RESEARCH ARTICLE

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A Comparative Analysis of Left Atrial Volume and Left Ventricular Mass Indices in Heart Failure Patients with Preserved versus Reduced Ejection Fraction

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Abstract

Background and Aim: Heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF) differ in their patterns of cardiac remodeling. This study aimed to compare left atrial volume index (LAVI), left ventricular mass index (LVMI), and left atrial (LA) strain between HFrEF and HFpEF, and to describe their clinical, biochemical, and echocardiographic correlates.

Materials and Methods: This prospective observational cohort study enrolled 100 patients (HFrEF, n=50; HFpEF, n=50) who underwent clinical, laboratory, electrocardiographic, echocardiographic, and speckle-tracking assessments, with a 6-month follow-up for echocardiographic parameters, functional status, re-hospitalization, and mortality.

Results: HFrEF patients had significantly higher left ventricular end-diastolic volume, left ventricular end-systolic volume, LVMI, and LAVI, and significantly lower EF and LA strain than HFpEF patients (all $P < 0.001$); E/e′ also differed between groups ($P = 0.005$). LA reservoir strain (LASr) was 6.10±2.53% in HFrEF versus 16.08±3.04% in HFpEF ($P < 0.001$), and remained significantly lower in HFrEF after excluding patients with atrial fibrillation ($P < 0.001$). N-terminal pro-B-type natriuretic peptide (NT-proBNP) was higher in HFrEF [median 4056 (IQR 1670-13183) vs. 2417 (1374-3804) pg/mL; $P = 0.007$]. In HFrEF, LVMI and LAVI correlated with LA strain, ventricular volumes, EF, E/e′, and NT-proBNP; in HFpEF, they correlated mainly with NT-proBNP and E/e′. At 6 months, 43 HFrEF and 44 HFpEF patients completed follow-up (7 and 6 patients, respectively, had died beforehand); LAVI decreased in both groups, and between-group differences in echocardiographic and LA strain parameters persisted.

Conclusion: HFrEF was associated with larger LAVI and LVMI and more impaired LA strain than HFpEF, reflecting distinct remodeling profiles. Because the groups were defined by EF and the HFpEF criteria included LAVI, LVMI, and E/e′, these differences are partly expected by design. Whether LA strain improves discrimination between the phenotypes beyond conventional indices was not tested and requires confirmation in larger studies.

Keywords: Heart failure, HFrEF, HFpEF, LAVI, LVMI, left atrial strain, echocardiography, speckle-tracking

INTRODUCTION

Heart failure (HF) is a major global health problem affecting approximately 2% of the population in developed countries. Although HF with reduced ejection fraction (HFrEF) has traditionally predominated, nearly half of HF patients have HF with preserved ejection fraction (HFpEF), particularly elderly women.[1] Community cohort data show that the incidence of HFpEF has increased relative to that of HFrEF and that long-term mortality is high in both phenotypes.[2,3] According to the European Society of Cardiology (ESC) guidelines and the HFA-PEFF diagnostic algorithm, the diagnosis of HFpEF

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requires objective evidence of cardiac structural and/or functional abnormalities consistent with raised left ventricular filling pressures.[4-6] Left atrial volume index (LAVI) and left ventricular mass index (LVMI) are central to this assessment, whereas left atrial (LA) strain derived from speckle-tracking echocardiography describes atrial function, which may be impaired before the atrium enlarges.[7]

Study Hypothesis and Primary Endpoint

We hypothesized that LA strain parameters would differ between HFrEF and HFpEF and would correlate with conventional structural indices (LAVI and LVMI) and with markers of disease severity. A formal comparison of the discriminatory ability of LA strain versus LAVI and LVMI (e.g., receiver operating characteristic analysis) was not part of the study design.

The primary objective was to compare LAVI, LVMI, and LA strain (reservoir, conduit, and contractile) between HFrEF and HFpEF patients. The primary endpoint was the difference in LA reservoir strain (LASr) between the two phenotypes. Secondary endpoints included the following: (1) differences in LAVI and LVMI; (2) correlations between structural indices and atrial strain parameters; (3) associations with biochemical and clinical variables; and (4) longitudinal changes in these parameters at 6-month follow-up. Exploratory analyses examined clinical outcomes, including re-hospitalization and mortality.

METHODS

This prospective observational cohort study enrolled 100 patients with chronic HF who were divided into HFrEF (Group 1, n=50) and HFpEF (Group 2, n=50) based on echocardiographic criteria. Enrolment began in May 2024, and the last 6-month follow-up assessment was completed in December 2025. Baseline data were collected prospectively, and all patients underwent comprehensive clinical evaluation, laboratory testing, electrocardiogram (ECG), transthoracic echocardiography, and speckle-tracking assessment. Patients were followed for 6 months, during which follow-up echocardiography and functional status assessments were performed, and re-hospitalization and mortality were documented. The baseline comparisons represent a cross-sectional analysis nested within the prospective cohort. The study protocol was approved by the Research Ethics Committee of Benha University Faculty of Medicine (protocol no: MS 28-1-2024, approval date: 28.01.2024). Written informed consent was obtained from all participants or their legal representatives in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.[8,9]

Clinical trial registration was not required because this study was a prospective observational cohort study without any therapeutic intervention, treatment allocation, or randomization. Speckle-tracking echocardiography was used solely as a non-invasive imaging assessment for research purposes and did not influence routine clinical management. Therefore, this study did not meet the definition of a clinical trial requiring prospective registration.

Diagnostic Criteria and Classification

HFrEF was defined as the presence of typical signs and symptoms of HF together with a left ventricular ejection fraction (LVEF) ≤40%. HFpEF was defined as the presence of signs and symptoms of HF with an LVEF ≥50% and objective evidence of cardiac structural and/or functional abnormalities consistent with elevated left ventricular filling pressures, including at least one of the following: (1) LAVI >34 mL/m^2; (2) LVMI >115 g/m^2 in men or >95 g/m^2 in women; (3) E/e′ ratio >15; or (4) elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels (>125 pg/mL in patients <75 years, or >450 pg/mL in those ≥75 years).[4,6] Patients with mildly reduced ejection fraction (HFmrEF; LVEF 41-49%) were excluded. Group assignment was based on the LVEF measured at enrolment (admission echocardiogram), which was ≤40% in all HFrEF patients. On the subsequent study echocardiogram, a small number of HFrEF patients had an LVEF of 41-42%, a difference within the recognized measurement variability of two-dimensional LVEF assessment between examinations.[10] To avoid post hoc reclassification and the selection bias it could introduce, these patients were retained in the HFrEF group according to the pre-specified classification.

To limit incorporation bias, the diagnostic algorithm for HFpEF was established before the index echocardiographic analysis, using clinical presentation, natriuretic peptide levels, and echocardiographic criteria. However, because LAVI, LVMI, and E/e′ were among the criteria that could qualify a patient for HFpEF, and because the groups were defined by EF, between-group differences in these variables are partly a consequence of the classification itself. LA strain was not part of the diagnostic criteria.

