Left Atrial Function Using Speckle Tracking: Beyond Volumetric Evaluation

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Abstract

Evaluation of left atrial function is currently an emerging method that may be related to patient prognosis. Classically, the static measures of diameter, area and volume are the most used for this purpose. The technique known as speckle tracking is capable of providing dynamic information of the left atrium throughout the cardiac cycle, as well as detecting abnormalities in left atrial function in subclinical phases, before volumetric increases or diastolic dysfunctions occur. Normality values for speckle tracking are being proposed, but the methodological differences and techniques make it difficult to standardize them. This literature review aims to discuss progress in the analysis of left atrial function, especially via speckle tracking.

Introduction

The association between left atrial (LA) size and increased clinical outcomes has been widely reported in the literature. Atrial fibrillation (AF),[1,2] cerebrovascular accident (CVA),[3] acute myocardial infarction (AMI), heart failure (HF) and hospitalization present high rates[4] and may be related to LA dysfunction. Modena et al.,[5] conducted a prospective study with a mean follow-up of 12 years (minimum of 7 years), whose cardiac mortality was 47.9%, of which 29% of patients had normal atrium and 54.3% in those with LA > 45 mm, with $p < 0.01$ significance.[5]

In people without this occurrence, LA has three basic functions: reservoir, which collects the venous return from the lung during ventricular systole; conduit, for the passage of blood stored in the atrium towards the ventricle during the onset of diastole; and pump, with atrial contraction at the end of diastole, contributing with about 30% of ventricular filling.[6]

Traditionally, LA size is evaluated by static morphological measures, such as diameter, area and volume (Figure 1). LA volume showed a more significant association with clinical outcomes compared to diameter, which is a one-dimensional measure.[7] Besides the dimensions,[8] LA can be evaluated in more detail with function parameters.

Keywords

Atrial Function, Left/physiology; Echocardiography/methods; Speckle Tracking; Atrial Fibrillation, Myocardial Infarction; Stroke; Heart Failure; Prognosis.

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Manuscript received August 10, 2018; revised August 24, 2018; accepted September 25, 2018.

DOI: 10.5935/2318-8219.20190009

Some echocardiographic techniques have been used to study left atrial function (LAF), such as LA volume variation (Table 1), transmitral spectral Doppler, pulmonary vein flow and tissue Doppler (Table 2)[4] as well as left atrial appendage velocities with transesophageal echocardiography.[9]

In 2013, Hsiao and Chiou[10] conducted a prospective study in which 1,735 patients with a history of dyspnea were submitted to transthoracic echocardiography to evaluate variables predictive of the combined outcome of hospitalization for heart failure and all-cause mortality in a 2-year follow-up. A combined outcome was seen in 91 patients, and the LA expansion index [IE = (maximum volume – minimum volume)/minimum volume, representing the LA reservoir function], with a C-statistic of 0.886, presented a better prognostic value compared to well-established echocardiographic parameters such as E/E' ratio (C-statistic of 0.741) and LA indexed volume (C-statistic of 0.723).[10]

Another technique to analyze LAF is called speckle tracking. The speckles were first described in the 1970s[11] as granular structures formed by a number of small speckles resulting from interfaces in tissues (such as the transition between a vessel and a muscle, for example), which reflect the echoes diffusely. These speckles are so small and numerous that, in a unit of ultrasound resolution, several of them are grouped. As the speckles are stable and form patterns for each Region of Interest (ROI), a software application was developed for echocardiography devices in order to track these speckles by analyzing myocardial or atrial strain.[12]

After being completely emptied at the end of diastole, the LA receives blood from the pulmonary veins during ventricular systole, increasing their size. Increase and reduction of LA size is due to the strain of the cavity walls. When the strain is reduced, the atrium decreases the ability to vary its size, indicating that the function is altered.

In the studies, normal values for LA global longitudinal strain (ε) range from 35.7% ± 5.8% to 42.2% ± 6.1%, and the LA systolic strain rate (SR) range from 1.43 S^{-1} ± 0.24 S^{-1} to 2.47 S^{-1} ± 0.55 S^{-1}[12]. Through speckle tracking, we can also study the three phases of atrial function.[13]

A meta-analysis of 40 studies on normal values for atrial speckle tracking, with 2,542 healthy individuals, suggested 39% (95% Confidence Interval – 95%CI 38%-41%) as a reference for reservoir strain ($LA\varepsilon\text{-}_S$), 23% (95%CI 21%-25%) for conduit strain ($LA\varepsilon\text{-}_E$) and 17% (95%CI 16%-19%) for pump strain ($LA\varepsilon\text{-}_A$), with heterogeneity among the studies on heart rate, body surface area and sample size (Table 3). There was no statistically significant difference as for the echocardiography device used for strain analysis, and most studies used EchoPac (GE Healthcare).[14] This meta-analysis also showed that the 40 studies analyzed reservoir function, but only 14 articles assessed the conduit function and 18 articles assessed pump function, suggesting that recording these three measurements is still not a common practice in the literature and in medical practice.

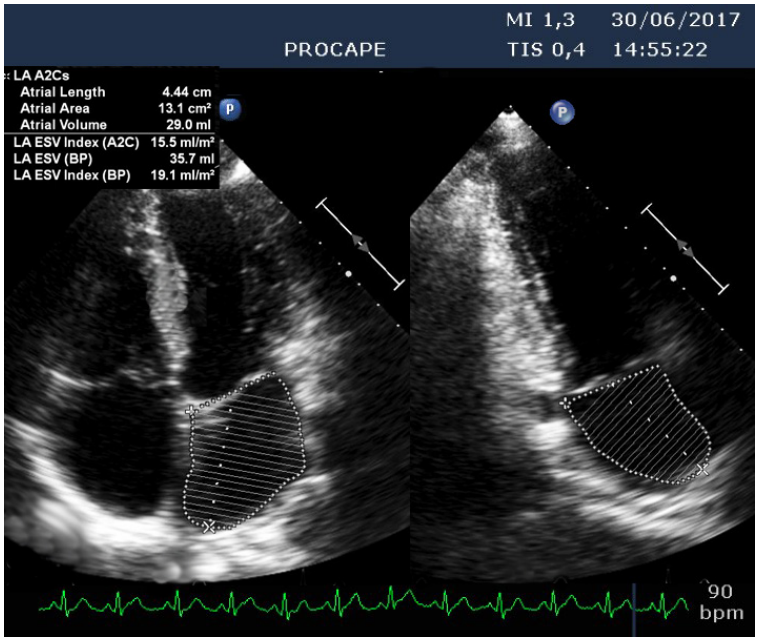

Figure 1 – *Maximum left atrial volume in two-chamber apical view: volumetric method.*

