Review Article

Echocardiographic Assessment of Left Atrial Function in Aging Adults

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Abstract

Cardiovascular diseases (CVD) are the main cause of death in Brazil, with aging being a major risk factor. Research indicates that there is a higher occurrence of cardiovascular disease as individuals age, impacting ventricular hypertrophy, diastolic dysfunction, and atrial fibrillation. Atrial myopathy, associated with aging, has received considerable attention, with oxidative stress and chronic inflammation under investigation as contributing factors. Left atrial function has been extensively studied, focusing on its role in cardiac performance. Modern echocardiographic techniques, such as speckle tracking, provide a detailed assessment of atrial function, offering advantages over traditional methods of assessing maximum atrial volume. Studies reveal the important role of atrial strain in predicting cardiovascular events. The aging process brings a progressive reduction in atrial functions, and new measures are being developed to detect atrial dysfunction early, with a potential impact on future guidelines and the definition of normal age-related standards.

Introduction

Cardiovascular diseases (CVD) are the main cause of death in Brazil, and the aging process is among the main risk factors for CVD. CVD prevalence increases with age, regardless of gender.[1] A study published in 2019[2] showed that the chance of an individual aged 65 or over having CVD is 4.7 times greater in Brazil. Data derived from the BLSA study (The Framingham Heart Study and the Baltimore Longitudinal Study on Aging)[3] revealed that aging individuals without concomitant CVD experience increased ventricular hypertrophy, diastolic dysfunction, declined physical fitness and increased prevalence of atrial fibrillation.

There has been a growing focus on the role of left atrial function in cardiovascular morbidity, with atrial myopathy recognized as an independent condition primarily linked to the aging process.[4] Animal models have demonstrated that aging is related to structural changes and modifications in atrial electrophysiological properties.[5] Oxidative stress, calcium dysregulation, and chronic inflammation leading to the final pathway of fibrosis[6] have been investigated as important agents of this process. The diseased atrium brings together conditions that predispose to blood stasis and endothelial dysfunction, favoring embolic phenomena.[4]

Besides recognizing atrial myopathy as the underlying cause of the well-established link between atrial fibrillation and cardioembolic events, there has been significant progress in understanding the impairment of atrial function itself, advancing to the extent that there is now recognition of atrial insufficiency as a distinct clinical entity. Atrial insufficiency is defined as any dysfunction of the atria – be it anatomical, mechanical, electrical, and/or rheological – leading to compromised cardiac function and associated symptoms.[7] The left atrium (LA) plays a fundamental role in ventricular filling. The physiology of the left atrium can be investigated and better determined through the analysis of the different phases of its contribution to ventricular filling, namely reservoir, conduit, and atrial contraction phases. The capacity of the atrial reservoir when filling during ventricular systole from the pulmonary veins corresponds to 40 to 50% of the systolic volume. Passive transfer during ventricular diastole (conduit function), by 20 to 30%. Active contraction of the atrium then transfers the remaining volume. Reduction in atrial function in any of these phases can lead to impaired overall cardiac performance and worse outcomes.[7]

Echocardiographic Analysis of Left Atrial Function

Biplanar measurement of maximum indexed left atrial volume (LAViMax) is widely utilized and recommended by guidelines for assessing atrial structure. This parameter is typically straightforward to obtain and has been extensively studied for its correlation with outcomes in patients with both preserved and reduced ejection fractions. The maximum atrial volume reflects the cumulative impact of processes contributing to atrial myopathy over time. Observational studies with more than 6 thousand patients have demonstrated that a maximum index volume of 34 ml/m² is an independent predictor of death, heart failure (HF), atrial fibrillation and ischemic stroke.[8,9] However, the development of new cardiovascular imaging techniques has allowed for a more detailed analysis of not only the structure but also the functional characteristics of the left atrium.

The advent of speckle tracking technology has enabled faster and more reproducible analysis of atrial myocardial deformation throughout the cardiac cycle, mainly due to its independence in relation to the insonation. It is currently possible to quantify, through dedicated software, atrial peak or reservoir function (PALS or LAS-r), conduit (LAS-cd), and atrial contraction (LAS-ct)[10] based on semi-automated analysis of apical images in two and

Keywords

Atrial cardiomyopathy; left atrial strain; speckle tracking echocardiography; aging.

