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Left atrial strain in patients without cardiovascular disease: uncovering influencing and related factors

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Abstract

Background Despite its proven prognostic value in different contexts, the precise implications of left atrial strain (LAS) assessment throughout different phases of the atrial cycle remain uncertain. A direct correlation between left atrial reservoir strain (LARS) and left ventricular global longitudinal strain (GLS) has been consistently demonstrated in several studies involving patients with various heart diseases. The objective of our study is to identify factors directly associated with LARS, left atrial conduction strain (LACS) and left atrial booster strain (LABS) in patients without cardiovascular (CV) disease.

Methods Transthoracic echocardiographic examinations in patients without CV disease were prospectively selected in two tertiary hospitals echocardiography labs for clinical purposes. LAS, maximal and minimal left atrial (LA) volumes and left atrial ejection fraction (LAEF) were measured using the two-dimensional strain analysis package provided by the EchoPAC Plugging workstation (AFI LA).

Results A total of 196 cases were included, median age of 54 (45–62) with 85 (43%) being men. The mean left ventricular ejection fraction (LVEF) was $61\% \pm 5$, and the median GLS was -18% (-17 to -20). Median indexed maximum volume of left atrium (LAVI) was 27 ml/m^2 (22 – 31), and LAEF was 64% (58 – 70). The mean LARS biplane was $35,1\% \pm 8$. Notably, LARS was greater in the 2-chamber view ($36,1\% \pm 10$) compared to the 4-chamber view ($34,1\% \pm 8$ $p < 0,05$). The multivariate analysis of LARS revealed that sex, GLS, LAEF and e'_{mean} are independently correlated with LARS. Multivariate analysis of LACS showed independent correlations between LACS and age, GLS, LAEF, E/A ratio and e'_{mean} . Conversely, the multivariate analysis of LABS demonstrated significant correlations among A wave, e'_{mean} and left atrial stiffness index (LASI).

Conclusions In patients without CV disease, GLS emerges as a crucial determinant of LARS and LACS. LAEF and e'_{mean} are directly and independently related to both LARS and LACS. LARS (univariate) and LACS (multivariate) exhibited a decline with older age in individuals without CV disease.

Keywords Left atrial strain, left atrial reservoir strain, global longitudinal strain, left atrial ejection fraction, speckle tracking echocardiography

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Background

Over the past fifteen years, the left atrial strain (LAS) has been increasingly analyzed by standardized transthoracic echocardiography [1, 2]. While numerous studies have demonstrated its prognostic significance in various clinical scenarios, the precise implications of LAS assessment throughout different phases of the atrial cycle remain uncertain [3]. LAS has been used as an indicator of atrial function [4], in the study of diastolic function in patients with preserved left ventricular ejection fraction (LVEF) [5, 6]. Some researchers have proposed its inclusion among the parameters of diastolic dysfunction instead of the indexed maximum volume of the left atrium (LAVI) [7]. Promisingly LAS evaluation has shown potential in predicting the progression of atrial fibrillation [8] and assessing stroke risk [9]. Several articles suggest that its incorporation into the CHA₂DS₂-VASc criteria enhances the predictive efficacy of the score [10].

Notably, a direct correlation between left atrial reservoir strain (LARS) and left ventricular global longitudinal strain (GLS) has been consistently demonstrated in several studies involving patients with various heart diseases [11, 12]. However, these data may seem to be inconsistent with the specificity of LARS as a marker of auricular disease. Concurrently, LAS has also been associated with left atrial stiffness, atrial fibrosis and elevated filling pressures. Nevertheless, most studies encompass patients with diverse heart diseases, hindering an unbiased assessment of determinants influencing LAS.

The objective of our multicentric study is to identify factors directly associated with LARS, left atrial conduction strain (LACS) and left atrial booster strain (LABS) in patients without any cardiac or cardiovascular (CV) disease.

Methods

We conducted a prospective study of consecutive transthoracic echocardiographic examinations from November 1, 2022, to February 1, 2023, involving patients aged 18 to 85 years, with no known CV disease, and in sinus rhythm. Evaluations were performed in two echocardiography laboratories in tertiary hospitals for clinical purposes.

