

Left Atrial Volume as an Index of Diastolic Function

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Congestive heart failure (CHF) is one of the main causes of death and hospital admissions in our country, according to data from Datasus¹. This clinical syndrome is progressive and characterized by complex cardiac and systemic adaptations, which vary during disease evolution².

It has been observed, however, that in approximately 30% to 50% of the individuals who develop CHF, the systolic function estimated through the left ventricular ejection fraction (LVEF) is normal or relatively normal³. Thus, the cause of cardiac decompensation in these patients is the left ventricular diastolic dysfunction, justifying the term "diastolic cardiac failure"⁴.

Little is known on the natural history of this disease, particularly regarding the mechanisms causing affected patients' death⁵, although its prevalence is known among certain groups, such as the elderly and women, as well as the fact that it usually precedes the systolic dysfunction in most cardiac affections, including Chagas' myocardiopathy⁶⁻⁹.

There have been few studies published in literature regarding the incidence of CHF in patients with diastolic dysfunction evidenced by Doppler echocardiography. It has been demonstrated, in a population of individuals older than 65 years with no clinical evidence of cardiac disease, that the detection of this type of dysfunction through Doppler echocardiography has a predictive value for the development of CHF in 11 a 15% of the cases within a five-year period¹⁰.

DIASTOLE AND TYPES OF DIASTOLIC DYSFUNCTION

According to the most generally employed clinical concept¹¹, the diastolic phase of the cardiac cycle, starting with the closing of the semilunar valves, comprises the largest part of the active ventricular relaxation, with periods of isovolumetric relaxation, and rapid ventricular filling, as well as diastasis or passive filling and, finally, the period that involves atrial contraction. The illustration of this concept is depicted in Figure 1.

Even though several independent factors affect the diastolic properties of the left ventricle (LV) its actions converge to the transmitral pressure gradient, which, in fact, is the physical determinant of the left ventricular filling¹².

During the isovolumetric relaxation period, the LV behaves as an isolated chamber, as the aortic and mitral valves are closed; thus, its volume is not altered when there is a progressive decrease of intracavitary pressure. The heart relaxation is also the main determinant of the rapid ventricular filling, which is caused by the opening of the mitral valve as a result of the pressure decrease inside the LV, which is lower than that observed in the left atrium (LA)¹³. It is an energy-dependent process, which corresponds to the active sequestration, contragradient, of calcium ions released from troponin during the contractile activation¹⁴.

The rapid ventricular filling, which under normal circumstances is responsible for 80% of the ventricular filling, is also due to the pressure in the left atrium at the moment of the mitral valve opening (preload) and elastic recoil (suction) of the left ventricle. This phenomenon occurs because the shortened muscle fibers at the end of the systole, together with the collagen matrix, act as a compressed coil to generate recoil forces at the initial phase of the diastole¹⁴, resulting in a decrease of LV pressure, despite the progressive increment of its volume. The LA emptying provides the manometric equalization between the left chambers, comprising the diastasis phase.

In this phase, which is influenced by the LV complacency (pressure/volume ratio), ventricular filling is basically originated from the pulmonary venous flow, as the LA behaves as a "passive conduit", enabling the direct passage of blood from the pulmonary valves to the LV¹⁵. The atrial contraction, which happens at the end of the diastolic period, contributes for 15% to 20% of ventricular filling in normal individuals¹⁶, and depends on interactions of the LV with the pericardium and the right ventricle (RV), on the atrioventricular synchronism (PR interval of the electrocardiogram), on the cardiac rhythm (loss of the atrial contraction in the presence of arrhythmias such as atrial fibrillation) and on the LA and LV pressures^{14,17,18}.

The normal LV must be capable of accommodating a significant volume of blood without causing the diastolic pressure elevation. Hence, the proportion of ventricular filling during the initial and final phases of diastole depends on the myocardial relaxation, the elastic retraction, the LV complacency and the LA pressure, which originate from the interaction between heart disease andolemia¹⁴.

