Review Article

Left Atrial Strain: Clinical Applications and Prognostic Implications

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Abstract

Left atrial (LA) strain, obtained using two-dimensional speckle tracking echocardiography (2DSTE), has emerged as an accurate method for evaluating LA function. Recently, it has gained prominence in clinical practice due to its significant prognostic value in various cardiovascular diseases, standing out due to its greater sensitivity compared to traditional methods of volumetric analysis and Doppler parameters.

This review article addresses the complex function of the LA and its close interdependence with left ventricular (LV) function, highlighting its relevance in cardiac performance. The LA performs three distinct functions, acting as a reservoir during ventricular systole, as a conduit in early diastole, and as a contractile chamber during the atrial contraction phase.

This review analyzes the normal patterns of LA strain and its application in various clinical conditions, such as atrial fibrillation (AF), heart failure, coronary artery disease, obesity, diabetes mellitus, hypertrophic cardiomyopathy, and cardiac amyloidosis. The crucial role of atrial strain in rheumatic mitral stenosis (MS) is highlighted due to its capacity to predict clinical outcomes.

LA function

LA function is closely interdependent with LV function, and it plays a crucial role in preserving optimal cardiac performance.[1] Assessment of LA function in both physiological and pathological states is essential to predict adverse outcomes in various cardiovascular conditions.[2] The LA performs three fundamental functions: it acts as a reservoir, functions as a conduit, and exerts a contractile function[3] (Figure 1).

1) Reservoir function: The LA functions as a reservoir receiving blood from the pulmonary veins. It begins with the closure of the mitral valve and encompasses ventricular systole, isovolumetric relaxation, and LA relaxation. This atrial function is modulated by ventricular contraction descending from the base of the LV, by right ventricular systolic pressure transmitted through pulmonary circulation, and by the properties of the LA, such as relaxation and chamber compliance.[3]

2) Conduit function: During early diastole, the LA acts as a conduit. The flow occurs passively, originating in the pulmonary veins and moving towards the LV. This function begins immediately after the opening of the mitral valve, encompassing the period of ventricular relaxation and diastasis. It ends shortly before atrial contraction, before the P wave is recorded on electrocardiogram. This function is especially modulated by LV diastolic properties in healthy individuals, considering LV relaxation and diastolic pressure.[3]

3) Contractile function: This phase occurs at the end of ventricular diastole. During atrial contraction, there is active emptying of the atrium, contributing 20% to 30% of cardiac output in the absence of heart disease. The effectiveness of this function is directly related to venous return (atrial preload), LV end-diastolic pressure (atrial afterload), and the intrinsic contractility of the atrial myocardium.[3]

Keywords

Global Longitudinal Strain; Left Atrial Function; Atrial Fibrillation; Echocardiography.

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Echocardiographic assessment of LA function

