marker, relying instead on a constellation of clinical, biochemical, and imaging criteria that are individually non-specific and collectively complex to apply at the point of care [16, 17]. The present study addresses this unmet clinical need by evaluating a deep learning-based automated echocardiographic platform for the quantification of LARS and its diagnostic utility in HFpEF, yielding three principal findings: the DL platform achieved accurate and highly reproducible automated LARS measurements with minimal systematic bias relative to manual measurements; DL-derived LARS demonstrated robust diagnostic performance for HFpEF comparable to manually derived LARS; and DL-derived LARS emerged as the strongest independent echocardiographic predictor of HFpEF after multivariate adjustment.

The left atrium functions as a dynamic barometer of left ventricular filling pressures and diastolic reserve, and its mechanical dysfunction has been increasingly recognized as a central feature of HFpEF pathophysiology [18, 19]. Unlike conventional volumetric measures such as LAVI, which reflect structural remodeling that may occur only after sustained pressure elevation, LA reservoir strain captures the deformation-based functional signature of atrial myopathy at an earlier and potentially more reversible stage [20]. Prior studies have demonstrated that LARS is significantly reduced in HFpEF patients compared with control subjects, correlates more strongly with invasively measured left ventricular filling pressures than conventional diastolic parameters, and provides incremental prognostic information beyond established echocardiographic indices [21, 22]. Consistent with this body of evidence, the current study observed markedly impaired LARS in the HFpEF group relative to controls, with the magnitude of impairment aligning closely with previous reports employing manual speckle-tracking methodology.

Of note, atrial myopathy, atrial fibrillation, and HFpEF share overlapping pathophysiological cascades, including myocardial fibrosis, neurohormonal activation, and chronic hemodynamic overload, and the presence of LA mechanical dysfunction as captured by impaired LARS may represent a unifying marker across these interrelated conditions [34]. Furthermore, LARS has potential clinical utility beyond conventional HFpEF diagnosis; in the setting of atrial functional mitral regurgitation (AFMR), LA strain assessment may contribute to improved diagnosis, longitudinal follow-up, and patient selection for valvular intervention [35]. These considerations support the broader clinical relevance of automated LA strain quantification beyond the specific diagnostic application evaluated in the present study.

A central contribution of the present work is the demonstration that a DL-based automated platform can generate LARS measurements with accuracy and reproducibility that compare favorably to experienced manual analysis. The strong Pearson correlation and narrow limits of agreement on Bland–Altman analysis between DL-derived and manual LARS, alongside near-perfect ICC for the automated approach, provide compelling evidence that the DL platform effectively eliminates the operator-dependent variability that has historically constrained the clinical adoption of strain imaging [23]. The substantially superior reproducibility of DL-derived LARS relative to manual inter-observer agreement supports prior observations that deep learning algorithms trained on large annotated datasets can markedly reduce intra- and inter-operator variability in echocardiographic strain measurements [24, 25]. Importantly, automated analysis required significantly less time per study compared with comprehensive manual analysis (mean 8.3 ± 1.4 min vs. 24.7 ± 5.6 min, $P < 0.001$), reflecting a workflow advantage of considerable relevance in high-volume clinical settings. Specifically, manual LARS measurement required operator-guided endocardial tracing, visual inspection of tracking quality, manual adjustment in a subset of cases, and repeated measurements across multiple views and cardiac cycles, whereas the DL platform completed view identification, chamber segmentation, speckle-tracking, and strain quantification in a fully automated pipeline following a single DICOM data upload without operator intervention [26].