Table 1 – Volumetric indexes of left atrial function (LAF)

LAF	LA volumetric fraction	Calculation	Normal value
Global function, reservoir	Total EF (%)	[(LAmax – LAmin)/LAmax]	70 ± 9
Reservoir	Expansion index (%)	[(LAmax – LAmin)/LAmin]	271 ± 126
Conduit	Passive EF (%)	[LAmax – LApreP)/LAmax]	44 ± 12
Pump	Active EF (%)	[LApreP – LAmin)/LApreP]	47 ± 12

LA: left atrium; EF: emptying fraction; LAmax: maximum left atrial volume; LAmin: minimum left atrial volume (after atrial contraction, at the end of diastole); LApreP: left atrial volume immediately before atrial contraction (preceding the P wave of electrocardiogram). Source: adapted from Hoit, 2014.

Table 2 – Left atrial function (LAF) by spectral and tissue Doppler

LAF	Transmitral flow	Pulmonary vein flow	Tissue velocity
Reservoir	-	S velocity	S´
Conduit	E, E/A velocity	D velocity	E´
Pump	A, E/A velocity	RevA	A´

RevA: reverse pulmonary vein velocity. Source: adapted from Hoit, JACC, 2014.[4]

Table 3 – Left atrial function (FAE) by speckle tracking

LAF	Normality values
Reservoir strain	39% (95%CI 38%-41%)
Conduit strain	23% (95%CI 21%-25%)
Pump strain	17% (95%CI 16%-19%)

95%CI: 95% confidence interval. Source: Adapted from Pathan et al. JASE, 2017.[14]

Analysis of left atrial function

In order to study the LA volumetric fractions, it is necessary to record the maximum volumes, the volume before atrial contraction (before the P wave on the electrocardiogram) and the minimum LA volume, assessing the three functions performed.[15] Regarding speckle tracking, specific software is necessary in the echocardiogram in order to record atrial strain and strain rate.

Volumetric method

In 4-chamber and 2-chamber echocardiographic view, two-dimensional mode, the three volumes should be recorded using the modified Simpson method, namely:[8] maximum LA volume (LAVmax, in mL) at the end of systole; minimum LA volume (LAVmin in mL) at the end of diastole; and volume before the P wave of the electrocardiogram (LAVpre, in mL), before the P wave. LA reservoir function is measured by the expansion index using the formula [EI = (LAVmax - LAVmin)/LAVmin] and total emptying fraction using the formula [TEF = (LAVmax - LAVmin)/LAVmax]. Conduit function is measured by the passive emptying fraction given by the formula [PEF = (LAVmax - LAVpre)/LAVmax], and the pump function by the active emptying fraction [AEF = (LAVpre - LAVmin)/LAVpre][15]. The inconvenience lies in the interobserver variability of the Simpson's method and the difficulty of accurately detecting the edge of the atrial wall.[16]

Speckle tracking method

The strain (ε) and strain rate (SR) represent the atrial strain magnitude and rate, respectively. They can be accessed by Tissue Doppler imaging (TDI) velocities or 2D speckle tracking echocardiography (2D STE), as detailed below.

The first strain description via echocardiography was derived from TDI velocity data using the Doppler equation to convert ultrasound frequencies into velocity information along the scan lines.[17] However, while temporal resolution is excellent and two-dimensional imaging of optimal quality is not required, TDI is highly angle-dependent, and signal-to-noise ratios can be problematic. Since the fundamental data produced by TDI are derived from velocities, the strain rate (strain per time unit) is a result of velocity data, according to the mathematical equation SR = (V1 - V2)/L, where SR = strain rate; V1 = speed at point 1, V2 = speed at point 2 and L = length, usually set at 10 mm.[18]

Later, to try to solve the problems of angle dependence, another echocardiographic tool for strain analysis came up. It is called speckle tracking and uses two or three-dimensional echocardiography. It is a computer algorithm for post-processing, which uses the gray scale of digital images. Although many manufacturers have created the algorithm itself, the approach is similar.[19,20] Digital gray-scale myocardial images contain speckle-specific patterns. A user-defined ROI is delimited on the myocardial wall, which may be ventricular or atrial, depending on the purpose of the scan. Within this ROI, the image processing algorithm automatically subdivides regions into pixel blocks, tracing stable speckle patterns. Subsequent frames are automatically analyzed by the software, searching for a new location of speckle patterns within each of the blocks, using correlation criteria and the sum of absolute differences in the echocardiographic windows used. The velocity-resulting vectors are then generated. Usually, the program calculates the mean of six segments for each window viewed, and the ε and SR values are the means obtained from each window.[18]

To calculate ε and SR, a frame rate ranging from 50 to 70 frames/second is required. It is also important to define the reference point, that is, the zero frame (Figure 2). If the ventricular cycle is chosen as a reference, the QRS complex is the zero frame, and the positive longitudinal peak corresponds to the reservoir function (εs), the ε during initial diastole (εe) represents the conduit function and the ε in late diastole late (εa), the pump. If the atrial cycle is chosen, the beginning of P wave of the electrocardiogram is the zero frame and the first negative peak of ε (εneg) represents the atrial pump function; the positive peak (εpos), the conduit function; and the total sum (εtotal), the reservoir function. SRs in ventricular systole (SRs), initial diastole (SRe) and late diastole (SRa) correspond to the reservoir, conduit and pump functions, respectively.[21,22]

Two models for ε atrial analysis have been proposed in the literature. The first, of 12 segments, using the apical 4 and 2-chamber windows.[23] The second one, of 15 segments, for a more detailed assessment of atrial strain, using the 4, 2 and 3-chamber windows.[10] This variability of models may be one of the technical factors for the different normality values found in the literature.