Patients meeting any of the following criteria were excluded: inadequate image quality, LVEF < 50%, GLS > -15%, septum or posterior wall thickness > 13 mm, segmental motility disorders, severe cardiac chambers dilation, pulmonary hypertension, pericardial effusion, valvular stenosis or more than trivial valvular regurgitation and known medical history of peripheral vascular disease, coronary heart disease, cardiac surgery, cardiomyopathies and atrial or ventricular rhythm disorders. Patients with stroke were not specifically excluded.

The study was registered and approved from the Regional Board for Ethics in Research with Humans CEI: IB 5212/23 Protocol CI 736–23 and adhered to the principles outlined in the Declaration of Helsinki.

All the studies were conducted using GE Vivid E9 or Vivid E95 echocardiographs and analyzed on EchoPAC Plugging on Centricity Cardio Workflow V7.0 SP 8.1.1 (GE Healthcare). Images were acquired at end-expiratory apnea with frame rate between 50–80/s.

Demographics, clinical and echocardiographic data collected included age, sex, systolic (SBP) and diastolic blood pressure (DBP), heart rate (HR), body surface area (BSA), basal septum, posterior wall, wall thickness (WT) = basal septum + posterior wall, left ventricular end-diastolic volume index (LVEDVi), left ventricular end-systolic volume index (LVESVi), LVEF (biplane Simpson's method), left ventricular 4-chambers strain (LV4cS), left ventricular 2-chambers strain (LV2cS), GLS, LAVI, left atrial ejection fraction (LAEF), 4-chambers LARS, 2-chambers LARS, biplane LARS, biplane LACS, biplane LABS, total atrial conduction time (PA-TDI), peak mitral E wave (E), peak mitral A wave (A), E/A ratio, E deceleration time (EDT), isovolumic relaxation time (IRT), e'_{septal} ($e's$), e'_{lateral} ($e'l$), e'_{mean} , E/e'_{mean} , left atrial stiffness index (LASI), peak gradient of tricuspid regurgitation (TR max) and tricuspid annular plane systolic excursion (TAPSE).

Echocardiographic measurements were made according to the American Society of Echocardiography criteria [13]. Volume data were indexed to BSA. PA-TDI was defined as the time from the beginning of the P wave on ECG to the peak of the A lateral mitral annulus wave on Tissue Doppler Imaging. LASI was defined as the ratio E/e'_{mean} /biplane LARS.

The measurement of volumes and longitudinal strain of left ventricle (LV) and left atrial (LA) were performed in the Core Lab by the same author*.

LAS, maximal and minimal LA volumes and LAEF were measured using a semi-automatic two-dimensional auricular strain analysis package provided by the EchoPAC Plugging workstation (AFI LA) with manual adjustments only if unsatisfactory tracking was observed. The starting point of the QRS wave of in the ECG served as the zero baseline. The two base points of the mitral annulus at 4 and 2 chambers view, and the top of the distal end of the LA were manually selected (Fig. 1) [14].

Statistical analysis

Analysis was performed using SPSS version 23.0 (IBM Corporation). Continuous variables were expressed as mean \pm SD or interquartile ranges, depending on their distribution; categorical variables were expressed as counts and percentages.

Univariate linear regression and Spearman correlation was performed to investigate the associations between