Exclusion criteria included age below 18 years, significant tachyarrhythmias or bradyarrhythmias [other than atrial fibrillation (AF)], significant structural valvular heart disease, and a documented history of ischemic heart disease, defined as prior myocardial infarction, prior coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting), or hemodynamically significant coronary artery stenosis confirmed by invasive or computed tomography (CT) coronary angiography. Ischemic heart disease was excluded on the basis of clinical history and the 12-lead ECG; invasive or CT coronary angiography was not performed routinely.

Patients with pathological Q-waves on surface ECG were not automatically excluded in the absence of a documented history of ischemic heart disease, because Q-waves may occasionally

be observed in non-ischemic cardiomyopathies (e.g., prior myocarditis, infiltrative diseases). The presence of Q-waves in the HFrEF group (Table 1) therefore reflects ECG findings in patients without a confirmed history of ischemic heart disease. Apart from the exclusion of ischemic heart disease, the underlying aetiology of HF was not systematically recorded.

All patients underwent a standard 12-lead ECG to assess Q-waves, left ventricular hypertrophy, and AF.

Comprehensive transthoracic echocardiography was performed using a Vivid E95 ultrasound system (GE Healthcare, Chicago, IL, USA) with an M5Sc phased-array transducer. All acquisitions were performed according to current recommendations of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI).[10] Images were obtained with patients in the left lateral decubitus position.

Table 1. Comparison between HFrEF Group and HFpEF Group regarding demographic data, clinical data, ECG and medications

		HFrEF Group (n=50)	HFpEF Group (n=50)	Test value	*P*-value
Age, years		62.80±6.77	62.38±7.31	0.298	0.766
Sex	Female	17 (34.0%)	33 (66.0%)	10.240	0.001*
	Male	33 (66.0%)	17 (34.0%)		
DM		34 (68.0%)	27 (54.0%)	2.060	0.151
HTN		25 (50.0%)	38 (76.0%)	7.250	0.007*
BMI (kg/m^2)		28.13±4.67	30.91±3.33	-3.431	<0.001**
Outpatients		20 (40.0%)	15 (30.0%)	0.703	0.402
Hospitalized		30 (60.0%)	35 (70.0%)		
NYHA	Class I	13 (26.0%)	10 (20.0%)	2.198	0.532
	Class II	23 (46.0%)	19 (38.0%)		
	Class III	11 (22.0%)	16 (32.0%)		
	Class IV	3 (6.0%)	5 (10.0%)		
SBP (mmHg)		116.80±18.23	113.60±16.99	0.908	0.366
DBP (mmHg)		68.00±9.90	68.20±11.01	-0.096	0.924
HR (bpm)		88.70±16.62	91.50±14.15	-0.907	0.367
NT-proBNP (pg/mL)		4056 (1670-13183)	2417 (1374-3804)	2.686	0.007*
Creatinine (mg/dL)		1.31±0.29	1.35±0.29	-0.751	0.454
AST (IU/L)		41.28±6.77	40.72±6.76	0.414	0.680
ALT (IU/L)		40.68±6.65	40.98±6.53	-0.228	0.820
Sodium (mmol/L)		135.84±5.94	136.82±6.05	-0.817	0.416
Potassium (mmol/L)		3.84±0.71	4.03±0.85	-1.246	0.216
Hb (g/dL)		10.86±0.92	11.01±0.97	-0.815	0.417
eGFR (mL/min/1.73 m^2)		69.61±16.68	67.55±15.29	0.644	0.521
AF		31 (62.0%)	28 (56.0%)	0.372	0.542
First-degree AV block		0 (0.0%)	4 (8.0%)		0.117
IVCD		6 (12.0%)	6 (12.0%)		1.000
LBBB		20 (40.0%)	7 (14.0%)		0.003*
Non-specific changes (poor R wave progression, incomplete LBBB, flat T anterior)		0 (0.0%)	14 (28.0%)		<0.001**
Q in anterior leads		6 (12.0%)	0 (0.0%)		0.027*
Q in inferior leads		4 (8.0%)	0 (0.0%)		0.117
RBBB		9 (18.0%)	8 (16.0%)		0.790
T inversion in anterior leads		5 (10.0%)	7 (14.0%)		0.538
T inversion in inferior leads		0 (0.0%)	3 (6.0%)		0.242
T inversion in lateral leads		0 (0.0%)	1 (2.0%)		1.000

Table 1. Continued

	HFrEF Group (n=50)	HFpEF Group (n=50)	Test value	*P*-value
ACEI/ARB/sacubitril/valsartan	44 (88.0%)	31 (62.0%)	9.013	0.003*
β-blockers	43 (86.0%)	40 (80.0%)	0.638	0.424
Diuretics	47 (94.0%)	46 (92.0%)	0.154	0.695
SGLT2 inhibitors	46 (92.0%)	43 (86.0%)	0.919	0.338
MRA	34 (68.0%)	20 (40.0%)	7.890	0.005*
CCB	5 (10.0%)	6 (12.0%)	0.102	0.749
Hospital duration (days)	9.00±1.98	9.36±2.05	-0.894	0.374

Data are mean ± SD, median (IQR), or n (%). Test value: t, independent-samples t-test (mean ± SD); Z, Mann-Whitney U test [median (IQR)]; χ^2, chi-square test [n (%)]; Fisher's exact test was used when any expected cell count was <5 (first-degree AV block, Q-waves, and T-wave inversion in the inferior and lateral leads). *$P < 0.05$ is significant; **$P < 0.001$ is highly significant. HFrEF: Heart failure with reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction, ECG: Electrocardiogram, DM: Diabetes mellitus, HTN: Hypertension, BMI: Body mass index, NYHA: New York Heart Association, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, NT-proBNP: N-terminal pro-B-type natriuretic peptide, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, Hb: Hemoglobin, eGFR: Estimated glomerular filtration rate, AF: Atrial fibrillation, AV: Atrioventricular, IVCD: Intraventricular conduction delay, LBBB: Left bundle branch block, RBBB: Right bundle branch block, ACEI: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker, SGLT2: Sodium-glucose cotransporter 2, MRA: Mineralocorticoid receptor antagonist, CCB: Calcium channel blocker, IQR: Interquartile range

Left ventricular end-diastolic volume (LVEDV) and end-systolic volume (LVESV) were calculated using the biplane Simpson's method of discs and are reported as absolute volumes (mL). LVM was calculated using the linear method according to the Devereux formula: $LVM=0.8\times\{1.04\times[(LVEDD+IVST+PWT)^3-LVEDD^3]\}+0.6$ g, where LVEDD is the left ventricular end-diastolic diameter, IVST the interventricular septal thickness (IVS), and PWT the posterior wall thickness (PWT), and was indexed to body surface area (BSA) to obtain LVMI (g/m^2). LA volume was calculated using the biplane area-length method from apical four-chamber and two-chamber views at left ventricular end-systole, when the LA reaches its maximal volume, and was indexed to BSA to obtain LAVI (mL/m^2).[10,11] Diastolic function was assessed using pulsed-wave Doppler of mitral inflow (E/A ratio) and tissue Doppler imaging of the medial and lateral mitral annular velocities (e′), and the average E/e′ ratio was calculated.[12,13] Because the A-wave is absent in AF and rhythm status could not be linked to individual patients in the study dataset, the E/A ratio was not included in the comparative analyses. All measurements were averaged over three consecutive cardiac cycles in sinus rhythm and over five cycles in AF and stored digitally for offline analysis.