Atrial strain during ventricular systole (ε_S) can be obtained at the beginning of the electrocardiogram QRS when it is chosen as a reference. Therefore, atrial strain during late diastole (εa) should be recorded at the beginning of the electrocardiogram P wave, and atrial strain during early diastole (εe) is obtained by subtracting the ε_S - εa values (Figure 3). SR at systolic peak (SR_S), SR at early diastolic peak (SRe) and SR at late diastolic peak (SRa) are obtained by outlining the entire LA contour. The speckles shown in Figure 4 correspond to the reservoir, conduit and pump functions, respectively.[4]

Before the final image processing, a preview confirms whether the inner lines follow the atrial endocardium during the cardiac cycle (Figures 3 and 4). Manual adjustments should be performed when the atrial endocardial tracing is not correctly circled. Atrial segment with inappropriate image should be excluded. It is suggested to consider the study as inadequate when more than one segment per view is unsatisfactory.[24]

The final ε and SR values are the mean values obtained in each apical window. If an apical 3-chamber view scan is chosen, the anterosteptal segments should be excluded from the analysis, as they represent the wall of the ascending aorta.[24]

From a technical point of view, the gain and the ROI should be adjusted. Adjusting the echocardiography device with a very low gain may artificially eliminate anatomical structures; on the other hand, excessive gain reduces resolution. Excessively increasing the ROI thickness may reduce the ε and SR values, possibly due to image contamination by the structures surrounding the LA.[25]

ε and SR have some limitations. They depend on frame rate and cannot be used in patients with poor quality two-dimensional imaging.[24] Also, the fact that some works use the P wave as zero frame and others use the QRS complex may interfere with the reference values.[26]

Structural interatrial septal (IAS) abnormalities may interfere with speckle tracking values, as in the case of IAS aneurysm[27] or septal defects. Significant pre- and post-load abnormalities may also influence the results.[28]

IAS properties can be influenced by right atrial pressures, which can modify the strain values of this area and, therefore, the global strain.[29] Motoki et al.,[30] compared ε and SR, derived from two different speckle tracking programs (EchoPAC, GE

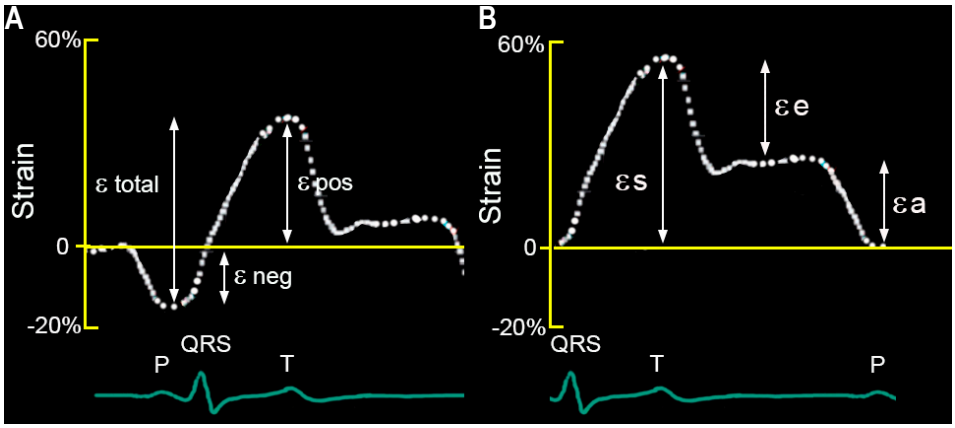

Figure 2 – *Speckle tracking method. (A) Atrial cycle as a reference. (B) Ventricular cycle as a reference.*