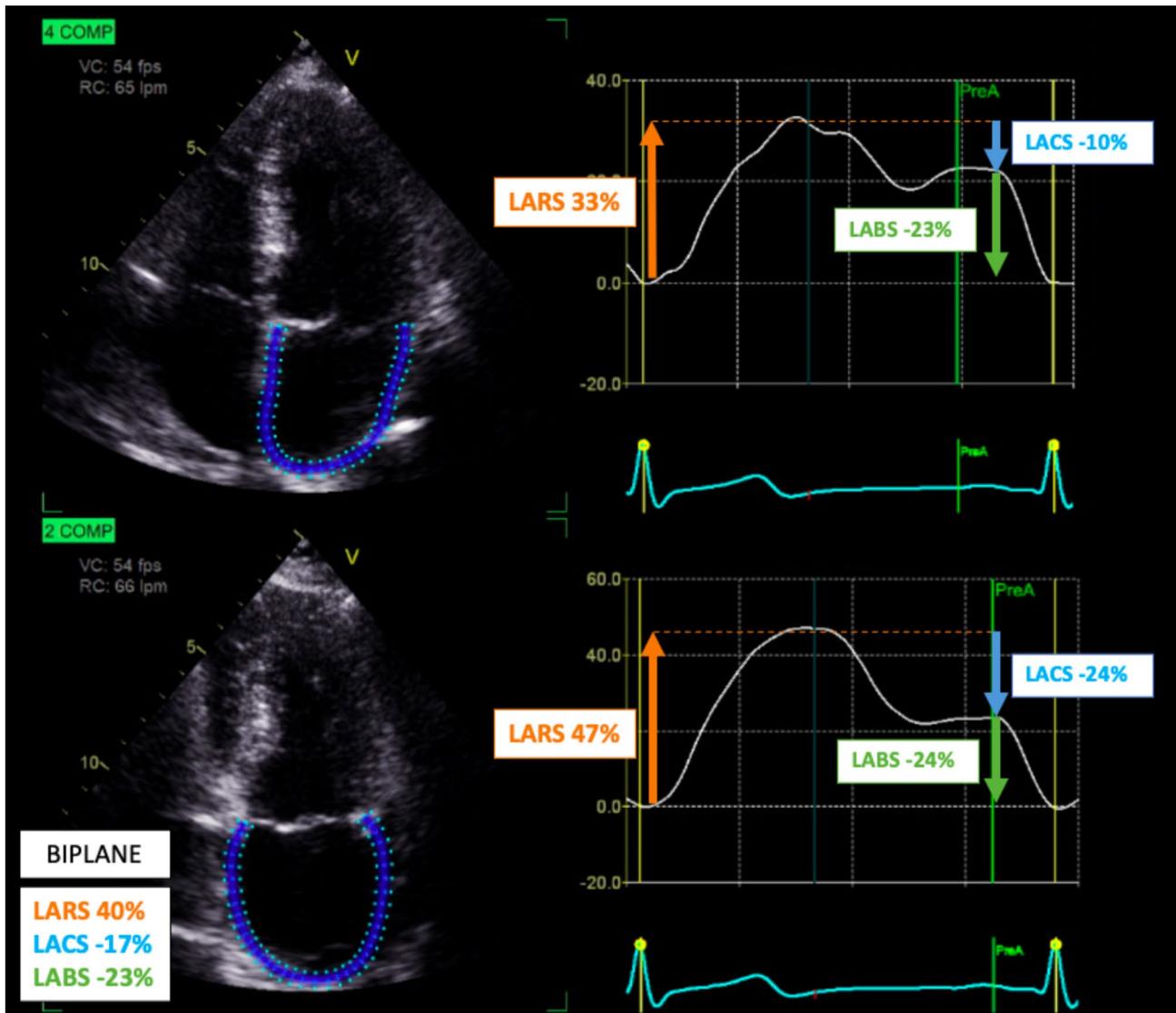


Fig. 1 Measurements of biplane left atrial strain using 2D echocardiography
Left atrial reservoir strain (LARS), left atrial conduction strain (LACS) and left atrial booster strain (LABS)

LARS, LACS and LABS and others clinical or echocardiographic parameters. Parameters associated with LAS (based on a conservative $p < 0.1$) were selected for inclusion in the multivariate model. A multivariate logistic regression model was constructed using a stepwise backward selection approach. We used the Akaike and Bayes information criteria to compare models [15, 16].

To establish reliability and reproducibility for the quantification of function and volume, 15 patients were randomly selected and re-analyzed at least 1 month after their initial assessments. Intraclass correlation coefficient (ICC) was calculated to evaluate intraobserver agreement for LA and LV volumes, LV4cS, LV2cS, GLS, and LAS.

