Echocardiographic Evaluation of Left Atrial Function: Physiological and Clinical Aspects

Afonso Yoshikiro Matsumoto[1,2], Frederico José N Mancuso[1,3], Solange Bernardes Tatani[1,3], Cristiano Vieira Machado[1,3], Viviane Tiemi Hotta[1,2,4], Valdir Ambrosio Moisés[1,3]

Laboratório Fleury Medicina e Saúde[1], Faculdade de Medicina da USP[2], Escola Paulista de Medicina, UNIFESP[3], Serviço de Ecocardiografia do InCor/FMUSP[4]

Abstract

The evaluation of left atrial function may provide important information regarding the pathophysiology of many heart diseases, especially when the left chambers are involved. However, as opposed to the left ventricular systolic and diastolic functions, widely exploited in many clinical conditions, the left atrial function is still poorly studied.

Basic concepts of the functions of left atrial reservoir, conduit and booster pump are discussed, highlighting the connections with ventricular filling. The methods of investigation of these functions are presented in summary form.

Introduction

As opposed to left ventricular (LV) systolic and diastolic functions, widely studied in various clinical and experimental conditions, the left atrial (LA) function has been little studied, despite its recognized importance in the overall LV performance [1].

The analysis of left atrial function associated with the study of left ventricular diastole may bring key information to help understanding the physiological and pathophysiological mechanisms involved in various cardiovascular conditions.

With the opening of the mitral valve, the LA and LV work basically as a single chamber, hence with mutual influence on the filling and emptying of these chambers [2].

Several factors contributed to the awakening of interest in the study of left atrial function. These factors include: 1) extensive use of procedures directly involving the LA, such as drug interventions, electronic devices, radioablation and surgeries intended to treat atrial fibrillation[3-5]; 2) recognition of LA electrical, ionic and mechanical remodeling[5]; 3) stunning after cardioversion[6,7]; and 4) the prognostic importance of left atrial size and function in heart failure[8-10]. With echocardiography, much information on atrial size and function can be obtained using recently validated techniques and methods in a simple and consistent way [11].

This revision addresses important aspects of LA physiology, which may help interpreting the mechanisms involved in left ventricular diastole in normal conditions and in diseases.

Keywords

Atrial Function Left/physiology; Echocardiography; Diastole; Left Ventricle.

Mailling Adress: Afonso Y. Matsumoto •
Rua Prof. Francisco de Faria Barcellos, 84, CEP 05396-090,
Parque dos Príncipes, São Paulo - SP - Brazil
E-mail: afonso.matsumoto@grupofleury.com.br, afonso.matsumoto@gmail.com
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Physiology

One of the LA functions is to provide blood to ventricular diastole.

This process involves relaxation, compliance and other functional LA characteristics, as well as LV systolic and diastolic functions. These particularities should be considered in an integrated way, since they are interdependent and therefore inseparable. However, for didactic purposes, the concepts will be discussed separately.

The LA plays a regulatory role in ventricular filling through three basic functions: 1) reservoir function during atrial diastole; 2) conduit function during passive emptying during ventricular relaxation and diastasis; 3) booster pump function in the contraction phase, or active emptying, provided that it is in sinus rhythm, which significantly contributes to cardiac output [12].

Reservoir Function

It is the storage capacity of blood volume during atrial diastole that is influenced by the following factors: 1) atrial contraction and relaxation[13,14]; 2) LV contraction that moves the mitral annulus in the caudal direction[13,15]; 3) atrial chamber rigidity and compliance[16-20]; and 4) right ventricular systole that influences the flow of pulmonary veins[20,21]. It is estimated that 42% of LV stroke volume is stored in the LA during ventricular systole, which makes evident the importance of LA reservoir function in cardiac output[1].

After atrial contraction and mitral valve closure, LA myocardial relaxation begins similarly in its characteristics as in LV relaxation. This cardiac cycle phase marks the end of diastole and the beginning of ventricular systole. These two phenomena (atrial relaxation and mitral annulus displacement) exert a suction effect and are important determinants of increased atrial blood volume from the pulmonary veins. Due to relaxation, the chamber expands and, even with a simultaneous increase in volume, there is an initial drop in the intra-atrial pressure. Therefore, the reservoir phase is made up by two parts: an initial one, related to myocardial relaxation resulting from previous atrial contraction; and a late one, which depends on the shortening of ventricular myocardial longitudinal fibers, and chamber rigidity[20,22].

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The initial reservoir function phase is responsible for approximately 37% of atrial filling and coincides with atrial relaxation. The late phase depends on the LA elastic characteristics and, just like in the LV, the pressure-volume ratio is exponential and curvilinear; 63% of atrial filling occurs in the late phase[14,20].

For better understanding atrial filling during the reservoir phase, it is crucial to understand some basic concepts of LA pressure and volume curves, LA pressure-volume ratio, and flow of pulmonary veins, whose dynamics is closely linked to LA and LV hemodynamic and physical characteristics[2,23].

LA Pressure and Volume Curves

The registration of pressure curve requires the use of a catheter with a micromanometer placed inside the LA [22]. Therefore, with atrial contraction, after the electrocardiogram P wave, wave **a** is followed by wave **c** at the beginning of ventricular systole. The latter results from the transmission of pressure wave during ventricular systole, starting the LA rapid filling phase. Wave **c** is followed by descent **x**, which arises from active atrial relaxation and mitral annulus caudal displacement, which are the main determinants of the initial phase of atrial filling (figure 1). In this phase, there is an increase in atrial volume, but with decreased intra-atrial pressure.