LA strain was evaluated from apical four- and two-chamber views using two-dimensional speckle-tracking echocardiography, in accordance with the EACVI/ASE/Industry Task Force consensus.[14] Images were exported in DICOM format and analyzed offline with QLAB software version 13 (Philips Healthcare). The LA endocardial border was traced at left ventricular end-systole, when the LA cavity is largest, and the zero-strain reference was set at left ventricular end-diastole (onset of the QRS complex). Each apical view was divided into six segments (12 segments in total), and reservoir, conduit, and contractile strain were calculated as the average of all segments. The frame rate was 50-90 frames per second. Because conduit strain is negative by convention, it is reported as an absolute (positive) value, so that lower values indicate worse function for both reservoir and conduit strain. Reported normal values are approximately 39% for reservoir, 23% for conduit, and 17% for contractile strain.[15]

Rhythm Status and LA Strain Acquisition

AF was present in 62% of HFrEF patients and 56% of HFpEF patients. For patients in sinus rhythm, LA strain measurements were performed during three consecutive cardiac cycles and averaged. For patients with AF, strain analysis was performed during episodes of controlled ventricular response (heart rate <100 beats/min) using five consecutive cardiac cycles with comparable R-R intervals, and the average of the valid cycles was reported; measurements during markedly irregular R-R intervals were excluded.[16]

Because organized atrial contraction is absent in AF, LA contractile strain cannot be meaningfully measured in these patients. As rhythm status could not be linked to individual patients in the study dataset, contractile strain could not be restricted to patients in sinus rhythm; it was therefore not included in the comparative analyses, and LA function is described by reservoir and conduit strain. A sensitivity analysis excluding patients with AF was performed for the primary endpoint (LASr).

Plasma NT-proBNP was measured using the Roche Modular System. Values >125 pg/mL in patients younger than 75 years and >450 pg/mL in those aged ≥75 years were considered elevated, according to the age-specific reference limits of the assay; 125 pg/mL is the threshold recommended in the ESC guidelines for the diagnosis of chronic HF.[4] In patients with AF, higher diagnostic thresholds are recommended for HFpEF

(e.g., NT-proBNP >660 pg/mL and LAVI >40 mL/m^2 as major HFA-PEFF criteria).[6]

Reproducibility and Observer Blinding

To assess measurement reproducibility, intra-observer and inter-observer variability for LA strain parameters were evaluated in a randomly selected subset of 20 patients (10 HFrEF and 10 HFpEF). To assess intra-observer variability, the same experienced echocardiographer repeated the LA strain analysis one month after the initial assessment while blinded to the previous results. To assess inter-observer variability, a second independent echocardiographer, blinded to the first observer's measurements and all clinical information, performed the analysis.

Reproducibility was quantified using intraclass correlation coefficients (ICC, two-way random effects model, absolute agreement) and Bland-Altman analysis (mean difference ±95% limits of agreement). ICC values were interpreted as follows: <0.50, poor; 0.50-0.75, moderate; 0.75-0.90, good; and >0.90, excellent reliability.[17] All primary speckle-tracking analyses were performed by observers blinded to the group allocation.

Sample Size Calculation: Sample size was calculated using MedCalc® version 12.3.0.0 with a 95% confidence level, 80% power, and 5% alpha error, based on an expected between-group difference in LVMI. At least 80 participants were required. To allow for a 10% dropout rate, 100 patients (50 per group) were enrolled. Because LVMI is a secondary endpoint, this calculation was not based on the primary endpoint (LASr); this is acknowledged as a limitation.

Clinical Outcome Definitions

Clinical outcomes at 6 months were categorized as follows: "Improved" was defined as an improvement in New York Heart Association (NYHA) functional class by at least one grade, without re-hospitalization for HF. "Still" was defined as an unchanged NYHA class without re-hospitalization. "Poor" was defined as a deterioration in NYHA class of at least one grade or re-hospitalization for HF. Patients who died before the 6-month assessment were recorded separately as deaths and were not included in the Improved/Still/Poor classification, which applied only to patients who survived to follow-up. Outcome adjudication was performed by two independent clinicians blinded to baseline echocardiographic data.

Statistical Analysis

Data were analyzed using SPSS version 26.0. Continuous variables are presented as mean ± standard deviation (SD), except NT-proBNP, which was markedly right-skewed (SD exceeding the mean) and is presented as median (interquartile range). Categorical variables are presented as frequencies and percentages.

Given the sample size of 50 patients per group, between-group comparisons of continuous variables were performed using the independent-samples t-test, except for NT-proBNP, which was compared using the Mann-Whitney U test. Categorical variables were compared using the chi-square test or Fisher's exact test (when any expected cell count was <5); the test used for each variable is indicated in the table footnotes. Within-group changes in echocardiographic parameters from baseline to follow-up were assessed using the paired-samples t-test.

Because several continuous variables (including NT-proBNP and E/e′) exhibited non-normal distributions, correlations were assessed using Spearman's rank correlation coefficient (rs). Correlation coefficients are reported with 95% confidence intervals (CIs) calculated using Fisher's z transformation.

Multivariable linear regression was used to identify independent determinants of LVMI and LAVI within each group. To avoid overfitting, the number of predictors was limited to four per model (approximately one predictor per 12 observations): age, sex, body mass index (BMI), and hypertension. Rhythm status could not be included as a covariate because it could not be linked to individual patients in the study dataset. Variance inflation factors (VIFs) were calculated; a VIF >5 indicated problematic collinearity. Regression coefficients (unstandardized β) are reported with 95% CIs and standard errors, together with model R^2, adjusted R^2, and F statistics.

Given the large number of comparisons, only the primary endpoint (difference in LASr between HFrEF and HFpEF) was treated as confirmatory and tested at α=0.05. All other analyses were considered exploratory, and no formal correction for multiple comparisons was applied; this is acknowledged as a limitation.

RESULTS

Participant Flow: Of 170 patients assessed for eligibility, 70 did not meet the inclusion criteria, and 100 were enrolled. No enrolled patients were excluded from the analysis. Of the 100 patients enrolled at baseline, 87 completed the 6-month follow-up echocardiographic assessment (43 HFrEF, 44 HFpEF). In the HFrEF group, 7 patients died before follow-up, and in the HFpEF group, 6 patients died before follow-up. No patients were lost to follow-up for reasons other than death. Among survivors, clinical outcomes (NYHA functional class and re-hospitalization) were ascertained by direct clinical review or telephone contact (Figure 1).