A p value less than 0,05 was considered statistically significant.

Results

Patient baseline characteristics

A total of 196 cases were included in the study. Descriptive statistics for the studied parameters are presented in Table 1. The study cohort had a median age of 54 (45–62) with 85 (43%) being men. The mean LVEF was $61\% \pm 5$, and the median GLS was -18% (-17 to 20). Median LAVI was 27 ml/m^2 (22 – 31), and LAEF was 64% (58 – 70). The mean LARS biplane was $35,1\% \pm 8$. Notably, LARS was greater in the 2-chamber view ($36,1\% \pm 10$) compared to the 4-chamber view ($34,1\% \pm 8$ $p < 0,05$). However, a strong correlation between LARS 4-chamber and LARS 2-chamber was observed, with a Pearson coefficient of 0,86.

Automated measurements of LA volumes by the AFI-LA software were lower than the manual measurement

Table 1 Sociodemographic, clinical and echocardiographic characteristics of the study population

	n = 196
Age	54 (45–62)
Male	85 (43%)
SBP, mmHg	131 (20)
DPB, mmHg	70 (9)
BSA, kg/m ²	1,8 (0–2)
HR, bpm	68 (62–77)
Echo parameters	
LARS, % (biplane)	35,1 (8)
LARS, % (4 C)	34,1 (8)
LARS, % (2 C)	36,1 (10)
LACS, % (biplane)	18,8 (8)
LABS, % (biplane)	16,3 (5)
GLS, %	-18 (-17 to -20)
E, cm/s	73 (17)
A, cm/s	67 (58–81)
E/A	1,06 (0,83 – 1,30)
e' mean, cm/s	9,5 (8–11,5)
E/e'	7,14 (6–8,84)
TR max, mmHg	22 (5)
TAPSE, mm	22 (4)
PA-TDI, msec	131 (115–143)
LASI	0,20 (0,16 – 0,28)
IRT, msec	104 (21)
EDT, msec	212 (181–239)
LAVI, ml/m ²	27 (22–31)
LAEF, %	64 (58–70)
WT, mm	18 (16–20)
LVEDVi, ml/m ²	56 (47–64)
LVESVi, ml/m ²	21 (17–27)
LVEF, %	61 (5)

Categorical values are presented as absolute numbers (and percentage) and continuous variables as mean and standard deviation (normal distribution) or as median and range for nonparametric

A=peak mitral inflow late velocity; DBP=diastolic blood pressure; E=peak mitral inflow early velocity; EDT=E deceleration time; e' mean=mitral annular early velocity; GLS global longitudinal strain; HR=heart rate; IRT=isovolumic relaxation time; LABS=left atrial booster strain; LACS=left atrial conduction strain; LAEF=left atrial ejection fraction; LARS=left atrial reservoir strain; LASI=left atrial stiffness index; LAVI=left atrial volume indexed to body surface area; LVEDVi=left ventricular diastolic volume indexed to body surface area; LVEF=left ventricular ejection fraction; LVESVi=left ventricular systolic volume indexed to body surface area; PA-TDI=total atrial conduction time; SBP=systolic blood pressure; TAPSE=tricuspid annular plane systolic excursion; TR max=peak gradient of tricuspid regurgitation; WT=wall thickness

performed by the operator. However, LAEF was considered valid, as the mismatch was consistent at both maximum and minimum LA volumes.

Reproducibility

Intra-observer variability was excellent, with ICC greater than 0.95 for all values studied.

All selected patients could be analyzed to obtain LAS and LAEF with a time consumption of less than two minutes.

Association between LAS and other parameters

Table 2 presents the results of univariate regression analyses for LARS, LACS and LABS. Table 3 displays the results of the multivariate analysis for LARS, LACS and LABS.

The multivariate analysis of LARS involved age, sex and statistically significant factors in the univariate analysis. It revealed that sex, GLS, LAEF (Fig. 2) and e' mean are directly and independently correlated with LARS.