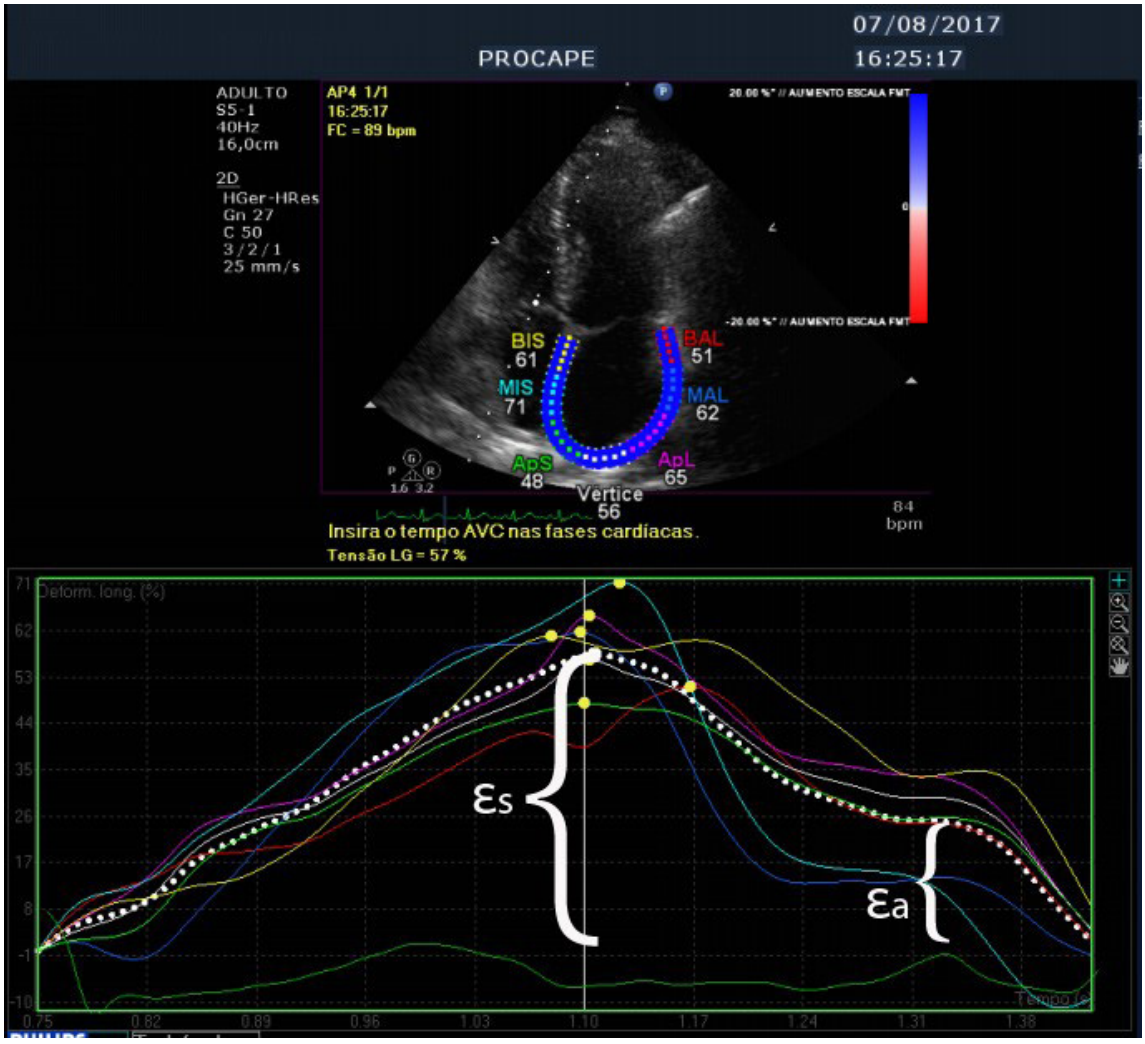

Figure 3 – *Left atrial strain by speckle tracking, using the QRS complex as a reference. ε S represents the reservoir function; ε e, the conduit function; and ε a, the pump function. We calculate the conduit function using the following mathematical formula: ε e = ε S – ε a. In the example image, ε e = 57% – 26% = 31%.*

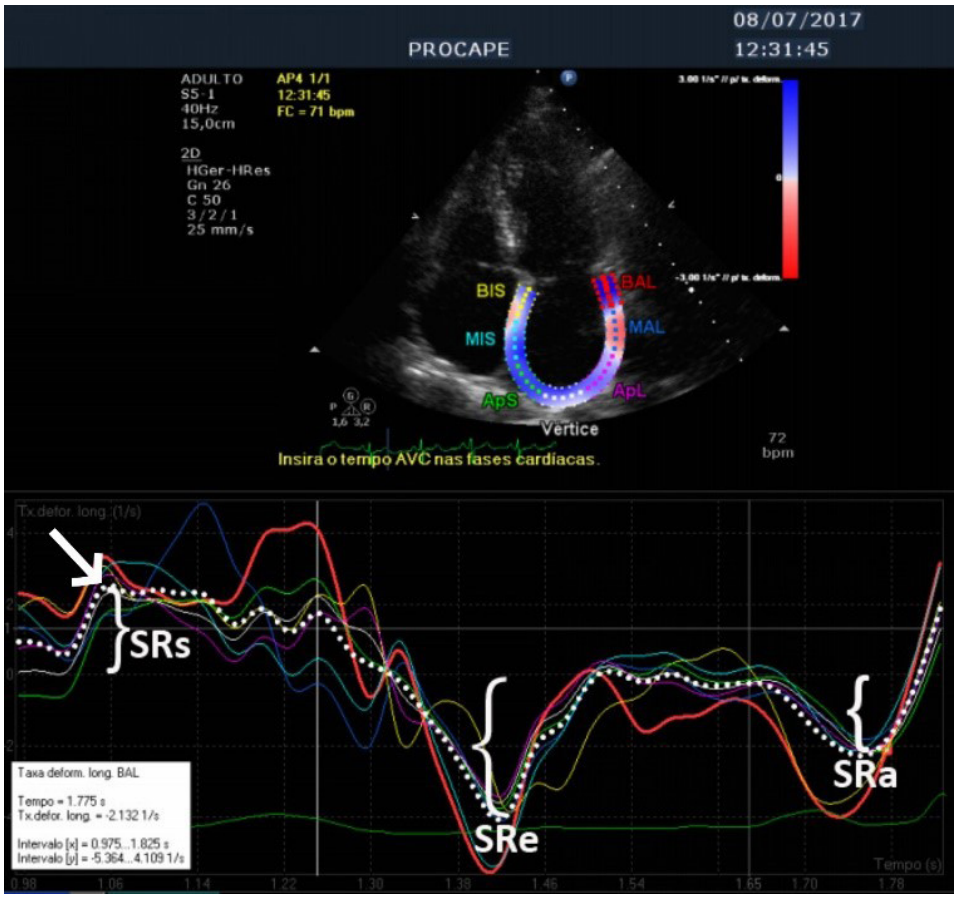

Figure 4 – *Left atrial strain rate (SR) by speckle tracking: SRs represents the reservoir function; SRe, the conduit function; and SRa, the pump function.*

Healthcare vs. Velocity Vector Imaging, Siemens Healthineers), and suggested that ε and SR, during late diastole, were comparable between the systems. However, there was a significant difference in ε and SR during ventricular systole and early diastole.[30] On the other hand, a meta-analysis of 2017, including 40 studies on normal values for atrial speckle tracking, found no significant difference among the manufacturers regarding strain values.[14]

As patients with AF do not present P wave, it would have been more appropriate to use the QRS complex as a reference to measure LA strain and this reference could be used as a standard. Using the apical 2 and 4-chamber views to assess the LA speckle tracking would be sufficient for the analysis and less laborious than using the apical 3-chamber view. Although the 3-chamber evaluation is more complete, using the 2 and 4-chamber views would make it easier to incorporate the technique into clinical practice.