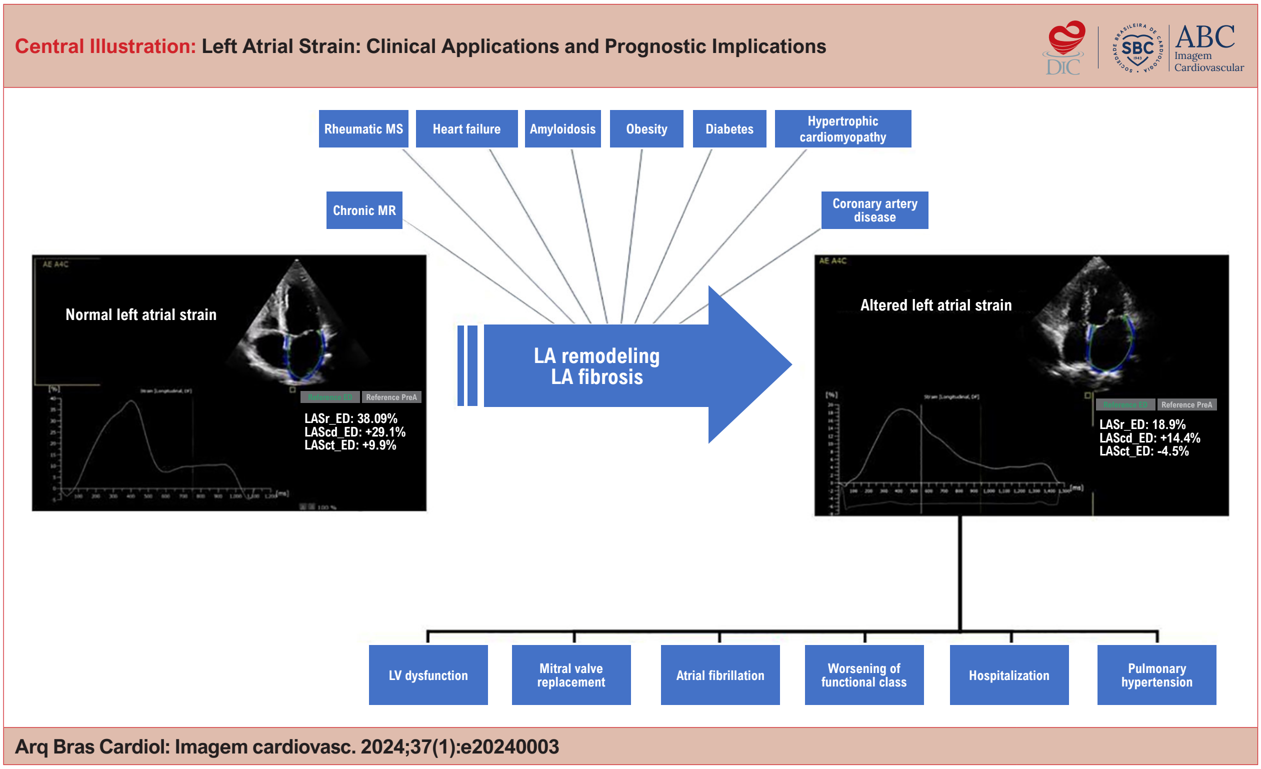
Non-invasive assessment of LA function has evolved considerably, surpassing volumetric analyses and Doppler parameters. Modalities such as computed tomography and magnetic resonance imaging have historically been used, but advanced echocardiographic techniques have recently gone on to provide more accurate assessment.

Analyses of atrial diameter and volume do not always reflect LA function, especially in later stages of pathological conditions, during which they may undergo changes. Thus, parameters that more accurately express LA function reveal complementary and incremental information in relation to traditional measures. [1]

The advent of advanced echocardiographic techniques has made it possible to better assess LA function. Strain measured by 2DSTE is a non-invasive method that allows automatic, frame by frame tracking of points in the myocardium throughout the cardiac cycle.[4,5]

The advantages of assessing LA function by means of strain are noteworthy. The capacity to discriminate between passive and active movement of myocardial tissue stands out. Furthermore, strain parameters are relatively independent from tethering effects and less dependent on load, making it possible to assess different phases of atrial function throughout the cardiac cycle.[6]

These advances represent a significant contribution to a more comprehensive understanding of LA function, offering valuable insights for clinical practice.



LA: left atrium; LAScd_ED: left atrial strain in the conduit phase in end diastole; LASct_ED: left atrial strain in the contractile phase in end diastole; LASr_ED: left atrial strain in the reservoir phase in end diastole; LV: left ventricle; MR: mitral regurgitation; MS: mitral stenosis.