Multivariate analysis of LACS showed direct and independent correlations between LACS and GLS, LAEF, E/A ratio and e' mean and inverse correlation with age (Fig. 3). Conversely, the multivariate analysis of LABS demonstrated significant direct correlation with A wave, and inverse correlations with e' mean and LASI.

Echocardiographic parameters such as LVEF, HR, PA-TDI, and LAVI did not show any significant correlation with LAS.

Table 2 Biplane univariate analysis to determine variables in LARS, LACS and LABS

Predictors	LARS		LACS		LABS	
	R		R		R	
Age	-0,47***		-0,64***		0,25***	
SBP	-0,21**		-0,34***		0,20*	
DBP	ns		-0,19*		0,22**	
WT	-0,26***		-0,33***		ns	
LVEDVi	0,25***		0,29***		ns	
LVESVi	0,19*		0,25**		ns	
GLS	0,43***		0,45***		ns	
LAVmin	-0,46***		-0,31***		-0,27***	
LAEF	0,72***		0,53***		0,33***	
E wave	0,25**		0,45***		-0,32***	
A wave	-0,15*		-0,37***		0,33***	
E/A	0,28***		0,55***		-0,40***	
IRT	-0,24**		-0,33***		ns	
e' mean	0,55***		0,76***		-0,28***	
E/e'	-0,36***		-0,37***		ns	
TAPSE	0,27***		0,27***		ns	
LASI			-0,59***		-0,26***	
LVEF	0,05 ns		0,02 ns		0,04 ns	

A=peak mitral inflow late velocity; DBP=diastolic blood pressure; E=peak mitral inflow early velocity; e' mean=mitral annular early velocity; GLS=global longitudinal strain; IRT=isovolumic relaxation time; LABS=left atrial booster strain; LACS=left atrial conduction strain; LAEF=left atrial ejection fraction; LARS=left atrial reservoir strain; LASI=left atrial stiffness index; LAVi=left atrial volume indexed to body surface area; LAVmin=left atrial minimum volume; LVEDVi=left ventricular diastolic volume indexed to body surface area; LVESVi=left ventricular systolic volume indexed to body surface area; SBP=systolic blood pressure; TAPSE=tricuspid annular plane systolic excursion; WT=wall thickness

*p<0,05; ** p<0,005; *** p<0,0005; ns: not significant

Table 3 Biplane multivariate analysis to determine variables in LARS, LACS and LABS

Predictors	LARS		LACS		LABS	
	Mean differences	p-value	Mean differences	p-value	Mean differences	p-value
Age			-13,79	0,001		
Sex	-1,54	0,034				
GLS, %	1,13	0,0005	0,64	0,0005		
LAEF, %	0,44	0,0005	0,28	0,0005		
e' mean,	0,53	0,002	0,99	0,008	-0,92	0,0005
E/A			2,54	0,003		
A					0,1	0,0005
LASI					-30,78	0,0005

A=peak mitral inflow late velocity; E=peak mitral inflow early velocity; e' mean=mitral annular early velocity; GLS=global longitudinal strain; LABS=left atrial booster strain; LACS=left atrial conduction strain; LAEF=left atrial ejection fraction; LARS=left atrial reservoir strain; LASI=left atrial stiffness index

Discussion

In recent years, numerous publications have studied the role of LAS for diagnostic and prognostic purposes in CV diseases. However, LAS determinants, especially in the absence of structural heart disease, remains unclear [3]. Our study aims to unveil the associated factors to the different components of LAS in this class of subjects without CV disease. The results may contribute to comprehend the mechanistic determinants of LA strain, which are more complex than just LA tissue properties, and constitutes a basis for further research in specific cardiovascular diseases.

2-chambers LARS was found to be greater than 4-chambers LARS, consistent with other studies, as the

evaluation of the inferior wall in 2-chamber view exhibits the highest strain [1]. In contrast, 4-chamber view involves the interatrial septum, thinner and with fewer myocytes, and the entrance of the pulmonary veins.

Ventricular longitudinal deformation represented as GLS emerged as a determining and independent factor of LARS and LACS in individuals without CV disease (p<0.0005). Notably, commonly used measures of LV systolic function like LVEF did not show any correlation. This finding could be because we have only included patients with preserved LVEF, so small differences in EF are not relevant in this population.