Clinical left atrial speckle tracking applications: beyond the volumetric measurement

The literature has shown that speckle tracking is an independent predictor of cardiovascular events, such as AF, HF, CVA, AMI and death, suggesting that it is superior to the traditional parameters of atrial analysis (LA diameter, area and volume).[31-33]

Cameli et al.,[32] in a prospective study with a mean follow-up of 3 years, suggested that atrial strain, with C-statistic of 0.83, as a predictor of cardiovascular events, was superior to: LA volume (C-statistic of 0.71), LA ejection fraction (C-statistic of 0.69), LA area (C-statistic of 0.64) and LA diameter (C-statistic of 0.59).[32]

Ancona et al.,[33] in a prospective 4-year study with 101 patients with pure mitral stenosis (asymptomatic) and 70 healthy controls, suggested that there were no significant differences between the patients who developed AF (20% of the total) regarding LA diameter, volume and ejection fraction, but the LA strain at systolic peak was significantly lower (C-statistic of 0.761, p = 0.002 — for cutoff value of 17.4%).[33]

A study by Debonnair et al.[34] suggested that patients who underwent mitral valve replacement and whose atrial reservoir strain (εs) after surgery was ≤ 24%, had a worse survival at 6.4 years (p = 0.02).[34] A longitudinal cohort study with 274 elderly individuals older than 85 suggested that reduced LAF is associated with increased mortality at 5 years, regardless of left atrial volume.[35] In addition to the prognostic value, speckle tracking can be used to assist in the diagnosis of systemic sclerosis, for example, by detecting atrial function abnormalities before any changes in cavity size and volume occur.[36]

Intense physical activity, as in high performance athletes, is associated with both ventricular and atrial hemodynamic abnormalities with increased cardiac chambers. When enlarged atria are found in an athlete, clinical and echocardiographic aspects must be considered to support the differentiation between physiological atrial remodeling in exercise and pathological remodeling, such as: (1) athletes usually have balance between atrial and ventricular increase; (2) athletes' atria may be as much enlarged as in pathological conditions, but rarely with a significant increase; (3) factors such as type of sport (usually those of high physical performance), years of practice and degree of conditioning may also contribute to remodeling; (4) both pathological and adaptive conditions of the sport may increase atrial volume, but the reservoir function has been normal in the athletes, which differentiates them from abnormal LAF under pathological conditions.[37]

Another study has suggested an association between obstructive sleep apnea (OSA) and abnormal LAF where, the stronger this association, the more severe is the degree of apnea.[38] In 2016, Haruki et al.[39] studied whether LAF in patients with HF and reduced ejection fraction differed between those with obstructive apnea and central sleep apnea. They concluded that central apnea significantly reduced reservoir and conduit functions compared to obstructive apnea.[39]

The adverse impact of systemic arterial hypertension (SAH) in LAF has been demonstrated by the measurement of atrial volume, which may be increased, using Doppler echocardiography.[40] However, this concept has been expanded, considering that LAF abnormalities can be detected by 2D STE, even with the normal LA volume, suggesting that dysfunction precedes the dilation that is recorded using traditional methods.[41] In fact, abnormalities found in 2D STE have already been reported in hypertensive patients, even in the absence of ventricular remodeling or of signs of diastolic dysfunction.[42]

Data published on the use of 2D STE in ischemic heart disease are conflicting, with a study suggesting a prognostic value[43] and another one which, after multivariate analysis, did not demonstrate any incremental prognostic value. This shows that LAF has no independent role and only reflects left ventricular longitudinal function as demonstrated by the global longitudinal strain.[44] Some conditions that may impair LAF include AF; valvulopathies; infiltrative diseases, such as amyloidosis; dilated and hypertrophic cardiomyopathies; SAH; obesity, diabetes etc. The main causes of atrial dysfunction are summarized in Table 4.[12,37,38,40]

Atrial cardiomyopathy: how to explain early left atrial abnormalities detected by speckle tracking?

The ASSERT study (Asymptomatic atrial fibrillation and Stroke Evaluation in pacemaker patients and the atrial fibrillation Reduction atrial pacing Trial) investigated the temporal relationship between subclinical AF and CVA in patients under continuous rhythm monitoring via implanted devices.[45] The result showed that AF events were detected 30 days before the CVA only in 8% of individuals, and that 16% of CVA victims had the first AF event after the CVA. A potential explanation for the poor temporal relationship between AF and CVA, as found in this study, is the presence of potential additional factors associated with atrial cardiomyopathy, such as hypocontractility and reduced atrial function, as contributors to CVA, other than the presence of AF.[46]

A situation that could illustrate how atrial cardiomyopathy and its reduced function could contribute to thromboembolism would be represented by patients with amyloidosis who, even

Table 4 – Pathologies that may affect left atrial function (LAF)

Pathology	LAF component mainly affected	Advantages
Atrial fibrillation	Reservoir and conduit reduction. No pump	Predict maintenance of sinus rhythm after cardioversion
Mitral stenosis	Reservoir	Predict adverse effect (AF, symptoms, hospitalization, thromboembolic events, valve surgery and percutaneous commissurotomy)
Mitral regurgitation.	Reservoir	Predict AF, cardiac surgery, atrial fibrosis and survival
Aortic stenosis	Pump	Predict adverse effects
Diastolic function	Conduit (initial stage); pump and reservoir (final stage)	Increased filling pressures
Dilated cardiomyopathy	Pump and reservoir	Responsiveness to resynchronization therapy
Diabetes mellitus	Reservoir, conduit and pump	Early sign of atrial fibrosis
Hypertrophic cardiomyopathy	Reservoir	Predictor of AF and onset of CHF symptoms
Amyloidosis	Reservoir	Early atrial involvement in the absence of classical echocardiographic findings
Systemic arterial hypertension	Reservoir	Predictor of myocardial involvement before atrial enlargement or ventricular hypertrophy
Athletes	Reservoir: normal	Enlarged left atrium with normal reservoir function to differentiate from pathological conditions, in which LAF is abnormal.
Obstructive sleep apnea	Reservoir and conduit reduction	Potential predictor of clinical outcomes