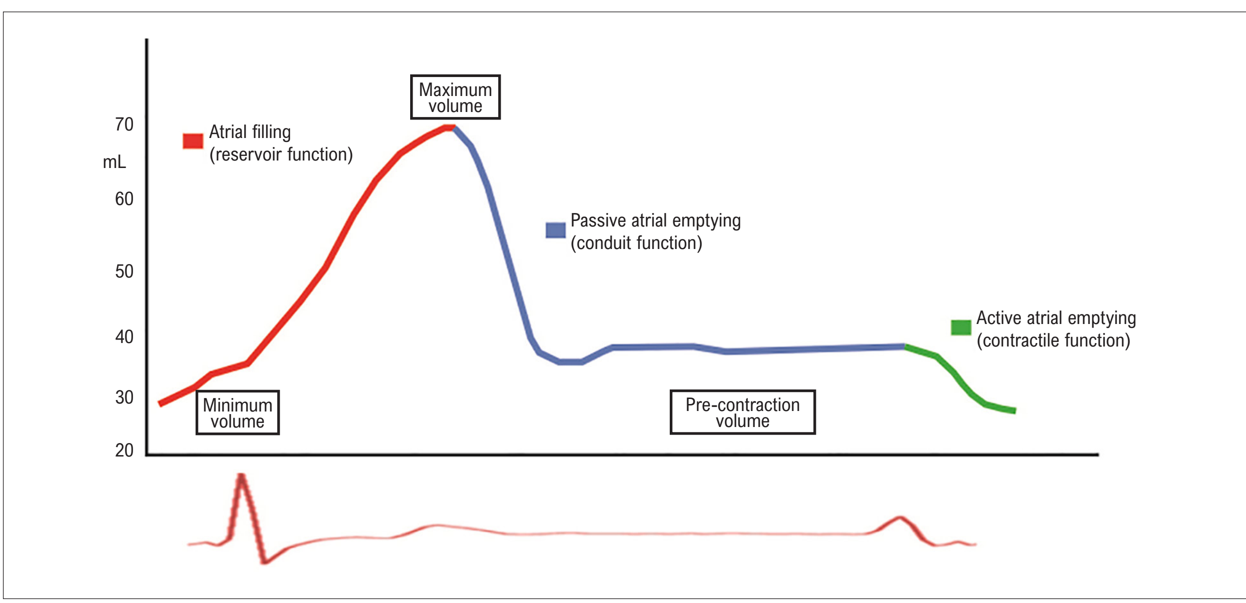


Figure 1 – *LA function: variation in LA volume during the cardiac cycle under physiological conditions.*

Assessment of atrial function by strain

During the reservoir phase, the LA expands as it fills with blood coming from the pulmonary veins. In this scenario, atrial longitudinal strain increases, reaching a positive peak at the end of atrial filling. After mitral valve opening, rapid emptying of the LA occurs, resulting in a decrease in atrial longitudinal strain, until it reaches a plateau, corresponding to the period of atrial diastasis. In the atrial contraction phase, an additional reduction in strain values is observed, due to the shortening of the wall of this chamber.[7]

The contributions of the reservoir, conduit, and contractile functions of the LA to LV filling are approximately 50%, 30%, and 20%, respectively, in healthy individuals.[2] There are differences in the nomenclature used to describe atrial strain that depend on which cycle (atrial or ventricular) is being used as a reference point, i.e., as baseline zero.[8] If the ventricular cycle is used, the QRS complex is the zero reference. Thus, the positive longitudinal peak corresponds to the atrial reservoir function (LASr), occurring during isovolumic contraction and relaxation of the LV. The periods of rapid filling and atrial contraction correspond, respectively, to the atrial conduit function (LAScd) and the pump or contraction function (LASct)[8] (Figures 2 and 3).

If the atrial cycle is used as a reference, the beginning of the P wave on electrocardiogram is the zero reference. The first negative peak represents the pump function; the positive peak corresponds to the conduit function, and their sum represents the reservoir function[8] (Figures 2 and 4).

There are some advantages to adopting end diastole as a reference point, such as the feasibility of obtaining measurements in all patients, regardless of heart rate. It is also worth emphasizing the ease of obtaining the reservoir strain measurement, which is clinically relevant, as it represents the parameter of atrial strain with most supporting evidence regarding its prognostic usefulness.[9,10]

Regarding normal LA strain values, a meta-analysis comprising 40 studies, including 2,542 healthy individuals, established the following reference values:[4] LASr: 39% (95% confidence interval: 38% to 41%), LAScd: 23% (95% confidence interval: 21% to 25%), and LASct: 17% (95% confidence interval: 16% to 19%).