Demographic characteristics, clinical presentation, electrocardiographic findings, laboratory parameters, and medications were compared between the HFrEF and HFpEF groups (Table 1). There were no significant between-group differences in age; diabetes mellitus; outpatient versus hospitalized status; hospital duration; creatinine; aspartate

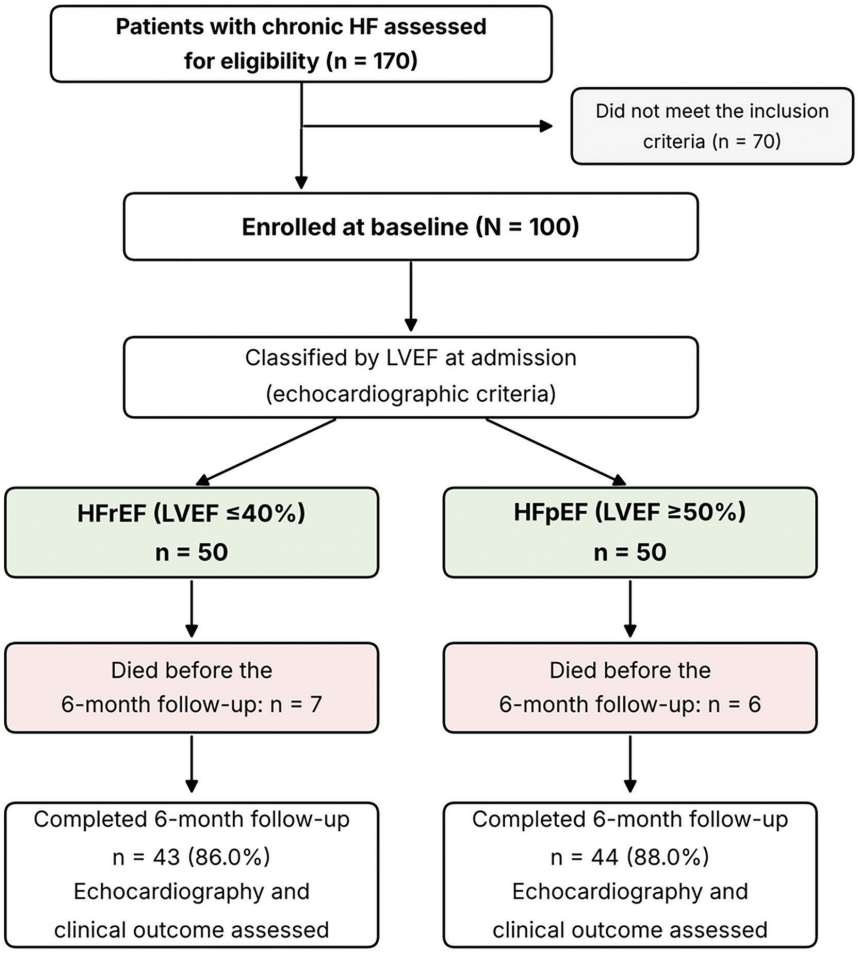

Figure 1. Flow chart of the study

HFrEF: Heart failure with reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction, ECG: Electrocardiogram, LVEF: Left ventricular ejection fraction

aminotransferase; alanine aminotransferase; sodium; potassium; hemoglobin; estimated glomerular filtration rate; intraventricular conduction delay; right bundle branch block; first-degree atrioventricular block; Q-waves in the inferior leads; T-wave inversion in the anterior, inferior, or lateral leads; NYHA functional class ($P = 0.532$); or use of β-blockers, diuretics, sodium-glucose cotransporter 2 inhibitors, or calcium channel blockers. Significant between-group differences were observed in sex, BMI, NT-proBNP, hypertension, left bundle branch block (LBBB), non-specific ECG changes, Q-waves in the anterior leads, and the use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or sacubitril/valsartan and of mineralocorticoid receptor antagonists. The prevalence of AF did not differ significantly between the groups (62.0% vs. 56.0%; $P = 0.542$).

Conventional echocardiography showed significantly greater IVS and PWT in the HFpEF group, whereas LVEDV and LVESV were significantly higher, and EF was significantly lower, in the HFrEF group. LVMI and LAVI were also significantly higher in patients with HFrEF. E/e′ was lower in HFrEF than in HFpEF ($P = 0.005$). LA reservoir and conduit strain were significantly lower in HFrEF ($P < 0.001$ for both) (Table 2).

Reproducibility: Intra-observer ICCs were 0.94 for LASr and 0.92 for LAScd (excellent), and inter-observer ICCs were 0.91 for LASr (excellent) and 0.89 for LAScd (good). Bland-Altman mean differences were -0.3% (95% limits of agreement: -2.1 to 1.5) for LASr and 0.2% (-1.8 to 2.2) for LAScd, indicating minimal systematic bias; the limits of agreement (approximately ±2 percentage points) were small relative to the between-group differences in strain (Supplementary Table 1).

At 6-month follow-up, echocardiographic data were available for 43 HFrEF and 44 HFpEF patients. LAVI decreased significantly in both HFrEF (45.86±6.48 to 42.38±6.51 mL/m^2; $P = 0.007$) and HFpEF (38.46±4.73 to 35.95±5.42 mL/m^2; $P = 0.014$). Although LVMI decreased in both groups, the within-group changes were not statistically significant (HFrEF, $P = 0.363$; HFpEF, $P = 0.060$). EF increased in both HFrEF (30.96±6.07% to 34.81±6.47%; $P = 0.002$) and HFpEF (56.76±3.69% to 59.14±3.35%; $P < 0.001$). LASr did not change significantly in HFrEF ($P = 0.277$) but increased significantly in HFpEF ($P = 0.006$), whereas LAScd increased significantly in both groups. Between-group differences remained significant at follow-up for LAVI, LVMI, EF, LASr, and LAScd (all $P < 0.001$; Tables 3-5).

Correlation between LV Mass and LA Volume Indices with HFrEF and HFpEF Groups

In the HFrEF group, LVMI and LAVI were strongly and inversely correlated with LASr and LAScd (all $P < 0.001$). Both LVMI and LAVI were positively correlated with NT-proBNP, LVEDV, LVESV, and E/e′, and negatively correlated with EF (all $P < 0.001$). NYHA class showed a weak positive correlation with LVMI (rs=0.323, $P = 0.022$), but not with LAVI (rs=0.250, $P = 0.080$). In the HFpEF group, neither LVMI nor LAVI correlated significantly with LA strain, LV volumes, or EF. However, both indices were positively correlated with NT-proBNP and E/e′ ($P \leq 0.002$). Other demographic, hemodynamic, and routine laboratory variables were not significantly correlated with LVMI or LAVI (Table 6).