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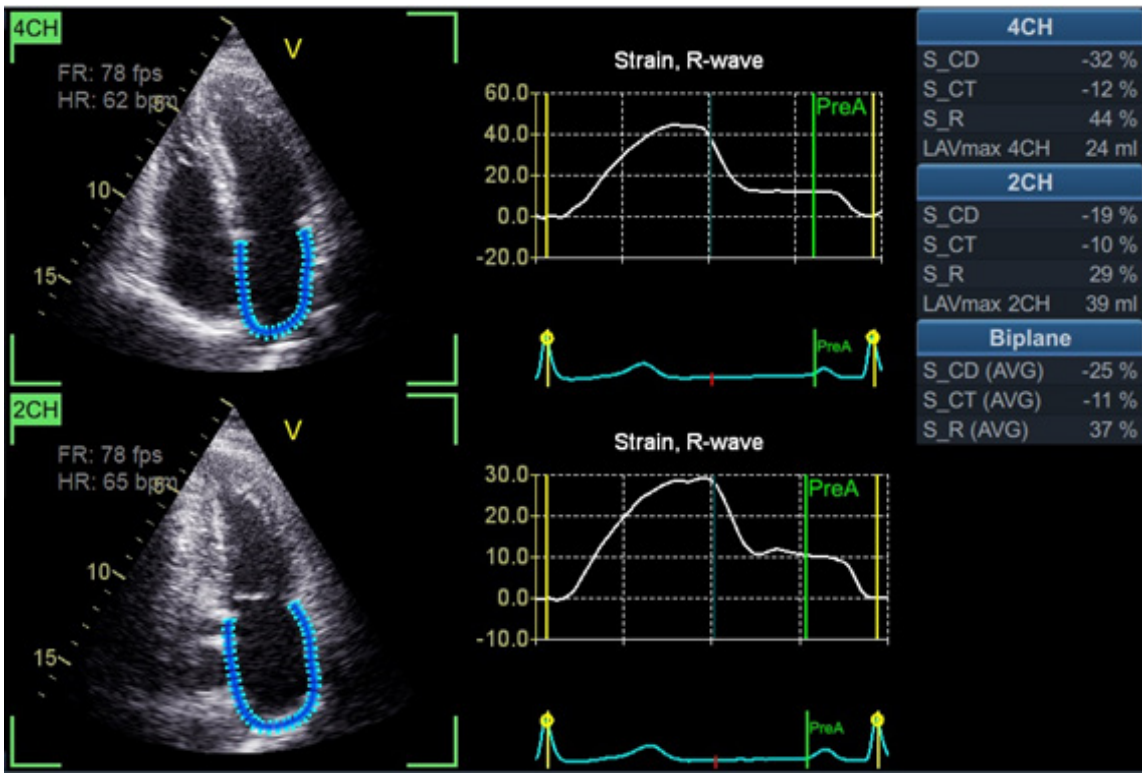
Central Illustration: **Echocardiographic Assessment of Left Atrial Function in Aging Adults**



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Exemplo de análise do strain atrial esquerdo nos cortes apicais de 4 e 2 câmaras com o software Echopac® (GE), utilizando o complexo QRS como referência para aferição. S_CD: strain de conduto; S_CT: strain de contração atrial; S_R: strain de reservatório. Notam-se os valores por corte e o valor médio considerando todos os seguimentos atriais.

four chambers focused on the left atrium (Central Illustration). Research has shown that evaluating atrial function, particularly reservoir function, offers significant advantages over summarizing maximum atrial volume alone, as functional changes often manifest before structural changes become apparent.[11]

Studies have demonstrated a noteworthy correlation between reduced LAS-r and the presence of atrial fibrosis, as assessed through magnetic resonance imaging and pathological studies.[11] An interesting study[12] analyzed the pre-operative atrial strain of 46 patients with mitral prolapse referred for cardiac surgery and who had histological atrial samples collected. LAS-r showed an important correlation with the degree of fibrosis in the anatomopathological study ($r = -0.82$, $p < 0.0001$). In contrast, atrial volume, atrial ejection fraction and Doppler-derived parameters (E/e' ratio) showed a weak correlation.