SAH: Systemic Arterial Hypertension. AF: atrial fibrillation; CHF congestive heart failure Source: Adapted from: Ancona R, et al.[12];SWJ,2014; D'Ascenzi F, et al.[37] JASE,2018; Altekin RE, et al.[38] CRC,2016; Cameli M, et al.[40], JCM,2016

Table 5 – Types of atrial cardiomyopathy

Atrial cardiomyopathy	Type I Cardiomyocyte	Type II Fibrosis	Type III Fibrosis + cardiomyocyte	Type IV Non-collagenous infiltrate
Atrial fibrillation		x	x	
Atrial amyloidosis				x
Muscular dystrophy	x	x	x	x
CHF		x	x	x
OSA	x		x	
Drug-induced	x	x	x	x
Myocarditis			x	x
Age		x		
SAH	x	x	x	
Obesity			x	x
Diabetes mellitus	x		x	x
Valvulopathy	x	x	x	x

CHF: congestive heart failure; OSA: obstructive sleep apnea; SHA: systemic arterial hypertension. [46] Source: Adapted from: Guichard JB, et al., [46]JACC,2017

under sinus rhythm, are at increased risk for embolisms, associated with severe atrial hypocontractility.[47]

A study in an animal model suggested that artificially produced OSA in rats was capable of causing deregulation of atrial connexin-43 and generating LA fibrosis, impacting atrial dysfunction.[48]

LAF parameters, such as ε and SR, are inversely proportional to the degree of atrial fibrosis, as found in cardiac magnetic resonance imaging, that is, the higher the degree of fibrosis, the lower the speckle tracking values.[49]

It is important to emphasize that not all atrial myocardiopathy results from fibrosis. Other remodeling processes may occur. Four classes of atrial myocardiopathy are known: cardiomyocyte-dependent, fibroblast-dependent, mixed, and deposition not deriving from collagen (Table 5).[46]

LAF evaluation in patients with LV pressure and volume overload suggests that the increase in LA volume correlates more with volume overload (mitral failure) than with pressure overload (hypertrophic, dilated and restrictive cardiomyopathies). Decreased atrial volume during atrial contraction is a sign of atrial cavity mechanical disorders. LA longitudinal strain, especially longitudinal LA SR, are decreased in pressure overloads when there is significant increase in LA pressure, and can be indicators of this condition when there is diastolic dysfunction of the left ventricular cavity.[50] Other studies[51,52] report a correlation between LA longitudinal strain reduction in the reservoir phase (maximum strain) and increased LA pressure. Moreover, there is evidence of a correlation between mitral flow E wave and mitral annulus tissue Doppler e' wave (increased E/e' ratio) and reduced LA maximum longitudinal strain in patients with cardiomyopathy and diastolic dysfunction, with increased LA pressure in the chronic phase of Chikungunya virus infection.[52]

Conclusion

Left atrial function evaluation using 2D STE has been shown to be a promising tool in recent years. However, major prospective studies are needed to confirm the incremental value of 2D STE for the clinical outcomes. Standardization of the method is also required, considering that the studies have used different methods to record atrial speckle tracking, from the reference point to be considered, to the number of echocardiographic windows in which the images will be recorded. For future studies, it would be interesting to standardize the reference values, corrected for sex and age, as well as to develop clinical trials to evaluate the impact of therapies on the reversal of atrial remodeling and clinical outcomes.

Acknowledgements

To Drs. Eugênio Soares de Albuquerque, Simone Cristina Soares Brandão and Dário Celestino Sobral Filho, for their insights to the construction of the idea that inspired us in this literature review study.

Authors' contributions

Creation and design: Medeiros MA, Pedrosa RP, Silveira ACM, Castillo JM; Data acquisition: Medeiros MA, Pedrosa RP, Castillo JM; Manuscript writing: Medeiros MA, Castillo JM. Critical revision of the manuscript for important intellectual content: Castillo JM.

Potential Conflicts of Interest

No relevant potential conflicts of interest.

Sources of Funding

This study had no sources of funding.

Academic Association

This study is associated with the Graduate Studies on Health Sciences of Universidade de Pernambuco and derived from a Master's dissertation.