Table 2. Comparison between HFrEF Group and HFpEF Group regarding echocardiography and speckle-tracking echocardiography

	HFrEF Group (n=50)	HFpEF Group (n=50)	Test value	*P*-value
Echocardiography				
IVS (cm)	1.00±0.18	1.26±0.15	-7.846	<0.001**
PWT (cm)	1.00±0.17	1.23±0.14	-7.385	<0.001**
LVEDV (mL)	205.82±34.22	97.98±19.04	19.472	<0.001**
LVESV (mL)	143.38±33.82	43.18±10.80	19.957	<0.001**
EF (%)	30.96±6.07	56.76±3.69	-25.682	<0.001**
LVMI (g/m^2)	151.05±35.78	107.62±14.05	7.989	<0.001**
LAVI (mL/m^2)	45.86±6.48	38.46±4.73	6.522	<0.001**
E/e'	9.55±2.12	10.78±2.12	-2.901	0.005*
Speckle-tracking echocardiography				
LASr %	6.10±2.53	16.08±3.04	-17.843	<0.001**
LAScd %	3.54±1.39	9.64±1.74	-19.368	<0.001**

Data are mean ± SD. Test value: t, independent-samples t-test. LAScd is presented as an absolute value; E/A ratio and LASc are not shown because they cannot be measured in AF. *$P < 0.05$ is significant; **$P < 0.001$ is highly significant. HFrEF: Heart failure with reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction, IVS: Interventricular septal thickness, PWT: Posterior wall thickness, LVEDV: Left ventricular end-diastolic volume, LVESV: Left ventricular end-systolic volume, EF: Ejection fraction, LVMI: Left ventricular mass index, LAVI: Left atrial volume index, E/e′: Ratio of early mitral inflow velocity to average early diastolic mitral annular velocity, LA: Left atrial, LASr: Left atrial reservoir strain, LAScd: Left atrial conduit strain

Table 3. Comparison between HFrEF Group and HFpEF Group regarding follow-up after 6 months

	HFrEF Group (n=50)	HFpEF Group (n=50)	Test value	*P*-value
Died	7 (14.0%)	6 (12.0%)	0.088	0.766
Alive at follow-up	43 (86.0%)	44 (88.0%)		
Clinical Outcomes (among patients who completed follow-up)				
Improved	26 (60.5% of 43)	31 (70.5% of 44)	-	0.372
Still	16 (37.2% of 43)	11 (25.0% of 44)	-	0.252
Poor	1 (2.3% of 43)	2 (4.5% of 44)	-	1.000

Percentages for "improved", "still", and "poor" are calculated among patients who completed the 6-month follow-up assessment (n=43 for HFrEF, n=44 for HFpEF); patients who died before follow-up are reported separately in the "died" row above and are not included in these percentages

Died/alive: chi-square test (test value, χ^2); clinical outcome categories: Fisher's exact test. $P > 0.05$ is insignificant

Effect estimates (HFrEF vs. HFpEF)—risk difference with 95% CI (OR with 95% CI): Died: 2.0% (95% CI -11.2 to 15.2; OR 1.19, 95% CI 0.37-3.84); Improved: -10.0% (95% CI -29.9 to 9.9; OR 0.64, 95% CI 0.26-1.56); Still: 12.2% (95% CI -7.1 to 31.5; OR 1.78, 95% CI 0.71-4.46); Poor: -2.2% (95% CI -9.8 to 5.4; OR 0.50, 95% CI 0.04-5.73, continuity-corrected for small cell counts). All CIs are wide and cross the null, consistent with the limited statistical power for these clinical outcome comparisons, as noted in the limitations section

HFrEF: Heart failure with reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction, SD: Standard deviation, CI: Confidence interval, OR: Odds ratio

Table 4. Comparison of changes in NYHA functional class from baseline to follow-up within each group and between HFrEF and HFpEF patients

NYHA Class	HFrEF Group			HFpEF Group			*P*-value between two groups at baseline	*P*-value between two groups at FU
	Baseline (n=50)	FU (n=43)	*P*-value	Baseline (n=50)	FU (n=44)	*P-value*		
Class I	13 (26.0%)	28 (65.1%)	-	10 (20.0%)	25 (56.8%)	-	0.532	0.729
Class II	23 (46.0%)	10 (23.3%)		19 (38.0%)	14 (31.8%)			
Class III	11 (22.0%)	4 (9.3%)		16 (32.0%)	3 (6.8%)			
Class IV	3 (6.0%)	1 (2.3%)		5 (10.0%)	2 (4.5%)			

Between-group comparisons: chi-square test. Within-group P-values are not shown because the paired patient-level data required for this comparison were not available.

HFrEF: Heart failure with reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction, FU: Follow-up, NYHA: New York Heart Association

Table 5. Comparison of changes in echocardiographic parameters (LAVI, LVMI, EF, and left atrial strain) from baseline to follow-up within each group and between HFrEF and HFpEF patients

Echocardiography parameters	HFrEF Group			HFpEF Group			*P*-value between two groups at baseline	*P*-value between two groups at FU
	Baseline (n=50)	FU (n=43)	*P*-value#	Baseline (n=50)	FU (n=44)	*P*-value#		
LAVI								
Mean ± SD	45.86±6.48	42.38±6.51	0.007*	38.46±4.73	35.95±5.42	0.014*	<0.001**	<0.001**
Range	37-59	33-57		30-49	27-50			
LVMI								
Mean ± SD	151.05±35.78	144.38±37.91	0.363	107.62±14.05	102.21±14.62	0.060	<0.001**	<0.001**
Range	98.5-252	95-248		74-156	72-143			
EF								
Mean ± SD	30.96±6.07	34.81±6.47	0.002*	56.76±3.69	59.14±3.35	<0.001	<0.001**	<0.001**
Range	20-42	18-48		50-64	52-65			
LASr								
Mean ± SD	6.10±2.53	6.81±3.88	0.277	16.08±3.04	17.76±2.92	0.006*	<0.001**	<0.001**
Range	2-11	-6 to 13		8-22	8-23			
LAScd								
Mean ± SD	3.54±1.39	4.21±1.54	0.023*	9.64±1.74	10.57±1.67	0.008*	<0.001**	<0.001**
Range	1 to 7	2 to 7		6 to 14	6 to 14			

#Within-group comparison (baseline vs. follow-up): paired-samples t-test; between-group comparisons: independent-samples t-test. LAScd is presented as an absolute value. $P > 0.05$ is insignificant; *$P < 0.05$ is significant; **$P < 0.001$ is highly significant.

HFrEF: Heart failure with reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction, LAVI: Left atrial volume index, LVMI: Left ventricular mass index, EF: Ejection fraction, SD: Standard deviation, LASr: Left atrial reservoir strain, LAScd: Left atrial conduit strain, FU: Follow-up. LAVI in mL/m², LVMI in g/m², EF and strain in %

Sensitivity Analysis Excluding AF Patients

To address the high prevalence of AF and its potential influence on LA strain measurements, a sensitivity analysis was performed, excluding all patients with AF at baseline. After exclusion of 31 HFrEF and 28 HFpEF patients with AF, the primary endpoint (LASr) remained significantly lower in HFrEF than HFpEF (HFrEF, sinus rhythm only, n=19: 7.42±2.81% vs. HFpEF, sinus rhythm only, n=22: 17.15±2.89%; mean difference -9.73%, 95% CI: -11.54 to -7.92; $P < 0.001$), indicating that the between-group difference in LASr was not explained by AF.