The analysis of atrial mechanics also reflects the important atrioventricular interaction, considering that mid-systole atrial distension is influenced by the mitral annulus movement, in addition to ventricular compliance also interfering with the atrial emptying process (passive and active).[13] Therefore, atrial strain is also an important parameter for ventricular function assessment. A study with 80 patients[14] referred for cardiac catheterization demonstrated that, among patients with an ejection fraction ≤ 30%, a LAS-r value < 18% was more accurate than the E/e' ratio in predicting a left ventricular end-diastolic pressure greater than 12 mmHg.

The close relationship between atrial and ventricular mechanics is also evidenced by the additional value of atrial strain analysis in the diagnosis of diastolic dysfunction, which may contribute to reducing the frequent diagnosis of "indeterminate diastolic function" according to current guidelines from the American Society of Echocardiography (ASE).[9] Among 517 patients considered at risk of developing diastolic dysfunction (with high blood pressure, diabetes, or history of coronary disease),[15] the reduction in LAS-r was more common than the increase in LAVI (36.9% vs. 15.5%; $p < 0.01$), and 29.4% of patients with normal LAViMax had reduced LAS-r. In this population, adding the LAS-r value < 23% as an additional diagnostic parameter for diastolic dysfunction alongside those determined by ASE, has increased the detection of diastolic dysfunction from 13.5% to 23.4% ($p < 0.01$). Furthermore, LAS-r < 23% was associated with the worst NYHA (New York Heart Association) functional class, even when LAViMax was normal.

Given the capacity for early detection of atrial and ventricular functional changes, the prognostic value of atrial strain has been demonstrated in several clinical contexts. A prospective study with 312 patients[16] demonstrated that LAS-r had the best capacity (area under the curve: 0.83) to predict in 3,1 ± 1,4 years the occurrence of atrial fibrillation, HF, stroke, transient ischemic attack, myocardial infarction, coronary revascularization, and cardiovascular death, in relation to LAVI (area under the curve: 0,71).

Atrial strain analysis also allows for a non-invasive assessment of the atrial stiffness index (LASI), defined as the relationship between mean E/e' and LAS-r. High atrial stiffness results from chronic exposure of the left atrium to high filling pressures. It represents a reduction in atrial compliance, with volumetric variations resulting in a large increase in atrial pressures. One study retrospectively evaluated 307 patients[17] with increased invasive measurement of final ventricular filling pressure (≥ 16 mmHg) and who underwent an echocardiogram within an interval of up to 7 days. In this population, a LASI > 0.26 showed better performance (area under the curve: 0.743; 95% CI: 0.681-0.806) to predict death from any cause or hospitalization due to HF in relation to the classic parameters for analyzing diastolic function (mean E/e', tricuspid regurgitation velocity, and LAViMax).

Volumetric data also continues to be explored. By employing three-dimensional echocardiography or atrial strain curves, it becomes feasible to accurately quantify the variation in left atrial volume throughout the entire cardiac cycle, rather than solely measuring the maximum volume at the end of systole, which is conventional. In an elderly population (71 ± 9 years), research has demonstrated that the minimum volume at the end of diastole, rather than the maximum volume, shows a stronger association with cardiovascular events, maybe because it represents the phase of the cardiac cycle when the atrium is most affected by ventricular filling pressures.[18]

Left Atrial Function and the Aging Process

Recent studies have aimed to establish normal values for atrial strain, considering its age-related variability. It is well-known that as individuals age, there is a gradual reversal in the relationship between rapid ventricular filling and atrial contraction. Starting from the fifth decade of life, there is a slowing of ventricular relaxation, leading to impaired early ventricular filling and a compensatory increase in late filling.[19] Interestingly, findings from the NORRE study (Normal Reference Ranges for Echocardiography)[20] have shown a progressive decline in reservoir (LAS-r) and conduit (LAS-cd) functions with age, accompanied by an increase in pump function (LAS-ct) and the atrial stiffness index. The minimum expected values for LAS -r were 31.1% for individuals aged 20 to 40 years, 27.7% for those aged 40 to 60 years, and 22.7% for those aged 60 and older. In contrast, the minimum values for LAS-ct were 7.2%, 9.3%, and 7.7%, respectively.