References

1. Tsang TSM, Barnes ME, Gersh BJ, Bailey KR, Seward JB. Risks for atrial fibrillation and congestive heart failure in patients \textgreater/=65 years of age with abnormal left ventricular diastolic relaxation. Am J Cardiol. 2004;93(1):54–58.
2. Tsang TSM, Gersh BJ, Appleton CP, Tajik AJ, Barnes ME, Bailey KR, et al. Left ventricular diastolic dysfunction as a predictor of the first diagnosed nonvalvular atrial fibrillation in 840 elderly men and women. J Am Coll Cardiol 2002;40(9):1636–44.
3. Benjamin EJ, D'Agostino RB, Belanger AJ, Wolf PA, Levy D. Left atrial size and the risk of stroke and death. The Framingham Heart Study. Circulation. 1995;92(4):835–41.
4. Hoit BD. Left atrial size and function: role in prognosis. J Am Coll Cardiol. 2014;63(6):493–505.
5. Modena MG, Muia N, Sgura FA, Molinari R, Castella A, Rossi R. Left atrial size is the major predictor of cardiac death and overall clinical outcome in patients with dilated cardiomyopathy: a long-term follow-up study. Clin Cardiol. 1997;20(6):553–60.
6. Delgado V, Di Biase L, Leung M, Romero J, Tops LF, Casadei B, et al. Structure and function of the left atrium and left atrial appendage: AF and Stroke Implications. J Am Coll Cardiol. 2017;70(25):3157–72.
7. Tsang TS, Barnes ME, Bailey KR, Leibson CL, Montgomery SC, Takemoto Y, et al. Left atrial volume: important risk marker of incident atrial fibrillation in 1655 older men and women. Mayo Clin Proc. 2001;76(5):467–75.
8. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1-39.e14.
9. Bansal M, Kasliwal RR. Echocardiography for left atrial appendage structure and function. Indian Heart J. 2012; 64(5):469-75.
10. Hsiao S-H, Chiou K-R. Left atrial expansion index predicts all-cause mortality and heart failure admissions in dyspnoea. Eur J Heart Fail. 2013;15(11):1245–52.
11. Burckhardt BC. Speckle in ultrasound B-mode scans. IEEEE Trans Sonics Ultrason. 1978;(1–25):1–6.
12. Ancona R, Comenale Pinto S, Caso P, D'Andrea A, Di Salvo G, Arenga F, et al. Left atrium by echocardiography in clinical practice: from conventional methods to new echocardiographic techniques. ScientificWorldJournal. 2014:ID 451042.
13. Leitman M, Lysyansky P, Sidenko S, Shir V, Peleg E, Binenbaum M, et al. Two-dimensional strain-a novel software for real-time quantitative echocardiographic assessment of myocardial function. J Am Soc Echocardiogr. 2004;17(10):1021–9.
14. Pathan F, D'Elia N, Nolan MT, Marwick TH, Negishi K. Normal ranges of left atrial strain by Speckle-Tracking echocardiography:a systematic review and meta-analysis. J Am Soc Echocardiogr. 2017;30(1):59-70.
15. Blume GG, Mcleod CJ, Barnes ME, Seward JB, Pellikka PA, Bastiansen PM, et al. Left atrial function: physiology, assessment, and clinical implications. Eur J Echocardiogr J Work Group Echocardiogr Eur J Echocardiogr. 2011;12(6):421–30.
16. Paul B. Left atrial volume. A new index in echocardiography. JAPI. 2009; 57:463-5.
17. Heimdal A, Stoylen A, Torp H, Skjaerpe T. Real-time strain rate imaging of the left ventricle by ultrasound. J Am Soc Echocardiogr. 1998; 11:1013–9.
18. Gorcsan J 3rd, Tanaka H. Echocardiographic assessment of myocardial strain. J Am Coll Cardiol. 2011;58(14):1401–13.
19. Bohs LN, Trahey GE. A novel method for angle independent ultrasonic imaging of blood flow and tissue motion. IEEE Trans Biomed Eng. 1991;38(3):280–6.
20. Notomi Y, Lysyansky P, Setser RM, Shiota T, Popovic ZB, Martin-Miklovic MG, et al. Measurement of ventricular torsion by two-dimensional ultrasound speckle tracking imaging. J Am Coll Cardiol. 2005;45(12):2034–41.
21. To ACY, Flamm SD, Marwick TH, Klein AL. Clinical utility of multimodality LA imaging: assessment of size, function, and structure. JACC Cardiovasc Imaging 2011;4(7):788–798.
22. Mor-Avi V, Lang RM, Badano LP, Belohlavek M, Cardim NM, Derumeaux G, et al. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. Eur J Echocardiogr. 2011;12(3):167–205.
23. Cameli M, Caputo M, Mondillo S, Ballo P, Palmerini E, Lisi M, et al. Feasibility and reference values of left atrial longitudinal strain imaging by two-dimensional speckle tracking. Cardiovasc Ultrasound. 2009 Feb 09;7:6.
24. Rimbas RC, Dulgheru RE, Vinereanu D. Methodological gaps in left atrial function assessment by 2D Speckle Tracking Echocardiography . Arq Bras Cardiol. 2015;105(6):625-36.
25. Rimbaş R, Mihaila S, Vinereanu D. Sources of variation in assessing left atrial functions by 2D speckle-tracking echocardiographyHeart Vessels.2016;31(3):370-81.
26. Olsen FJ, Bertelsen L, de Knegt MC, Christensen TE, Vejlstrup N, Svendsen JH, et al. Multimodality Cardiac Imaging for the Assessment of Left Atrial Function and the Association With Atrial Arrhythmias. Circ Cardiovasc Imaging. 2016;9(10):e004947.
27. Demir M, Aktas I, Camci S. Left atrial mechanical function and stiffness in patients with atrial septal aneurysm: a speckle tracking study. Cardiol J. 2015;22(5):535–40.
28. Yuda S, Muranaka A, Miura T. Clinical implications of left atrial function assessed by speckle tracking echocardiography. J Echocardiogr. 2016;14(3):104–12.
29. Donal E, Lip GYH, Galderisi M, Goette A, Shah D, Marwan M, et al. EACVI/EHRA Expert Consensus Document on the role of multi-modality imaging for the evaluation of patients with atrial fibrillation. Eur Heart J Cardiovasc Imaging. 2016;17(4):355–83.
30. Motoki H, Dahiya A, Bhargava M, Wazni OM, Saliba WI, Marwick TH, et al. Assessment of left atrial mechanics in patients with atrial fibrillation: comparison between two-dimensional speckle-based strain and velocity vector imaging. J Am Soc Echocardiogr. 2012;25(4):428–35.
31. Caso P, Ancona R, Di Salvo G, Comenale Pinto S, Macrino M, Di Palma V, et al. Atrial reservoir function by strain rate imaging in asymptomatic mitral stenosis: prognostic value at 3 year follow-up. Eur J Echocardiogr. 2009;10(6):753–9.
32. Cameli M, Lisi M, Focardi M, Reccia R, Natali BM, Sparla S, et al. Left atrial deformation analysis by speckle tracking echocardiography for prediction of cardiovascular outcomes. Am J Cardiol 2012;110(2):264–9.
33. Ancona R, Comenale Pinto S, Caso P, Di Salvo G, Severino S, D'Andrea A, et al. Two-dimensional atrial systolic strain imaging predicts atrial fibrillation at 4-year follow-up in asymptomatic rheumatic mitral stenosis. J Am Soc Echocardiogr. 2013;26(3):270–7.
34. Debonnaire P, Leong DP, Witkowski TG, Al Amri I, Joyce E, Katsanos S, et al. Left atrial function by two-dimensional speckle-tracking echocardiography in patients with severe organic mitral regurgitation: association with guidelines-based surgical indication and postoperative (long-term) survival. J Am Soc Echocardiogr. 2013;26(9):1053–62.
35. Koslowsky J, Gilon D, Stessman J, Jacobs J, Leibowitz D. Left atrial function and mortality in the elderly. Eur Heart J. 2017;38(suppl_1):ehx502.P2079-ehx502.P2079.
36. Agoston G, Gargani L, Miglioranza MH, Caputo M, Badano LP, et al. Left atrial dysfunction detected by speckle tracking in patients with systemic sclerosis. Cardiovasc Ultrasound 2014 Aug 5 ;12:30.