LV volumes also increase in univariate LARS and LACS as previously described [11].

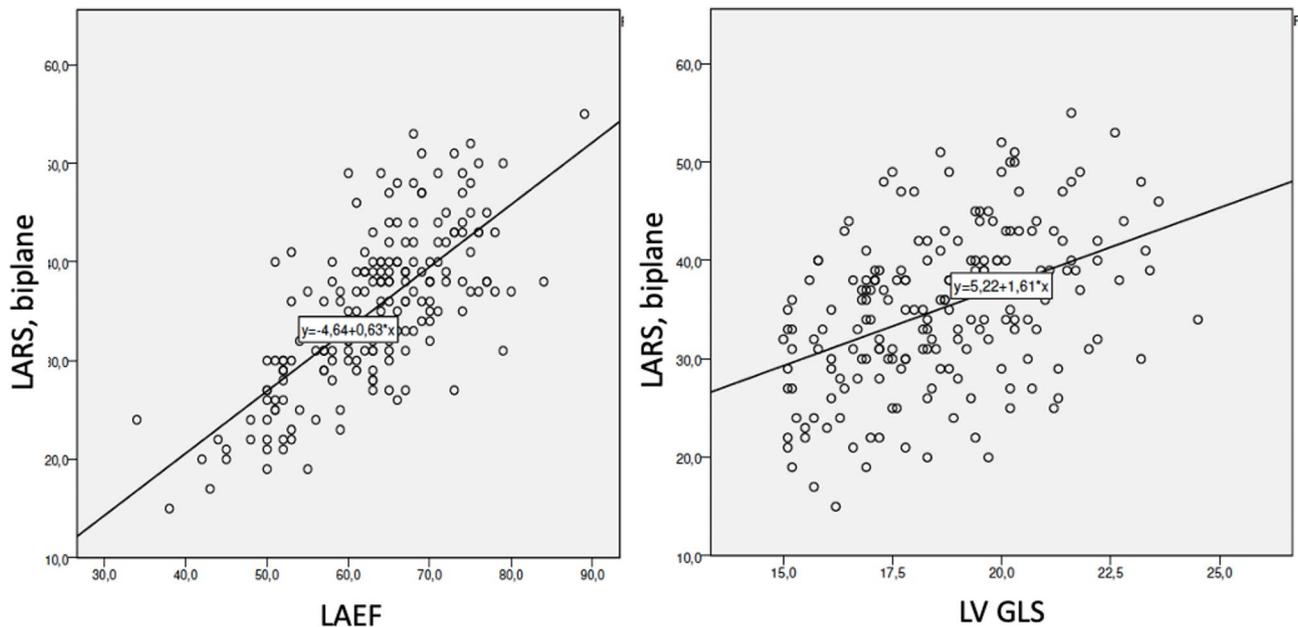


Fig. 2 Scatter plot of the correlation of biplane left atrial reservoir strain (LARS) and left atrial ejection fraction (LAEF) and left ventricle global longitudinal strain (LV GLS)