A more recent study[21] based on HUNT4Echo (The Echocardiographic substudy of the 4th wave of the Trøndelag Health Study), including 1329 patients, also sought to determine normal values for atrial strain. Unlike the NORRE study, which used the VIS software (Tomtec), the HUNT4Echo data were analyzed by Echopac (GE). The results also reveal a negative association between age and reservoir and conduit strains.

Finally, a study published in the Journal of the American College of Cardiology in April 2022 specifically explored the behavior of atrial structure and function in elderly patients.[22] In the article by Inciardi et al., the LAViMAx measurement is initially emphasized as the most commonly used measure to measure the LA, being recommended by the main international cardiology societies. However, they emphasize the potential of incorporating new measurements and functional analyses using advanced techniques to provide additional insights for the early detection of atrial dysfunction, potentially identifying issues before structural changes become evident.

This is the analysis of a multicenter cohort of patients from the ARIC study (Atherosclerosis Risk in Communities Study), using new LA assessment measures in a population of 4901 participants over 65 years of age, presenting sinus rhythm and without HF. The objectives of the study were to evaluate variations in LA structural and functional measurements and their correlation with NT-proBNP and incidence of the combined outcome of death or HF in an average prospective follow-up of 5.5 years.

In addition to the conventional structural measurement of LAViMax, two other measurements were performed: the minimum LA volume (LAViMin) and the LA emptying fraction (LAEF). Functional measurements of the LA reservoir, conduit and contractile derived from two-dimensional strain were also performed. Interestingly, an initial cohort of 301 patients without pre-existing CVD was studied to establish the normal limits of the assessed parameters, defined as values between the 10th and 90th percentiles.

After a mean follow-up time of 5.5 years and adjustments for clinical confounding factors, ventricular function, and NT-proBNP, with the exception of LAViMax, all other structural and functional parameters under investigation (including LAViMin) remained significantly associated with a greater incidence of the combined outcome. The variables were identified as predictors of unfavorable outcomes, even when excluding patients with increased LAViMax or analyzing the outcomes separately between the groups of patients who developed HF with reduced or preserved ejection fraction.

Reservoir and conduit atrial strains showed a non-linear relationship between outcomes, with a significant increase in the combined incidence of death and HF with values below 28% and 11%, respectively. Thus, the conventional measurement of left atrial dimension was found to be less reliable in this elderly population compared to the measurement of minimum indexed atrial volume and functional parameters derived from atrial strain. It is important to note that the upper normal values (90th percentile) identified in this group for LAViMax were 37.8 ml/m^2 for women and 42.7 ml/m^2 for men, indicating that current guidelines may underestimate normal values for older people.

Conclusion

The development of new echocardiographic techniques has allowed a more detailed analysis of left atrial function. The integration of functional data with structural analysis enabled the characterization of left atrial function throughout the entire cardiac cycle, in addition to establishing its relationship with left ventricular function and determining the changes resulting from pathological processes and aging. Previously viewed primarily

as a "buffer chamber" affected by ventricular dysfunction, the assessment of dynamic parameters has revealed the early onset of atrial dysfunction, actively contributing to reduced overall cardiac performance and holding prognostic significance across various contexts. Advancements in technology and the adoption of more automated methods, including artificial intelligence, are expanding the accessibility of functional analysis of the left atrium. Future studies should integrate these insights into guidelines to enhance understanding of the anticipated variations in normal values due to aging.

Author Contributions

Conception and design of the research and critical revision of the manuscript for intellectual content: Oliveira FRC, Resende MVC, Vieira MLC; acquisition of data, analysis and interpretation of the data and writing of the manuscript: Oliveira FRC.

Potential Conflict of Interest

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

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This study is not associated with any thesis or dissertation work.

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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