LA strain in the clinical context

LA strain as a predictor of AF

Atrial dysfunction is associated with the presence of fibrosis, especially in cases of AF.[7,11] Although nuclear magnetic resonance is considered the gold standard for evaluating atrial fibrosis, its cost and availability limitations have led to a search for alternatives. The measurement of LA strain by 2DSTE has revealed an inverse correlation with the extent of fibrosis, presenting itself as a viable alternative.[12] Correlations between LA strain and histological fibrosis have been established in patients with mitral valve disease, highlighting a negative relationship between strain values and extent of fibrosis.[8] A recent study also showed that LA reservoir strain was correlated with the occurrence of paroxysmal AF, preceding atrial dilation.[13]

In patients with AF undergoing catheter ablation, peak systolic LA strain has been shown to be related to recurrence of AF after the procedure. These findings highlight the potential of LA strain as a predictor of AF and its clinical usefulness in different cardiovascular contexts.[14,15]

Hauser et al.[16] conducted a prospective study with 4,466 participants with the primary objective of evaluating the incidence of AF over an average follow-up of 5 years. During this period, 154 (4.3%) participants developed AF. In univariate analyses, they observed that peak atrial longitudinal strain (PALS), peak atrial contraction strain (PACS), and strain during the conduit phase were significantly associated with the development of AF. The results of multivariate analyses indicated that both PALS and PACS remained independent predictors of AF. Furthermore, PALS and PACS maintained a significant association with the development of AF, even in participants with normal LA size and preserved LV systolic function. Patients with atrial strain below 23% had a 6.8 times greater risk of developing AF compared to those with strain of 23% or greater.

In another study, Candan et al.[17] included 53 patients with significant mitral regurgitation in sinus rhythm who underwent mitral valve surgery. During the postoperative period, 15 patients (28.3%) developed AF. The results

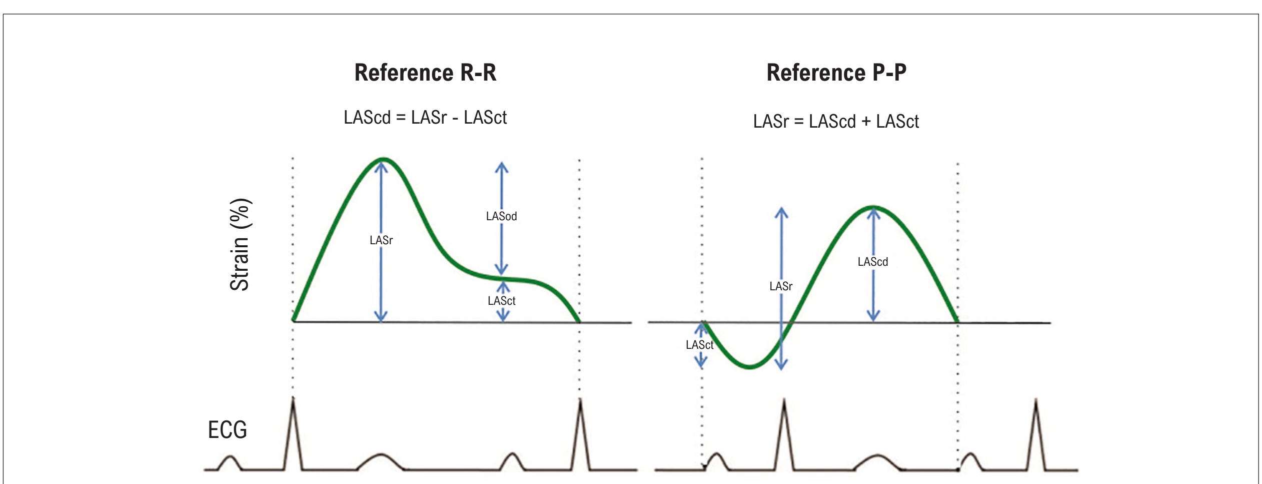


Figure 2 – *Nomenclature of strain based on the choice of the zero reference point. ECG: electrocardiogram; LAScd: left atrial strain in the conduit phase; LASct: left atrial strain in the contractile phase; LASr: left atrial strain in the reservoir phase.*