Multivariable linear regression models including age, male sex, BMI, and hypertension as predictors of LVMI or LAVI within each group are shown in Table 7. None of the individual predictors was statistically significant, and model-level significance was not reached for HFrEF-LVMI ($R^2 = 0.061$, $P = 0.577$), HFrEF–LAVI ($R^2 = 0.106$, $P = 0.272$), HFpEF-LVMI ($R^2 = 0.084$, $P = 0.404$), or HFpEF-LAVI ($R^2 = 0.099$, $P = 0.309$). All VIF values were <1.3.

Table 6. Spearman correlations (rs, 95% CI) of LV mass index and LA volume index with clinical, laboratory, and echocardiographic variables in the HFrEF and HFpEF groups

	LV mass index		LA volume index	
	r-value	*P*-value	r-value	*P*-value
HFrEF Group				
LASr %	-0.805 (-0.885 to -0.679)	<0.001	-0.870 (-0.924 to -0.781)	<0.001
LAScd %	-0.751 (-0.851 to -0.598)	<0.001	-0.825 (-0.897 to -0.710)	<0.001
Age (years)	-0.119 (-0.385 to 0.165)	0.410	-0.086 (-0.356 to 0.197)	0.552
BMI	0.081 (-0.202 to 0.351)	0.578	0.115 (-0.169 to 0.381)	0.426
NYHA class	0.323 (0.049 to 0.552)	0.022	0.250 (-0.030 to 0.494)	0.080
SBP (mmHg)	-0.047 (-0.321 to 0.234)	0.748	-0.125 (-0.390 to 0.159)	0.387
DBP (mmHg)	-0.103 (-0.371 to 0.181)	0.476	-0.104 (-0.372 to 0.180)	0.473
HR (bpm)	-0.046 (-0.320 to 0.235)	0.749	-0.044 (-0.318 to 0.237)	0.762
NT-proBNP (pg/mL)	0.830 (0.717 to 0.900)	<0.001	0.929 (0.878 to 0.959)	<0.001
Creatinine (mg/dL)	-0.105 (-0.372 to 0.179)	0.467	0.008 (-0.271 to 0.286)	0.959
AST (IU/L)	0.066 (-0.216 to 0.338)	0.646	0.055 (-0.227 to 0.328)	0.704
ALT (IU/L)	-0.076 (-0.347 to 0.207)	0.601	-0.103 (-0.371 to 0.181)	0.477
Sodium (mmol/L)	-0.163 (-0.422 to 0.121)	0.258	-0.145 (-0.407 to 0.139)	0.315
Potassium (mmol/L)	0.079 (-0.204 to 0.350)	0.586	0.201 (-0.082 to 0.454)	0.162
Hb (g/dL)	0.167 (-0.117 to 0.426)	0.246	0.150 (-0.134 to 0.411)	0.299
Hospital duration (days)	0.037 (-0.244 to 0.312)	0.800	0.087 (-0.196 to 0.357)	0.549
IVS (cm)	0.107 (-0.177 to 0.374)	0.460	0.196 (-0.087 to 0.450)	0.172
PWT (cm)	0.118 (-0.166 to 0.384)	0.414	0.106 (-0.178 to 0.373)	0.465
LVEDV (mL)	0.637 (0.436 to 0.777)	<0.001	0.636 (0.435 to 0.777)	<0.001
LVESV (mL)	0.767 (0.621 to 0.861)	<0.001	0.849 (0.747 to 0.912)	<0.001
EF (%)	-0.810 (-0.888 to -0.686)	<0.001	-0.909 (-0.948 to -0.844)	<0.001
E/e′	0.493 (0.249 to 0.678)	<0.001	0.592 (0.376 to 0.747)	<0.001
Follow-up NYHA	0.101 (-0.182 to 0.369)	0.486	0.110 (-0.174 to 0.377)	0.449
HFpEF Group				
LASr %	0.091 (-0.192 to 0.360)	0.528	0.025 (-0.255 to 0.301)	0.861
LAScd %	-0.055 (-0.328 to 0.227)	0.703	-0.061 (-0.334 to 0.221)	0.673
Age (years)	-0.190 (-0.445 to 0.093)	0.186	-0.192 (-0.446 to 0.091)	0.183
BMI	0.159 (-0.125 to 0.419)	0.270	0.125 (-0.159 to 0.390)	0.387
NYHA class	0.149 (-0.135 to 0.410)	0.302	0.104 (-0.180 to 0.372)	0.472
SBP (mmHg)	-0.196 (-0.450 to 0.087)	0.173	-0.179 (-0.436 to 0.105)	0.213
DBP (mmHg)	-0.209 (-0.461 to 0.074)	0.144	-0.251 (-0.495 to 0.029)	0.079
HR (bpm)	0.052 (-0.230 to 0.326)	0.720	0.173 (-0.111 to 0.431)	0.229
NT-proBNP (pg/mL)	0.725 (0.560 to 0.835)	<0.001	0.851 (0.750 to 0.913)	<0.001
Creatinine (mg/dL)	0.112 (-0.172 to 0.379)	0.440	-0.057 (-0.330 to 0.225)	0.692
AST (IU/L)	0.102 (-0.182 to 0.370)	0.479	0.097 (-0.186 to 0.365)	0.502
ALT (IU/L)	0.199 (-0.084 to 0.452)	0.166	0.223 (-0.059 to 0.472)	0.120
Sodium (mmol/L)	0.100 (-0.183 to 0.368)	0.491	0.106 (-0.178 to 0.373)	0.464
Potassium (mmol/L)	0.160 (-0.124 to 0.420)	0.268	0.175 (-0.109 to 0.432)	0.225
Hb (g/dL)	0.026 (-0.254 to 0.302)	0.859	-0.022 (-0.299 to 0.258)	0.882
Hospital duration (days)	0.007 (-0.272 to 0.285)	0.960	-0.033 (-0.309 to 0.248)	0.820
IVS (cm)	0.080 (-0.203 to 0.351)	0.581	0.122 (-0.162 to 0.387)	0.398

Table 6. Continued

	LV mass index		LA volume index	
	r-value	*P*-value	r-value	*P*-value
HFpEF Group				
PWT (cm)	-0.153 (-0.414 to 0.131)	0.290	-0.160 (-0.420 to 0.124)	0.266
LVEDV (mL)	-0.168 (-0.426 to 0.116)	0.243	-0.190 (-0.445 to 0.093)	0.186
LVESV (mL)	-0.057 (-0.330 to 0.225)	0.696	-0.049 (-0.323 to 0.233)	0.737
EF (%)	-0.011 (-0.288 to 0.268)	0.941	0.000 (-0.278 to 0.278)	0.999
E/e'	0.423 (0.164 to 0.627)	0.002	0.560 (0.334 to 0.725)	<0.001
Follow-up NYHA	0.132 (-0.152 to 0.396)	0.361	0.209 (-0.074 to 0.461)	0.146