The diagnostic performance of DL-derived LARS for HFpEF identification, as reflected by an AUC exceeding 0.80, was numerically higher than that of established echocardiographic parameters including LAVI, E/e' ratio, and LVGLS, although these pairwise differences did not reach statistical significance by DeLong test. This finding is consistent with the broader literature demonstrating that no single echocardiographic parameter provides definitive diagnostic separation in HFpEF, and that multiparameter integration is typically necessary [17, 27]. The optimal DL-LARS cutoff for HFpEF identification identified in this study is broadly consistent with thresholds reported in prior investigations employing manual LARS measurement. A previous large exercise stress echocardiography study demonstrated that resting LAS reservoir independently predicted exercise-induced elevation in left ventricular filling pressure in patients with intermediate HFA-PEFF scores, establishing LAS as a valuable supplementary tool when standard diagnostic algorithms

yield indeterminate results [21]. Similarly, a study examining the relative importance of LARS within the HFA-PEFF diagnostic framework found that LARS impairment was a more influential predictor of high-probability HFpEF than several individual HFA-PEFF components including septal E/e' and left ventricular mass index [28]. The present findings corroborate and extend these observations to the automated DL context, suggesting that DL-derived LARS may serve as a viable alternative to manual strain analysis within existing diagnostic pathways without significant loss of diagnostic accuracy.

The finding that DL-derived LARS was the strongest independent echocardiographic predictor of HFpEF in multivariate logistic regression, outperforming LAVI, average E/e', and LVGLS after adjustment for relevant clinical covariates, adds further support to the diagnostic primacy of atrial deformation imaging in this condition. It should be acknowledged that LARS, LAVI, and E/e' reflect interrelated aspects of diastolic dysfunction, and some degree of collinearity among these variables is expected; however, variance inflation factors for all predictors remained below 3.0, suggesting that the multivariate model was reasonably stable and the independent contribution of DL-derived LARS was not substantially inflated by collinearity. This result aligns with a recent systematic review and meta-analysis identifying impaired LA reservoir strain as one of only three echocardiographic parameters that consistently predicted adverse cardiovascular outcomes across all HFpEF subgroup analyses [22]. The mechanistic basis for this observation relates to the left atrium's unique position as both a reservoir and pressure transducer: chronic exposure to elevated left ventricular filling pressures impairs atrial longitudinal strain through a combination of myocardial fibrosis, atrial dilation, and neurohormonal activation, processes that precede and may be more sensitive indicators of diastolic pathology than conventional parameters dependent on transmitral flow patterns [19, 29]. The stepwise reduction in DL-derived LARS across increasing HFA-PEFF diagnostic score strata further confirms the construct validity of this automated measurement, demonstrating that DL-derived LARS tracks with pathophysiological disease severity in a clinically coherent manner.

Beyond its diagnostic utility, LARS may also serve as a therapy-responsive biomarker reflecting myocardial and atrial reverse remodeling under treatment. Recent evidence has demonstrated that sodium-glucose cotransporter 2 inhibitors, including empagliflozin and dapagliflozin, exert favorable effects on arrhythmias, sudden cardiac death, and cardiac function in heart failure populations [36], suggesting that serial LARS assessment could potentially track treatment response and cardioprotective benefit. Similarly, vericiguat, through its effects on soluble guanylate cyclase stimulation, has been associated with cardiac strain modifications that may reflect improvements in myocardial compliance and ventricular-arterial coupling [37]. These observations support the broader potential of LA strain as not merely a static diagnostic discriminator but as a dynamic marker that may evolve with therapeutic intervention, a concept that warrants further investigation in prospective treatment trials. Furthermore, the need for more sensitive echocardiographic phenotyping extends beyond conventional heart failure workflows; for example, prevention and risk assessment of cardiac device-related infections increasingly benefit from comprehensive strain-based imaging protocols that may detect subclinical functional changes not captured by conventional parameters [38].

The present study utilized a commercial DL platform (EchoGo Pro, Ultromics) that has been previously validated in multiple external cohorts for automated echocardiographic interpretation, including systolic and diastolic function assessment across diverse clinical populations [26, 27]. The algorithm was trained on a large annotated dataset encompassing a broad range of image qualities and patient phenotypes; however, it should be noted that the training data composition has not been fully disclosed by the vendor, and the extent to which it encompasses populations with significant obesity, advanced valvular disease, or non-Western ethnic representation remains uncertain. While the platform demonstrated a 100% technical success rate in the current cohort, this may partly reflect the study's exclusion of patients with suboptimal acoustic windows, and performance may differ in unselected clinical populations with more variable image quality.