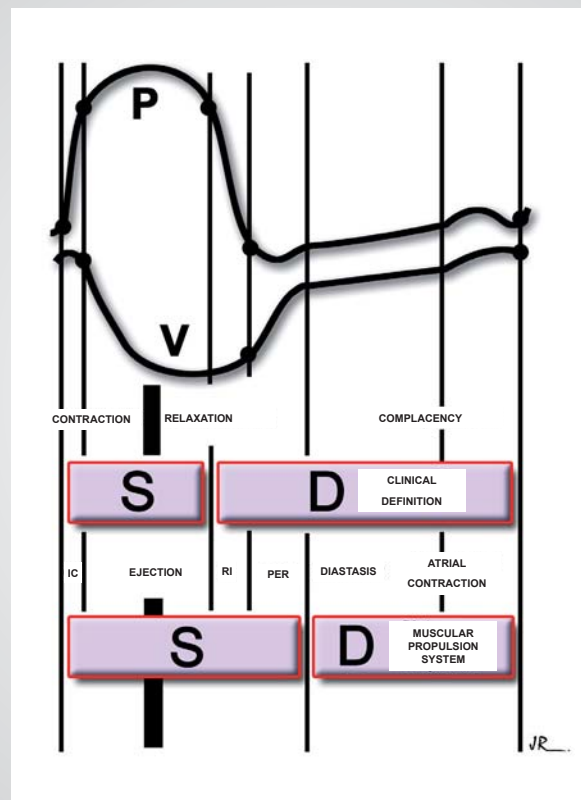


Fig. 1 – Cardiac cycle divided in periods corresponding to the clinical definition and the conception of the heart as a muscular propulsion system, of the systolic (S) and diastolic (D) events; P=ventricular pressure curve; V=ventricular volume curve; IC=isovolumetric contraction; IR=isovolumetric relaxation; RVF= rapid ventricular filling period. Observe that, in the mechanical conception of the heart, the systole comprehends not only the contraction and ejection phases, but also the whole of the active relaxation period, including, as well, the rapid ventricular filling. Adapted from Marin-Neto and Sousa (1988).

Many patients with CHF and preserved systolic function predominantly present the diastolic mechanisms that determine the symptoms of dyspnea and fatigue. In these individuals, the LV is not dilated and contracts normally; however, the diastolic function is compromised¹⁹. In diastolic heart failure, the LV has decreased complacency and it is unable to fill adequately with normal pressures. This condition results in the reduction of the final diastolic volume, which causes the decrease in the systolic volume and symptoms of low cardiac output and/or final diastolic pressure elevation, which, in turn, determines the onset of symptoms of pulmonary congestion. Thus, the characteristics of CHF (incapacity of the heart in pumping blood to maintain the tissue metabolic needs, preserving the filling pressures) can be mainly due to lusitropic abnormalities⁹.

There are three types of diastolic dysfunction: a) increase of ventricular rigidity, which is common in ischemic heart disease in the elderly, in cardiac amyloidosis and endomyocardiofibrosis; b) ventricular hypertrophy, of which the main cause is systemic arterial hypertension (SAH); c) mechanical obstructions, caused

by mitral stenosis, LA myxoma, constrictive pericarditis and cardiac tamponade¹⁹.

EVALUATION OF THE DIASTOLIC FUNCTION

Part of the difficulty in studying the diastolic function of the LV is due to the fact that its main determinants (relaxation and complacency) act in different phases of the diastole, with an overlap of the time of action. In addition to undergoing mutual interaction, they are also influenced, as mentioned above, by the LV systolic function, by the heart frequency (HF) and the heart conduction system.

The analysis of the ventricular filling pattern provides important information on the diastolic performance of the LV. Historically, the hemodynamic study through cardiac catheterism has been the reference standard for the acquisition of such information²¹. However, its invasive nature makes this methodology unfeasible in routine clinical practice. Diastolic function assessments can also be obtained by non-invasive techniques, such as the determination of the LV volume of dimensions during the cardiac cycle, by radioisotope angiography²², or by Doppler echocardiography^{12,23}.