LV: Left ventricular, LA: Left atrial, HFrEF: Heart failure with reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction, LASr: Left atrial reservoir strain, LAScd: Left atrial conduit strain (absolute value), NYHA: New York Heart Association, NT-proBNP: N-terminal pro-B-type natriuretic peptide, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, Hb: Hemoglobin, EF: Ejection fraction, CI: Confidence interval (Fisher's z transformation), BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, PWT: Posterior wall thickness, LVEDV: Left ventricular end-diastolic volume, LVESV: Left ventricular end-systolic volume, IVS: Interventricular septal thickness

Table 7. Multivariable linear regression analysis of determinants of LVMI and LAVI within each group

Model	Predictor	β	SE	95% CI	*P*-value	VIF	R^2	Adjusted R^2	F-statistic	Model *P*-value
HFrEF-LVMI	Age (years)	-0.274	0.553	-1.388 to 0.839	0.622	1.053	-	-	-	-
	Male sex	-6.239	8.450	-23.257 to 10.779	0.464	1.230	-	-	-	-
	BMI	0.765	0.855	-0.957 to 2.486	0.376	1.197	-	-	-	-
	Hypertension	2.144	7.365	-12.689 to 16.977	0.772	1.041	-	-	-	-
	Model statistics	-	-	-	-	-	**0.061**	**-0.023**	**0.729**	**0.577**
HFrEF-LAVI	Age (years)	-0.022	0.217	-0.459 to 0.415	0.920	1.053	-	-	-	-
	Male sex	-3.955	3.317	-10.636 to 2.725	0.239	1.230	-	-	-	-
	BMI	0.410	0.336	-0.265 to 1.086	0.228	1.197	-	-	-	-
	Hypertension	0.958	2.891	-4.864 to 6.781	0.742	1.041	-	-	-	-
	Model statistics	-	-	-	-	-	**0.106**	**0.026**	**1.333**	**0.272**
HFpEF-LVMI	Age (years)	-0.541	0.381	-1.308 to 0.226	0.162	1.030	-	-	-	-
	Male sex	1.105	6.212	-11.407 to 13.618	0.860	1.172	-	-	-	-
	BMI	1.282	0.899	-0.529 to 3.092	0.161	1.186	-	-	-	-
	Hypertension	-6.440	6.645	-19.823 to 6.943	0.338	1.090	-	-	-	-
	Model statistics	-	-	-	-	-	**0.084**	**0.002**	**1.026**	**0.404**
HFpEF-LAVI	Age (years)	-0.218	0.114	-0.448 to 0.012	0.063	1.030	-	-	-	-
	Male sex	-0.150	1.863	-3.902 to 3.601	0.936	1.172	-	-	-	-
	BMI	0.303	0.270	-0.240 to 0.846	0.268	1.186	-	-	-	-
	Hypertension	-0.125	1.992	-4.138 to 3.888	0.950	1.090	-	-	-	-
	Model statistics	-	-	-	-	-	**0.099**	**0.019**	**1.235**	**0.309**

All models included four predictors: age, sex (male), BMI, and hypertension. Each model was based on n=50 participants per group. VIF values were <1.3 for all predictors, indicating no relevant collinearity.

β: Unstandardized regression coefficient, HFrEF: Heart failure with reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction, SE: Standard error, CI: Confidence interval, VIF: Variance inflation factor, LVMI: Left ventricular mass index, LAVI: Left atrial volume index

DISCUSSION

HF remains a major global health problem characterized by substantial morbidity and mortality despite advances in medical therapy. Although HFrEF and HFpEF share similar clinical manifestations, they differ considerably in their underlying pathophysiology, patterns of cardiac remodeling, and clinical outcomes.[4] Conventional echocardiography remains the cornerstone of cardiac assessment; however, it may not fully characterize atrial mechanical dysfunction, which has emerged as an important determinant of disease severity and prognosis.[7] This study therefore combined conventional echocardiographic measurements with speckle-tracking-derived LA strain to evaluate structural and functional remodeling in patients with HFrEF and HFpEF.

The present study demonstrated distinct demographic characteristics of the two HF phenotypes despite comparable age distributions. HFrEF was predominantly observed in men, whereas HFpEF occurred more frequently in women. In addition, patients with HFpEF had significantly higher BMI and were more likely to have hypertension, reflecting the well-recognized clinical profile of HFpEF as a syndrome strongly associated with obesity and multiple cardiovascular comorbidities.[4] These findings are consistent with those of Gehlken et al.,[18] who reported a predominance of men in HFrEF and a higher prevalence of hypertension and higher BMI among patients with HFpEF.

Although symptom severity, as assessed by NYHA functional class, was comparable between the two groups, laboratory evaluation revealed significantly higher NT-proBNP concentrations in patients with HFrEF, reflecting the greater myocardial wall stress and neurohormonal activation associated with advanced systolic dysfunction. This is consistent with previous studies showing higher natriuretic peptide concentrations in HFrEF than in HFpEF.[19] Renal function, liver enzymes, electrolyte levels, and hemoglobin concentrations were comparable between the groups. However, because the groups also differed in sex, BMI, and the prevalence of hypertension, the observed differences in cardiac remodeling cannot be attributed solely to the HF phenotype.

Electrocardiographic findings further highlighted the different remodeling patterns between the two phenotypes. LBBB was significantly more frequent in patients with HFrEF, consistent with the advanced ventricular remodeling, myocardial fibrosis, and electrical dyssynchrony that accompany systolic dysfunction. AF was common in both groups, and its prevalence did not differ significantly between HFrEF and HFpEF, which emphasizes the close relationship between atrial remodeling and HF irrespective of ejection fraction. Because the association between rhythm status and LA size was not analyzed separately, this relationship should be interpreted with caution. Collectively, these demographic, biochemical, and electrocardiographic findings are consistent with HFrEF and HFpEF being distinct clinical entities with different patterns of myocardial remodeling.

Conventional echocardiography demonstrated distinct patterns of cardiac remodeling between HFrEF and HFpEF. Patients with HFrEF exhibited significantly greater left ventricular dilatation, as evidenced by increased end-diastolic and end-systolic volumes, markedly reduced LVEF, and higher LVMI and LAVI, a pattern consistent with chronic volume overload and progressive systolic dysfunction. In contrast, patients with HFpEF demonstrated significantly greater interventricular septal and PWT, in keeping with hypertrophic remodeling related to pressure overload. Because relative wall thickness was not reported, left ventricular geometry (eccentric vs. concentric remodeling) could not be formally classified.

Our findings are in line with those of Gehlken et al.,[18] who found that in HFpEF, LAVI was independently associated with age, AF, NT-proBNP, and LVMI, supporting a close link between atrial and ventricular remodeling. In the echocardiographic substudy of PARAGON-HF, Shah et al.[20] reported LA enlargement in 83% and an elevated E/e′ ratio in 53% of patients with HFpEF, whereas left ventricular hypertrophy was present in 21%. In a community population with mildly reduced or preserved EF, Zhang et al.[21] showed that EF indexed to LVM was associated with cardiac event risk, supporting the relevance of ventricular mass-related remodeling.