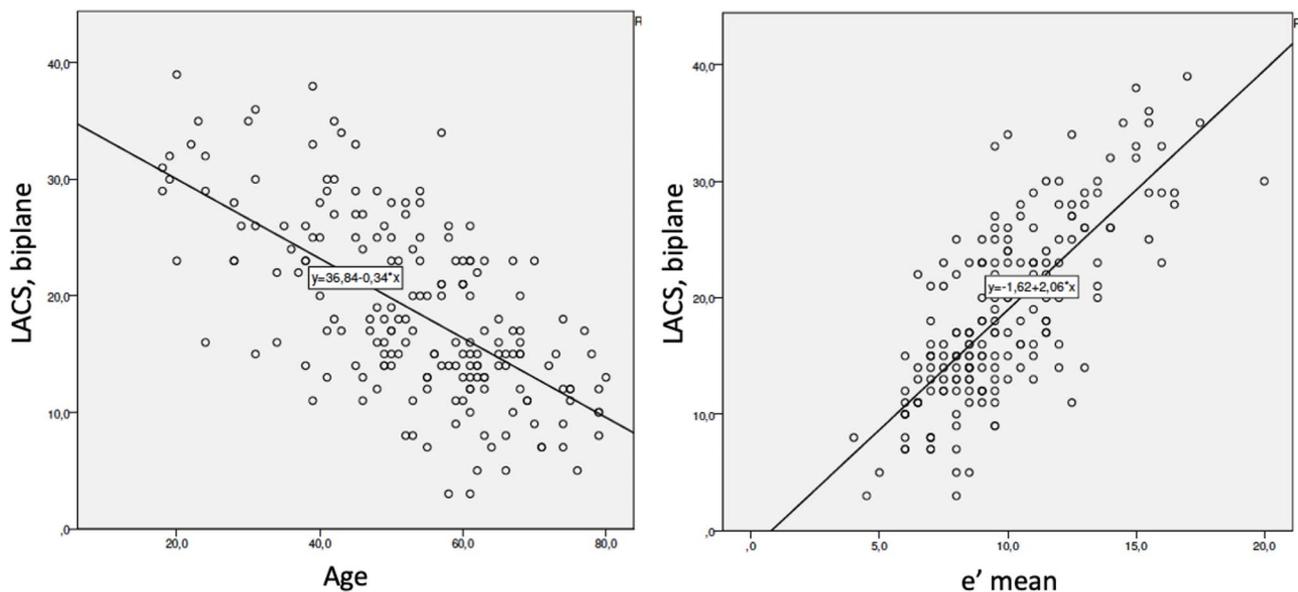


Fig. 3 Scatter plot of the correlation of biplane left atrial conduction strain (LACS) and age and e' mean

LAEF was closely related to LARS and LACS ($p < 0.0005$), although in this case it is logical to infer that LARS and LACS influence LAEF, with LAEF being the consequence of atrial wall strain.

The protodiastolic velocity of mitral annulus (e'_{mean}) correlated with three phasic LAS. This relationship is understandable in the context of LACS, where e' serves as a surrogate of ventricular relaxation, favoring atrial emptying in early diastole. The correlation with LARS demonstrates how the interaction between atrial and ventricular strain occurs through the mitral annulus.

We did not measure annulus velocity during ventricular systole which should have a stronger relationship with LARS. Thus, the movement of the mitral annulus due to myocardial deformation appears to be the interface between the longitudinal function of LV and LA.

The correlation between e'_{mean} and LABS was inverse, indicating the compensatory role of atrial systole when relaxation is slow.

Age exhibited an inverse correlation with LARS and LACS in univariate analysis and direct correlation with LABS. In multivariate analysis it remained significant

in LACS ($p < 0.0005$), suggesting that in older patients without CV disease, conduction strain declines along with e'_{mean} , EDT and other parameters related to slower relaxation, in older individuals. This mirrors the known decrease in both ventricular and atrial relaxation with age.

LA maximal volume was not related to LAS in patients without CV disease. Conversely LA minimal volume was directly related in the univariate analysis to all three LAS components, although it did not appear in the multivariate analysis due to probable interference with LAEF. However, it behaves as a more sensitive parameter of atrial function and ventricular diastolic function than maximum volume of LA [17].

Sex did not show correlation with any component of LAS in the univariate analysis. However, in the multivariate analysis of LARS, a weak significance appears ($p = 0.034$) difficult to interpret. It has been reported that the reduction of LARS with age is more prominent in women than in men [18, 19], which may explain its significance in the multivariate.

SBP, DBP and WT exhibited a slight inverse correlation with LARS and a more intense correlation with LACS in the univariate analysis; LABS has weak direct correlation with SBP and DBP.

The E/A filling pattern was directly related to LACS and inversely related to LABS. The multivariate analysis of LABS demonstrated its direct relationship with the A wave of mitral filling and its inverse relationship with e'_{mean} and LASI. LABS was the atrial strain least related to LV function or volumes.