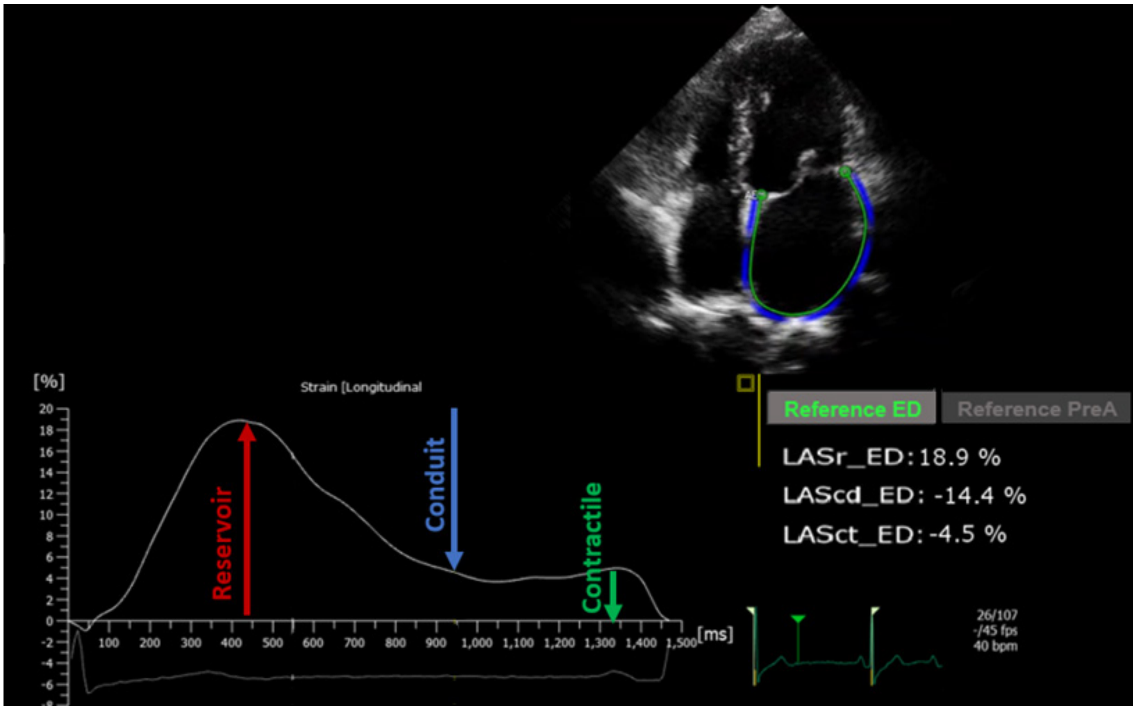


Figure 3 – *Analysis of LA strain using the QRS as a reference. Conduit: conduit phase; Contractile: contractile or pump phase; LAScd_ED: left atrial strain in the conduit phase _ end diastole; LASct_ED: left atrial strain in the contractile phase _ end diastole; LASr_ED: left atrial strain in the reservoir phase _ end diastole; Reservoir: reservoir phase.*

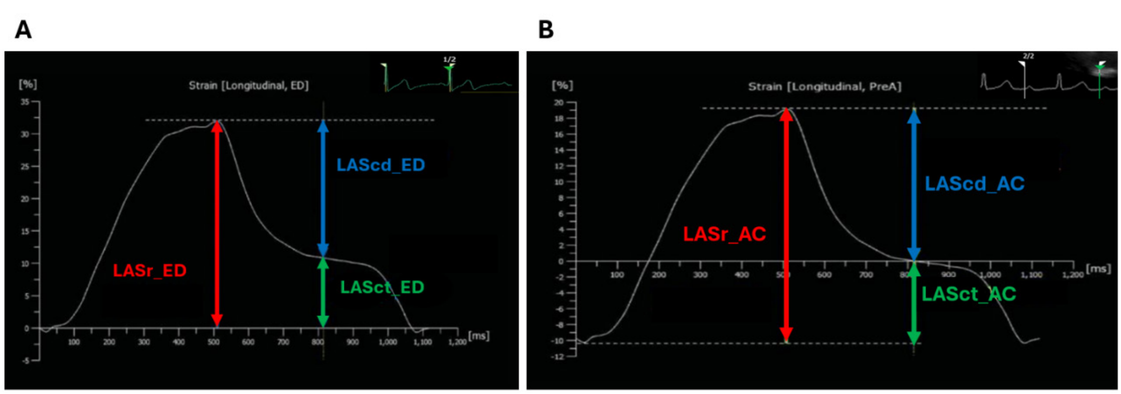


Figura 4 – *LA strain measurements using the QRS as a reference; B) LA strain measurements using the P wave as a reference. LAScd_AC: left atrial strain in the conduit phase _ pre-atrial contraction; LAScd_ED: left atrial strain in the conduit phase _ end diastole; LASct_AC: left atrial strain in the contractile phase _ pre-atrial contraction; LASct_ED: left atrial strain in the contractile phase _ end diastole; LASr_AC: left atrial strain in the reservoir phase _ pre-atrial contraction; LASr_ED: left atrial strain in the reservoir phase _ end diastole.*

revealed that both PACS and PALS were significantly lower in the group of patients who developed AF.