37. D'Ascenzi F, Anselmi F, Focardi M, Mondillo S. Atrial enlargement in the athlete's heart: assessment of atrial function may help distinguish adaptive from pathologic remodeling. J Am Soc Echocardiogr. 2018;31(2):148–57.

38. Altekin RE, Yanikoglu A, Karakas MS, Ozel D, Kucuk M, Yilmaz H, et al. Assessment of left atrial dysfunction in obstructive sleep apnea patients with the two dimensional speckle-tracking echocardiography. Clin Res Cardiol.2012;101(6):403-15.

39. Haruki N, Tsang W, Thavendiranathan P, Woo A, Tomlinson G, Logan AG, et al. Sleep Apnea and Left Atrial Phasic Function in Heart Failure With Reduced Ejection Fraction. Can J Cardiol 2016;32(12):1402-10.

40. Cameli M, Ciccone MM, Maiello M, Modesti PA, Muiesan ML, Scicchitano P, et al. Speckle tracking analysis: a new tool for left atrial function analysis in systemic hypertension: an overview. J Cardiovasc Med (Hagerstown) 2016;17(5):339–43.

41. Mondillo S, Cameli M, Caputo ML, Lisi M, Palmerini E, Padeletti M, et al. Early detection of left atrial strain abnormalities by speckle-tracking in hypertensive and diabetic patients with normal left atrial size. J Am Soc Echocardiogr .2011;24(8):898–908.

42. Cameli M, Righini F, Benincasa S. Left atrial strain in patients with arterial hypertension early effects of arterial hypertension: left atrial deformation analysis by two- dimensional speckle tracking echocardiography - Semantic Scholar [Internet]. 2013 [Citado 4 de junho de 2018]. Disponível em: https://www.semanticscholar.org/paper/Left-atrial-strain-in-patients-with-arterial-early-Cameli-Righini/e0e3414d4bd42c7ef8b6e80c4a6d825161c79aab

43. Antoni ML, ten Brinke EA, Atary JZ, Marsan NA, Holman ER, Schalij MJ, et al. Left atrial strain is related to adverse events in patients after acute myocardial infarction treated with primary percutaneous coronary intervention. Heart . 2011;97(16):1332–7.

44. Ersboll M, Andersen MJ, Valeur N, Mogensen UM, Waziri H, Moller JE, et al. The prognostic value of left atrial peak reservoir strain in acute myocardial infarction is dependent on left ventricular longitudinal function and left atrial size. Circ Cardiovasc Imaging. 2013;6(1):26–33.

45. Brambatti M, Connolly SJ, Gold MR, Morillo CA, Capucci A, Muto C, et al. Temporal relationship between subclinical atrial fibrillation and embolic events. Circulation. 2014;129(21):2094–9.

46. Guichard J-B, Nattel S. Atrial cardiomyopathy. J Am Coll Cardiol 2017;70(6):756 –65.

47. Hausfater P, Costedoat-Chalumeau N, Amoura Z, Cacoub P, Papo T, Grateau G, et al. AL cardiac amyloidosis and arterial thromboembolic events. Scand J Rheumatol 2005;34(4):315–9.

48. Iwasaki Y-K, Kato T, Xiong F, Shi Y-F, Naud P, Maguy A, et al. Atrial fibrillation promotion with long-term repetitive obstructive sleep apnea in a rat model. J Am Coll Cardiol. 2014;64(19):2013–23.

49. Kuppahally SS, Akoum N, Burgon NS, Badger TJ, Kholmovski EG, Vijayakumar S, et al. Left atrial strain and strain rate in patients with paroxysmal and persistent atrial fibrillation. Circ Cardiovasc Imaging. 2010;3(3):231-9.

50. Henein MY, Holgren A, Lindqvist P. Left atrial function in volume and pressure overloaded left atrium. Int J Cardiovasc Imaging.2015;31(5):659-65 Kurt M, Wang J, Torre-Amione G, Nagueh SF. Left atrial function in diastolic heart failure. Circ Cardiovasc Imaging. 2009;2(1):10-5.

51. Wakami K, Ohte N, Asada K, Fukuta H, Goto T, et al. Correlation between left ventricular end-diastolic pressure and peak left atrial wall strain during left ventricular systole. J Am Soc Echocardiogr. 2009;22(7):847-51.

52. Del Castillo JM, Alencar GMP, Nóbrega MVD, Mazzarollo C, Diniz JV, Albuquerque E S, et al. Avaliação ecocadiográfica das alterações ecocardiográficas tardias provocadas pela febre Chicungunya. Arq Bras Cardiol Imagem Cardiovasc. 2018;31(3):183-90.