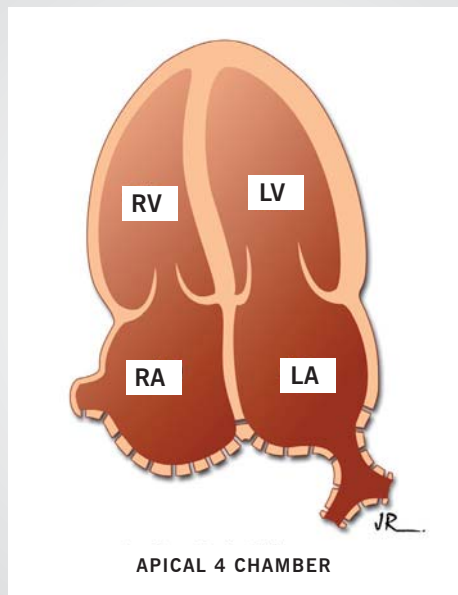


Fig. 2 – Schematic representation of the bidimensional echocardiogram obtained at the apical four-chamber position. Observe that in the diastolic period, with the mitral valve open, the left atrium is directly exposed to the filling pressures of the left ventricular chamber.

The use of Doppler echocardiography in diastolic function assessment started in the seventies with Gibson & Brown²⁴, who developed an analysis method of the continuous variation of the LV dimension, using a computerized system of reutilization of echocardiographic tracings. In our country, this technique was standardized by Marin-Neto and Sousa²⁵ and utilized in the demonstration of early diastolic dysfunction in Chagas disease⁶, showing it to be reproducible, but also time-consuming, which, in a way, limits its routine utilization.

LEFT ATRIUM VOLUME

As mentioned before, alterations in the relaxation and complacency of the LV secondary to a defect in the actin-myosin interaction and increase in collagen deposition or the viscoelastic properties of the heart cause an elevation of the left ventricular end-diastolic pressure (LVDP) and consequently, elevation of pressure in the LA to maintain the ventricular filling²⁶. The parietal tension increase leads to the dilation of the atrial chamber, which consequently reflects the diastolic dysfunction of the LV^{27,28}. The LA behaves as a reservoir during the ventricular systole, as a conduit that allows the passage of blood from the pulmonary veins to the LV at the beginning of the diastole, and as an active contractile chamber at the end of the diastole.

During the diastolic period, this atrial chamber is directly exposed to the pressures of the LV through the open mitral valve²⁸, as shown in Fig. 2. Hence, the size of the LA is greatly influenced by same factors that determine ventricular filling²⁶, so constituting a stable parameter that reflects the duration and severity of the lusitropic dysfunction²⁹. Consequently, it has been considered that the LA dimension is a potent predictor

of adverse events in several clinical situations such as: a) ischemic stroke³⁰; b) chronic atrial fibrillation (AF)³¹; c) left ventricular failure³²; d) mitral regurgitation³³ and e) diastolic dysfunction²⁹.

The routinely available methods for the determination of the LA size through Doppler echocardiography are the measurement of the anteroposterior dimension obtained at the parasternal projection of its long axis and volume calculation, also utilizing the apical two-chamber and the apical four-chamber views³⁴. The uniplane measurement of the anteroposterior dimension has decreased accuracy and low reproducibility in the quantification of the left atrial dimension, which are caused by technical limitations such as the ultrasound beam angulation, the irregular geometry of the LA and the fact that the growth of this chamber is not a uniform one, due to the physical limitation imposed by the sternum and vertebral column³⁵.

This can, in part, explain the conflicting results described in the specialized literature regarding the size of the LA when assessed by its anteroposterior dimension, as a variable, in order to establish the prognosis in certain clinical situations; in patients with chronic AF, who took part in the AFASAK³⁶ study, the anteroposterior dimension did not have a predictive value for thromboembolism (TE), whereas another study (SPAF)³⁷ showed that this variable was the best predictor for stroke, when assessing a similar population.