In a study conducted by Park et al.,[18] which analyzed 2,461 patients with acute heart failure over 5 years of follow-up, 397 patients (16.1%) developed new-onset AF. The incidence of AF was significantly higher in patients with reduced LA longitudinal strain values compared to those with normal strain values. These findings suggest an association between atrial dysfunction, measured by strain, and the development of AF in patients with acute heart failure.

In the evaluation of cryptogenic ischemic stroke, Pathan et al.[19] included 538 patients who underwent transthoracic echocardiography with LA strain. During follow-up, 61 (11%) developed AF. These patients had significantly lower atrial strain values compared to those who did not develop AF during follow-up.

Strain indices, especially LASr with a cutoff of ≤ 21.4% and LASct with a cutoff of > 10.4%, have been identified as high-risk markers. The isolated analysis of these indices revealed a subgroup of patients at considerably higher risk, making them candidates for empirical anticoagulation. This is due to the incremental and independent value of atrial strain in predicting the risk of thromboembolic events, superior to the CHA2DS2-VASc score.[20]

LA strain in rheumatic MS

LA function plays a crucial role in rheumatic MS, influencing blood flow through the stenosed valve.[21,22]

In MS, the reservoir function of the LA, which is essential for ventricular filling during diastole, is impaired due to the compensatory elevation in atrial pressure, fibrosis, and dilation. The conduit function, which is responsible for passive filling of the LV, is also affected due to reduced duration of ventricular diastole. In patients with MS, an initial increase is observed in the contractile function of the LA as a compensatory response; however, this function decreases with the progression of the disease.[23] Studies have shown that, even in mild MS, the LA reservoir and conduit strain may be reduced.[24-26]

LA strain assessment has shown to be valuable in predicting adverse events in patients with MS, such as hospitalizations, AF, thromboembolism, symptoms of heart failure, and the need for mitral valve intervention.[26] LASr has emerged as a significant prognostic indicator, which is reduced even in early stages of mild MS.[26] In follow-up studies, LASr was shown to be a consistent predictor of AF and other adverse outcomes.[27]

Table 1 displays an overview of the main studies that have used LA strain to evaluate rheumatic MS, highlighting its role in risk stratification and prognosis of these patients.

LA strain in heart failure

Increased filling pressures represent a crucial condition in the pathophysiology of heart failure. In this context, LA strain can be used as a diagnostic and prognostic tool, especially in heart failure with reduced ejection fraction.[33]

Reduced LASr (LA strain in the reservoir phase) is associated with increased LV systolic dysfunction, as well as right ventricular systolic and diastolic dysfunction, risk of AF, elevated levels of brain natriuretic peptide, and worsening of NYHA functional class. It is also an important predictor of death and hospitalization due to heart failure.[33-35]

In addition to these prognostic associations, LA strain can be used to evaluate therapeutic response. Optimized therapy reduces pre- and afterload, in addition to reducing the metabolic demand of the myocyte, reducing myocardial work. These effects lead to reduced LA overload, improving strain parameters.[2]

LA strain has also shown to be a promising prognostic marker in heart failure with preserved ejection fraction. Patients with heart failure with preserved ejection fraction have reduced LASr and LASct values, which are strongly associated with increased pressure and resistance in the pulmonary artery, reduced cardiac output, and low exercise tolerance.[36]

Despite the aforementioned evidence, the value of LA strain as a predictor of hospitalization and death in HF, regardless of LV strain, remains uncertain.[37,38]

LA strain in various cardiovascular conditions

LA dysfunction in the context of coronary artery disease, despite initially being mild, can be identified through analysis of LA strain.[39] Atrial strain in the reservoir phase (LASr) has been observed to be is significantly reduced in patients with involvement of the anterior descending artery, and reduced values are correlated with greater severity of the coronary lesion. This evidence supports the view that LA strain not only plays a diagnostic role, but also provides crucial prognostic information. Therefore, when weighing between conservative and interventional treatment approaches, the inclusion of LA strain analysis can contribute to clinical decision-making.[40]