Factors influencing LAS vary depending on cardiovascular physiology or pathology. In a multicentric study carried out on different stages of heart failure (HF), the influence of GLS and age over LARS decreased as HF progressed; conversely as HF increases maximal atrial size and filling pressures became more related on LAS [20].

Our results align with other studies emphasizing the significant and direct relationship between GLS and LARS [11, 12], these studies incorporate patients with different heart diseases; however, our series only includes cases without known CV disease, reinforcing the physiological interdependence between the longitudinal functions of LV and LA.

The relationship of LAS with age and blood pressure coincides with the results of a multicenter Asian study [21], although in ours it did not reach significance in the multivariate analysis.

Limitations

It cannot be definitively ruled out that some patients may have underlying conditions such as hypertension, diabetes or vascular disease, especially among the elderly.

In any case, there would be few and echocardiographic exclusion criteria were designed to eliminate cases with significant cardiac involvement.

Mitral annulus systolic data such as systolic velocity by pulsed tissue Doppler or mitral annular plane systolic excursion (MAPSE) were not collected in this study because these parameters are not routinely assessed in our laboratories. It is conceivable that including these measures might have revealed a greater correlation with LARS than the currently assessed e'_{mean} .

Intrinsic determinants such as LA relaxation and stiffness are not directly achievable. Instead, we relied on clinical and echocardiographic data that could be serve as surrogates for these intrinsic determinants.

The multivariate analysis does not establish the plausibility of the cause-effect relationship; depending on the methodology used, the results could be subject to partial variations.

These limitations should be considered when interpreting the findings of our study, and future research endeavors could explore these aspects in greater detail.

Conclusions

1. In patients without CV disease, GLS emerges as a crucial determinant of LARS and LACS.
2. LAEF and e'_{mean} are directly and independently related to both LARS and LACS.
3. LARS (univariate) and LACS (multivariate) exhibits a decline with older age in individuals without CV disease.
4. LABS demonstrates a compensatory effect when relaxation is slow.
5. Parameters such as LVEF, LAVI, HR or PA-TDI do not exhibit significant correlations with LAS in patients without CV disease.

Abbreviations

A	Peak mitral inflow late velocity
BSA	Body surface area
CV	Cardiovascular
DBP	Diastolic blood pressure
E	Peak mitral inflow early velocity
EDT	E deceleration time
e'_{mean}	Mitral annular early velocity
GLS	Left ventricular global longitudinal strain
HF	Heart failure
ICC	Intraclass correlation coefficient
IRT	Isovolumic relaxation time
LA	Left atrial
LABS	Left atrial booster strain
LACS	Left atrial conduction strain
LAEF	Left atrial ejection fraction
LARS	Left atrial reservoir strain
LAS	Left atrial strain
LASI	Left atrial stiffness index
LAVI	Indexed maximum volume of left atrium
LAVmin	Left atrial minimum volume
LV	Left ventricular

LVEF	Left ventricular ejection fraction
LVEDVi	Left ventricular diastolic volume indexed to body surface area
LVESVi	Left ventricular systolic volume indexed to body surface area
LV2cS	LV 2-chambers Strain
LV4cS	LV 4-chambers Strain
MAPSE	Mitral annular plane systolic excursion
PA-TDI	Total atrial conduction time
SBP	Systolic blood pressure
TAPSE	Tricuspid annular plane systolic excursion
TR max	Peak gradient of tricuspid regurgitation
WT	Wall thickness

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12947-024-00334-y>.

Supplementary Material 1

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None.

Author contributions

JFF: conceptualization, methodology, validation, data curation, writing-original draft, writing-review & editing, supervision; YR: writing-original draft, writing-review & editing, validation; AL: formal analysis, validation; PP: conceptualization, validation, writing-review & editing; FGC: conceptualization, validation, writing-review & editing; LRC: data curation, visualization; LGG: data curation, visualization; ARF: visualization; VPD: visualization.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was registered and approved from the Regional Board for Ethics in Research with Humans CEI: IB 5212/23 Protocol CI 736–23 and adhered to the principles outlined in the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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