On the other hand, the LA volume (LAV) can generally be obtained by several means: a) the cube³⁸ method, according to which the atrial chamber has a spherical shape, through the following formula: $LA = 4/3 \pi \times (\text{anteroposterior dimension}/2)^3$; b) ellipsoid method³⁹, assuming an elliptical shape of the LA, according to the formula: $4/3 \pi \times \text{anteroposterior dimension}/2 \times \text{length}/2 \times \text{mediolateral dimension}/2$, in which the length is the

distance between the point of coaptation of the mitral valve cuspids and the upper wall of the LA and the mediolateral dimension is the transverse dimension, obtained at the apical 4-chamber position. All calculations must be performed at the end of the systole; c) the biplane area-length measurement⁴⁰, using the formula $0.85 \times 4\text{-chamber area} \times 2\text{-chamber area/perpendicular axis}$, in which the areas are obtained at the apical positions, by excluding the left atrial appendix and the confluence of the pulmonary veins; the perpendicular length is measured between the plane of the mitral valve (MV) ring and the upper portion of the LA; d) uniplane or biplane Simpson's disks method⁴¹, in which the technician performs the tracing of the left atrial endocardium at the apical 2- and 4-chamber positions, as shown in Fig. 3.

The methodologies for measurement of the left atrium volume (LAV) that best apply to clinical practice are those that utilize Simpson's technique, either uniplane³⁴ or biplane⁴².

Lester and cols.³⁴ observed that the uniplane technique, derived from the apical 4-chamber position, represents an accurate measurement of the factual size of the LA. According to Schiller & Foster⁴³, the LA volume, normalized for the body surface, is an index of the left atrial size that seems to be a better indicator of the factual size of this cavity, and concluded, based on personal experience, that the normal value for the LA volume index in both sexes was 21 ml/m², with 32 ml/m² being the upper limit of normality (with a confidence interval of 90% of the 95th percentile). Simpson's method for obtaining LAV has been validated in clinical trials utilizing the biplane angiography technique⁴⁴ and cine computed tomography (CT)⁴⁵. More recently, Khankirawatana e cols.⁴², comparing several methods of measuring LAV, also

demonstrated the great accuracy of Simpson's method.

Some studies^{46,47} reported that the LA size would naturally increase with age. These observations are supported by the evidence that 70% of the patients with AF are 65 years or older⁴⁸. Therefore, senescence can cause alterations that would eventually culminate with LA dilation and dysfunction, thus increasing the predisposition to atrial arrhythmias⁴⁹. However, these studies utilized M-mode-derived parameters to evaluate atrial dimension, which is a technique that has been shown to be geometrically less exact. Thomas and cols.⁵⁰ did not find significant variations in LAV produced by aging when utilizing Simpson's method, thus suggesting that the confirmation of LA increase indicates a pathological manifestation, and not a physiological aging process. The same authors verified that, in order to compensate for the decrease of ventricular filling that occurs in the initial phases of diastole (which depends on the relaxation), the elderly individual increases the volume of active emptying volume (atrial contraction), so that the total draining volume remains unaltered. The increased velocity of the A wave of the mitral flow chart observed in elderly individuals (see below) reflects such phenomenon.

The LAV has been considered to be an index independent from the acute variations of pre-load, and therefore, it provides a more accurate evaluation of ventricular dysfunction^{18,34}. However, Barberato and cols.⁵¹, in a recent publication, demonstrated for the first time that the index of LAV is affected by acute pre-load modifications, by utilizing a clinical model of volume variation offered by hemodialysis. Nevertheless, it is noteworthy that this observed pre-load dependence was less than that observed in Doppler-derived indexes.