Obesity leads to increased cardiac output and stroke volume, increased afterload, systemic inflammation (with myopathic effect), in addition to the paracrine effect of epicardial fat. These factors are associated with the occurrence of atrial remodeling, which can be detected early by analyzing LA strain.[41-44] In a study carried out by Chirinos et al.,[43] involving 1,531 patients, increased body mass index was associated with reduced LASr and LASct (atrial strain in the reservoir and conduit phases), and a compensatory increase in contractile strain (LASct), when adjusted for age and sex. The authors also observed that, as body mass index increases, there is a decrease in this atrial compensatory contractile function, which increases the likelihood of developing heart failure.

Diabetes mellitus is an important cardiovascular risk factor, and its prevalence is growing significantly.[45] Long-standing diabetes mellitus is associated with LV diastolic dysfunction, LA dilation, and greater predisposition to heart failure.[46] Previous studies have shown reduced LA strain in the reservoir and conduit phases (LASr and LASct) in patients with diabetes,[47] even in the absence of systemic arterial hypertension and LV hypertrophy.[48] The impact of diabetes mellitus on atrial remodeling contributes to a greater risk of developing AF in patients with diabetes.[49]

Hypertrophic cardiomyopathy induces progressive LV diastolic dysfunction, with a consequent increase in filling pressures, which are transmitted to the LA, culminating in the remodeling and progressive dilation of this chamber. As a clinical manifestation, patients present heart failure, AF, ventricular arrhythmias, and sudden death.[50] Previous studies have shown that hypertrophic cardiomyopathy leads to a progressive stiffening of the LA myocardium with reduced reservoir function in this chamber.[51] A study with 76 patients with hypertrophic cardiomyopathy provided evidence of an association between this condition and reduced indices of LA conduit and contractile strain (LAScd and LASct).[52] This study also found that lower LASct values correlated with a significant increase in the rates of hospitalization for heart failure and AF.

Cardiac amyloidosis leads to progressive thickening of the LV myocardium with consequent diastolic dysfunction and elevated filling pressures.[53] This increase in LV filling

Table 1 – Main studies using atrial strain in the context of rheumatic MS

Study	Population	Objectives	Main findings
Ancona et al., 2013 [27]	101 asymptomatic patients with MS 70 controls	Assess the function of the LA in MS using LA strain and its value in predicting AF at 4 years of follow-up.	LA dimensions, volumes, and PASP were significantly increased, and LA strain was significantly decreased in patients with MS. Patients who progressed to AF (20%) were older, with no difference in LA dimensions or volumes. The best predictor of AF at 4 years of follow-up was LA peak systolic strain, with a cutoff value of 17.4%.
Pourafkari et al., 2015 [28]	603 patients with MS (33% with AF)	Establish a mathematical model for predicting the risk of AF in patients with MS.	The factors independently associated with AF were LA strain, right atrial pressure, age, and ejection fraction.
Chien et al., 2018 [29]	69 stable patients with MS	Identify the determinants of NYHA functional class in patients with MS and assess the relationship between atrial strain and HF symptoms.	In multivariate analyses, adjusted for the use of diuretics, LASr was an independent predictor of NYHA functional class.
Mahfouz et al., 2020 [24]	75 patients with mild MS in sinus rhythm 40 healthy controls	Assess atrial strain in patients with mild MS and correlate it with exercise tolerance.	Patients with mild MS had significantly lower LASr and LAScd values. Patients with exercise intolerance (MET < 8) had lower LASr, LAScd, and LASct values. LASr ≤ 26.5% was an independent predictor of low exercise capacity in patients with mild MS.
Vriz et al., 2021[30]	101 patients with severe MS	Determine the correlation between atrial strain, PASP, and other parameters of RV function Verify whether atrial strain is a predictor of development of AF.	With the increase in LASr there was a decrease in PASP and PVR. RV function increased significantly with the increase in LASr. LASr was one of the best predictors of AF.
Kaur V et al., 2021 [31]	83 patients with MS undergoing PTMC	Assess the association between LA-RAs and increased PVR measured by hemodynamics.	Low LA-RAs correlated with more severe MS, higher mean pulmonary artery pressure, and pulmonary capillary wedge pressure, when compared with patients with high LA-RAs. LA-RAs showed a strong correlation with PH. LA-RAs increased significantly after PTMC.
Stassen et al., 2022 [32]	125 patients with MS, with no history of AF	Assess the association of atrial strain with the development of AF in the follow-up of patients with MS.	During a mean follow-up period of 32 months, 41 patients (32.8%) developed new-onset AF. Patients who developed AF had significantly more impaired LASr than those who remained in sinus rhythm. LASr < 21% was independently associated with the development of AF during follow-up.
Mehta et al., 2022 [25]	80 patients with severe MS in sinus rhythm 40 controls	Assess LA function using strain and its correlation with NYHA functional class and echocardiographic parameters in patients with severe MS and PH, compared with the control group.	The mean LASr, LAScd, and LASct values in patients with MS were significantly lower than in controls.