Several considerations should contextualize the interpretation of these findings. First, the retrospective single-center design and relatively modest sample size limit the generalizability of the results to other clinical environments, patient populations, and echocardiographic platforms. External multicenter validation is required before DL-derived LARS can be incorporated into routine diagnostic workflows. Second, the study enrolled patients with established HFpEF diagnoses and control subjects without heart failure, a case–control design that optimizes signal detection but may overestimate apparent diagnostic performance relative to what would be expected in a real-world consecutive screening scenario with a broader spectrum of dyspneic patients presenting with diagnostic uncertainty. Prospective validation in unselected populations with unexplained dyspnea is therefore essential to establish the true clinical utility of DL-derived LARS. Third, although the DL platform demonstrated high technical success in this cohort, the

performance of automated algorithms may degrade in suboptimal acoustic windows or in phenotypically distinct HFpEF populations, such as those with concomitant significant valvular disease or obesity-predominant phenotypes, which were either excluded or underrepresented in this study [30]. Fourth, the absence of invasive hemodynamic validation means that the present results rely on clinically and echocardiographically established HFpEF diagnoses, which, while consistent with guideline criteria, introduce the possibility of diagnostic misclassification particularly in borderline cases. This is an inherent limitation of the study's reference standard, and it should be noted that the use of echocardiographic criteria to both define HFpEF and evaluate a novel echocardiographic parameter introduces potential circularity; accordingly, future studies should evaluate DL-derived LARS against catheterization-derived filling pressure measurements to establish its hemodynamic correlates and to provide a truly independent reference standard. Fifth, the current analysis focused on LA reservoir strain as the primary DL endpoint; whether DL-derived LA conduit and contractile strain components provide additional independent diagnostic information in HFpEF warrants dedicated investigation. Sixth, the exclusion of patients with atrial fibrillation at the time of echocardiographic examination, while necessary to ensure reliable strain quantification, significantly limits the generalizability of the present findings, given that atrial fibrillation is highly prevalent in HFpEF populations; in particular, the current results cannot be extrapolated to patients with permanent atrial fibrillation, and future studies should evaluate the feasibility and diagnostic accuracy of DL-derived LARS in patients with ongoing atrial fibrillation or in those with paroxysmal atrial fibrillation captured during the arrhythmia.

Conclusion

DL-based automated LARS analysis provides accurate, highly reproducible, and time-efficient quantification of LA reservoir function that is comparable to expert manual measurement. DL-derived LARS demonstrates robust diagnostic performance for HFpEF identification that is comparable to manually derived LARS, and it shows numerically favorable but not statistically superior discrimination relative to conventional diastolic parameters while serving as the strongest independent echocardiographic predictor of HFpEF in multivariate analysis. These findings support the potential clinical integration of automated DL-based LARS into echocardiographic workflows to facilitate timely and standardized HFpEF diagnosis, although prospective validation in unselected dyspneic populations is warranted to confirm real-world diagnostic utility.

Author contributions

Libo Wang: Conceptualization, Data Curation, Investigation Haiyang Mu: Methodology, Formal Analysis, Software Ye Tian: Investigation, Validation, Visualization Ying Lin: Writing – Original Draft, Data Curation, Investigation Jian Wang: Methodology, Formal Analysis, Validation Liye Zhang: Visualization, Data Curation, Resources Xingying Wu: Investigation, Validation, Resources Mei Chen: Writing – Original Draft, Data Curation Meiling Yang: Visualization, Investigation, Validation Chaofei Zhou: Conceptualization, Methodology, Supervision, Writing – Review & Editing, Funding Acquisition.

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Data availability

The data used to support the findings of this study are available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Hainan Hospital of Chinese PLA General Hospital. The requirement for informed consent was waived due to the retrospective nature of the study.

Competing interests

The authors declare no competing interests.

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