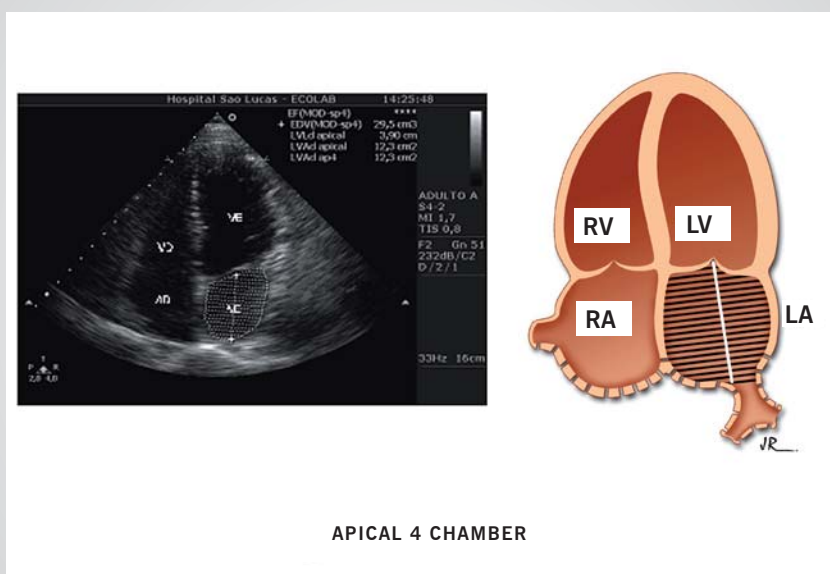


Fig. 3 – Left atrium volume (LAV) measurement utilizing the uniplane Simpson's method at the end of the systole, in the apical four-chamber view. A 25-year old normal individual is depicted on the left, presenting LAV=40 mL and LAV index =21 mL/m²; the schematic representation of the procedure can be seen on the right.

Several clinical studies have demonstrated the usefulness of LAV in the prognosis of several pathologies. Tsang and cols.⁵², evaluating a group of patients with no history of valvulopathies, showed that this variable translates a sensitive morphophysiological expression of the degree of LV diastolic dysfunction, and also constitutes a useful marker of cardiovascular risk. Cioffi e cols.⁵³, studying the connection between left ventricular geometry and LA dimension in patients with systemic arterial hypertension, verified that the concentric LV hypertrophy is associated to a higher LAV, thus indicating a higher degree of diastolic function involvement, also evaluated by the mitral flow chart, than the eccentric hypertrophy. In this study, the degree of the atrial chamber increment was similarly correlated to the LV mass at the two patterns of ventricular geometry. However, the same group, in a previous study, had demonstrated that in individuals with chronic aortic valve disease, the LA volumetric increase is directly associated with LV mass, within the context of concentric geometry. Its value as an AF predictor has also been disclosed. Tsang and cols.⁵⁴, by studying an elderly population of both gender who were, in the beginning of the investigation, in sinus rhythm and did not present significant cardiac diseases, observed that an increase of 30% of the LAV was followed by an increment of 43% in the risk of presenting AF. The authors also verified that the predictive value of this variable for AF occurrence in apparently healthy elderly individuals is higher than that obtained by a combination of clinical factors and M-mode LA measurement. Moller and cols.⁵⁵ concluded that the LAV index is a strong predictor of early mortality after acute myocardial infarction (AMI) and that it also added prognostic information to the clinical parameters and the conventional measurements of systolic and diastolic LV function. This investigation also showed that, if this index was normal, the patient's prognosis was favorable, even when his or her systolic function was compromised. Beinart and cols.⁵⁶ observed, in a similar population, that

when this index was obtained within the first 48 hours of hospital admission, it was also an independent predictor of late mortality, incorporating additional information to the clinical and echocardiographic ones. Recently, Sabharwal⁵⁷ reported that, in ischemic cardiomyopathy ($EF \leq 0.40$), the LAV was an independent factor in predicting mortality among several clinical and echocardiographic parameters evaluated, which is in accordance to the results previously described by Rossi and cols.⁵⁸ in patients with dilated cardiomyopathy.

Barnes and cols.⁵⁹, studying a population of elderly individuals, demonstrated the importance of LAV as an independent predictor of the first ischemic stroke and death, in individuals with no previous AF. Although the conception that the increase of LA dimension gives rise to a higher incidence of AF, and consequently, a higher incidence of stroke is appealing, the investigators postulate the existence of another mechanism to explain such association, as only 15% of all ischemic brain strokes are attributed to AF⁶⁰. In a recently published population-based study, Prichett e cols.⁶¹ observed that the diastolic dysfunction is associated to the increase of LAV, regardless of the presence of cardiovascular disease, left ventricular systolic dysfunction and ventricular hypertrophy, and also that this index is a reliable indicator of the presence of lusitropic dysfunction of a significant degree.

CONCLUSIONS

The left atrial volume (LAV) evaluation by Doppler echocardiography is a sensitive index that expresses the severity of the left ventricular diastolic function, as well as providing prognostic information on several cardiopathies. This methodology is increasingly being incorporated into the routine practice, due to its relative technical simplicity and its potential for providing relevant information, making the management of the patient undergoing the technique easier for the physician.

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