LA: left atrium; AF: atrial fibrillation; HF: heart failure; MS: mitral stenosis; LA-RAs: left atrial to right atrial strain ratio; LAScd: left atrial strain during the conduit phase; LASct: left atrial strain during the contractile phase; LASr: left atrial strain during the reservoir phase; NYHA: New York Heart Association; PASP: pulmonary artery systolic pressure; PH: pulmonary hypertension; PTMC: percutaneous mitral commissurotomy; PVR: pulmonary vascular resistance; RV: right ventricle.

pressures, associated with the deposition of amyloid proteins in the atrial myocardium, causes progressive LA dysfunction and dilation.[54] Mohty et al.,[55] in a study with 77 patients with cardiac amyloidosis (type AL, light chain amyloidosis), showed reduced LA reservoir strain values (LASr), with significantly lower 2-year survival in patients with LASr < 14%. Another study conducted by Nochioka et al.,[56] found reduced values of atrial strain in the reservoir, conduit, and contractile phases in individuals with cardiac amyloidosis, regardless of the subtype.

Mitral regurgitation causes progressive dilation and dysfunction of the LA, leading to an increased risk of developing AF.[57] In a study conducted by Yang et al.,[58] involving patients with severe primary mitral regurgitation, the reduction in LA strain in the reservoir phase was associated with higher mortality rates and need for mitral valve replacement surgery or repair after a follow-up period of 13.2 months. In another study, Ring et al.[59] evaluated 192 patients with mitral prolapse and regurgitation, observing that LA strain values in the reservoir and contractile phases were independent predictors of the need for mitral valve replacement. Although small, these studies show the relevance of atrial strain measurements for risk stratification and possible optimization of the ideal time to perform surgical interventions in this group of patients.

Challenges in current clinical applications of LA strain

The routine, widespread application of LA strain as a prognostic marker in different cardiovascular conditions is still limited. Comprehensive assessment of LA function requires joint analysis of both atrial pressure and volume. In the absence of modalities for direct assessment of LA pressure, estimates are made indirectly, which can be influenced both by LV dysfunction and by primary abnormalities in the LA.[2] Furthermore, it is worth highlighting the variation in LA strain values obtained by different software platforms.

Conclusions and future perspectives

LA strain has emerged as a promising tool in the assessment of various cardiovascular conditions, offering valuable insights for risk stratification and for monitoring the progression of heart diseases.

Notwithstanding its potential, it is crucial to recognize the need for prospective multicenter studies, in addition to the standardization of techniques and the development of specific guidelines on the interpretation and clinical application of atrial strain.

The establishment of specific guidelines will guarantee consistency and reliability in the interpretation of LA strain, leading to its widespread use in clinical practice.

Author Contributions

Conception and design of the research: Figueiredo Fernanda A, Figueiredo Flávio A, Chavez LMT, Teixeira MFA, Nunes MC; acquisition of data: Barbosa WS, Bronzatto PH, Nunes MC; analysis and interpretation of the data: Figueiredo Fernanda A, Nunes MC; obtaining financing: Nunes MC; writing of the manuscript: Figueiredo Fernanda A, Costa Filho AL, Figueiredo Flávio A, Chavez LMT, Cintra PR, Nunes MC; critical revision of the manuscript for intellectual content: Figueiredo Fernanda A, Figueiredo Flávio A, Nunes MC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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