LA remodeling also differed substantially between the two groups. Patients with HFrEF exhibited significantly greater LA enlargement than those with HFpEF, consistent with the cumulative effects of chronic volume overload, elevated filling pressures, and progressive ventricular dysfunction. Although LAVI is a well-established marker of chronic diastolic burden, it does not fully characterize atrial mechanical performance. Functional impairment of the left atrium may precede substantial structural enlargement,[7] suggesting that volumetric assessment alone may underestimate the degree of atrial dysfunction. Consistent with this concept, Okada et al.[22] showed that an index integrating LA volume with LA mechanical function provided prognostic information in patients with HFpEF.

Speckle-tracking echocardiography provided additional insights into atrial mechanical dysfunction that were not evident from conventional echocardiographic parameters alone. Patients with HFrEF demonstrated markedly lower LA reservoir and conduit strain than patients with HFpEF, indicating more advanced impairment of atrial mechanical function. These findings parallel those of the meta-analysis by Jin et al.,[23] in which LASr was worse in HFrEF than in HFpEF despite a higher

burden of AF in HFpEF, suggesting that LA myopathy is not specific to HFpEF. Atrial dysfunction in HFrEF may therefore reflect more extensive remodeling of both atrial and ventricular myocardium, rather than isolated atrial enlargement.

The present findings are also consistent with growing evidence supporting LA strain as a marker of cardiac dysfunction. Reddy et al.[24] showed that LASr was reduced in HFpEF and improved its diagnostic evaluation, whereas Kanagala et al.[25] found that LA function, assessed as LA ejection fraction by cardiac magnetic resonance, was associated with adverse outcomes in HFpEF. Likewise, Benfari et al.[26] reported that an index coupling LA volume with LA mechanical function provided incremental prognostic information in HFrEF. Together, these data support further evaluation of LA function as an adjunct to conventional echocardiographic assessment.

In the present study, HFrEF retained higher LAVI and LVMI, and a more impaired LA strain profile at follow-up than HFpEF. However, LAVI decreased in both groups, and LVMI did not change significantly within either group. Because baseline measurements were largely obtained during hospitalization, the decrease in LAVI may partly reflect recompensation and lower filling pressures rather than structural reverse remodeling. Thus, the current findings support persistent phenotypic differences between groups rather than progressive remodeling. Okada et al.[22] observed that better preservation of LA mechanical function relative to LA size in HFpEF was associated with more favorable clinical outcomes. Longer follow-up is needed to determine how LA dysfunction evolves over the course of the disease.

Clinical Implications

The present findings highlight the complementary value of conventional echocardiography and speckle-tracking imaging in HF assessment. LA strain may provide functional information beyond conventional volumetric indices and contribute to phenotypic characterization and longitudinal follow-up. Whether LA strain adds incremental diagnostic or prognostic value beyond conventional parameters was not tested in this study and should be examined in future work.

Study Limitations

The strengths of this study include its prospective design, standardized echocardiographic protocol, and assessment of both conventional and speckle-tracking parameters in HFrEF and HFpEF. Several limitations should be acknowledged. First, this single-center study had a relatively small sample, which may limit generalizability, and its observational design precludes causal inference. Second, the sample size was calculated for LVMI, a secondary endpoint, rather than for the primary endpoint (LASr); although the observed difference in LASr was large, the study may be underpowered for secondary and exploratory analyses, particularly multivariable regression. Third, because the groups were defined by EF and the HFpEF criteria included LAVI, LVMI, and E/e′, between-group differences in these variables are partly circular; in addition, sinus-rhythm diagnostic thresholds were applied, whereas higher thresholds are recommended in AF.[6] Fourth, no receiver operating characteristic or incremental-value analysis was performed, so the discriminatory value of LA strain relative to LAVI and LVMI was not tested. Fifth, the high prevalence of AF may have influenced LA volume and strain measurements; because rhythm status could not be linked to individual patients, the E/A ratio and contractile strain were not analyzed and the analyses could not be adjusted for rhythm, and the sensitivity analysis excluding patients with AF was limited to the primary endpoint. Sixth, ischemic heart disease was excluded on the basis of clinical history and ECG without routine coronary imaging, so unrecognized coronary artery disease cannot be ruled out, particularly in HFrEF patients with Q-waves, and the non-ischemic aetiology of HF was not recorded; in addition, excluding ischemic heart disease limits generalizability to the broader HFrEF population, in whom ischemic cardiomyopathy is a major cause.

Seventh, group assignment was based on the LVEF at enrolment, and a small number of HFrEF patients had an LVEF of 41-42% on the study echocardiogram, within the HFmrEF range. Eighth, imbalances in sex, BMI, and hypertension between the groups may confound comparisons of cardiac remodeling, and residual confounding cannot be excluded. Ninth, differences in guideline-directed medical therapy (particularly ACE inhibitors/ARBs and MRAs) between groups may have influenced remodeling during follow-up. Tenth, baseline measurements were largely obtained during hospitalization, so the decrease in LAVI at follow-up may partly reflect recompensation rather than structural reverse remodeling; moreover, follow-up data were available only for survivors, which introduces possible survivor bias. Eleventh, many comparisons were performed without correction for multiplicity, so findings other than the primary endpoint should be regarded as exploratory. Twelfth, the study was underpowered for clinical outcomes given the small numbers of deaths (7 HFrEF, 6 HFpEF) and re-hospitalizations; non-significant *P*-values should not be interpreted as evidence of equivalence between groups. Finally, follow-up was short; LA strain measurements depend on image quality and analysis software, and images acquired on one vendor's system were analyzed with another vendor's software after DICOM export, which may affect comparability with vendor-specific reference values; and functional exercise testing and continuous rhythm monitoring were not performed. Larger multicenter studies with longer follow-up are warranted to confirm these findings.

CONCLUSION

HFrEF and HFpEF exhibit distinct patterns of cardiac remodeling. Compared with HFpEF, HFrEF is characterized by greater ventricular dilatation, more advanced structural remodeling, and more severe impairment of LA mechanics, including significantly lower LASr. Speckle-tracking echocardiography detected between-group differences in LA mechanics and correlations between these mechanics and markers of cardiac remodeling; whether LA strain adds incremental diagnostic or prognostic value beyond conventional echocardiographic parameters was not formally tested in this study, and therefore remains hypothesis-generating. These findings support further evaluation of LA strain as a potential adjunct to conventional echocardiographic assessment in HF, pending confirmation in larger, adequately powered multicenter studies.

Ethics

Ethics Committee Approval: The study protocol was approved by the Research Ethics Committee of Benha University Faculty of Medicine (protocol no: MS 28-1-2024, approval date: 28.01.2024).

Informed Consent: Written informed consent was obtained from all participants or their legal representatives in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Footnotes

Authorship Contributions

Medical Practices: M.H.H., A.E.E., Concept: M.H.H., A.E.E., Design: M.H.H., Data Collection or Processing: M.H.H., H.H.E., S.S.E., G.E., A.E.E., Analysis or Interpretation: M.H.H., H.H.E., S.S.E., G.E., Writing: M.H.H., S.S.E., G.E.

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