As atrial relaxation ends, filling proceeds continuously, from the final phase of isovolumetric contraction, ejection, and much of the LV isovolumetric relaxation[24], being influenced by atrial compliance and by mitral annulus displacement[20,22]. However, as opposed to what occurs in the initial phase, there is a progressive increase in left atrial chamber pressure and volume, reaching a peak in wave **v**.

In the following phase, with the opening of the mitral valve, the LA empties quickly, with immediate drop in atrial pressure and volume, forming the **y** descent. Simultaneously, atrial filling continues slowly due to the blood volume from the pulmonary veins. Then, during slow LV filling there is a slow and gradual LA pressure and volume increase until point **d**. Note that until the **y** descent, and from the **y** descent to point **d**, the two chambers are filled passively. In this filling phase, the pressure difference between the two chambers is zero or close to zero. What determines the LA flow to the LV is the greater compliance of the latter (about two to three times)[22].

LA Pressure-Volume Relationship

Simultaneous measurement of LA volume and pressure helps establishing the temporal relationship between the two variables, which is key to understand the dynamics of atrial filling. However, it is an invasive and expensive procedure that is virtually restricted to research purposes.

Continuous LA measures were initially done by sonomicrometry, or LA coronary angiography, which are presently being replaced by two-dimensional echocardiography measurements, for example, LA area variation during atrial diastole [20]. Measuring volume variation using three-dimensional echocardiography is another option.

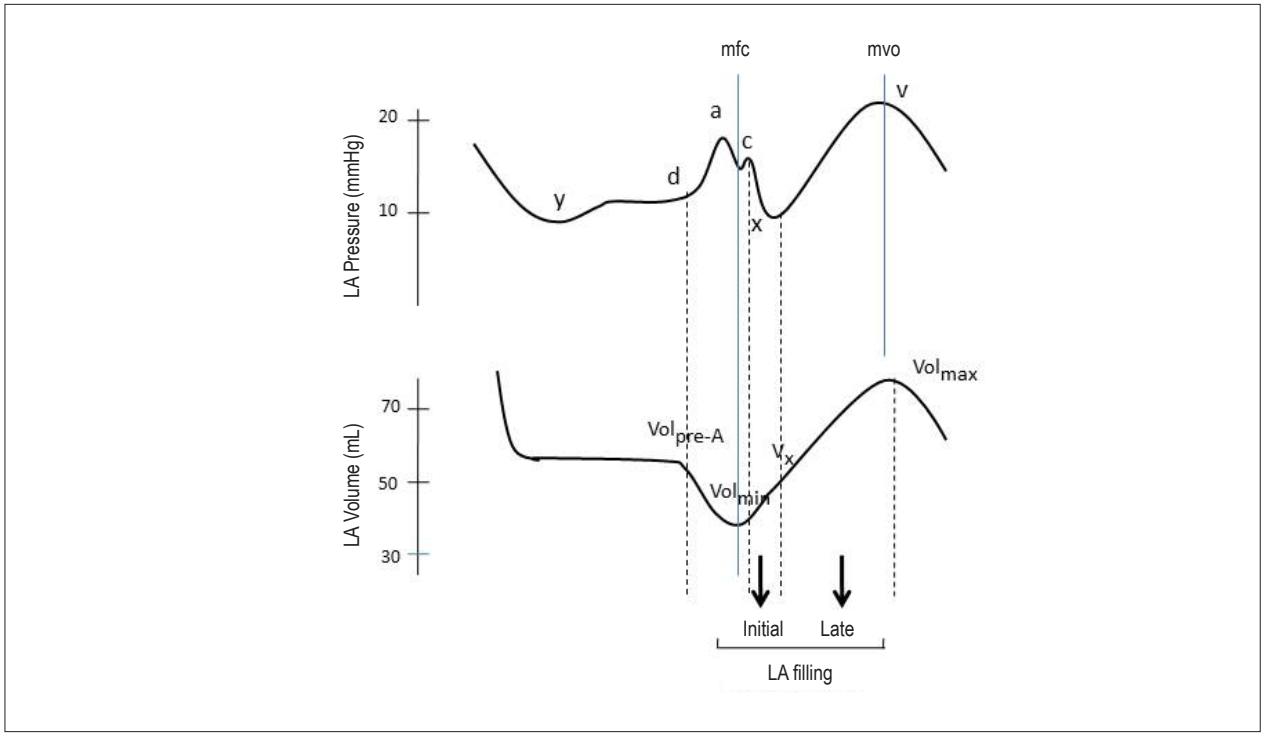

Figure 1 - *Schematic representation of left atrial pressure and volume curves. The upper curve represents the pressure, highlighting waves a, c, d and v, and the x and y descents. The lower curve represents the volume Volmin = minimum volume Volmax = maximum volume Vol pre-A = volume before atrial contraction mvc = mitral valve closure mvo = mitral valve opening. See description of the curves in the text.*

On a diagram, analyzing a cardiac cycle, the pressure-volume relationship is expressed by two loops making up a horizontal eight-shape. The first one (loop A), with anti-clockwise rotation, represents the active component, and the second one (loop V), with clockwise rotation, stands for the reservoir atrial function (Figure 2). The ascending portion of loop V is an exponential and curvilinear function that is similar to the LV pressure-volume curve; it is the only way to analyze and measure atrial compliance. Similarly to the LV pressure-volume curve, in the initial portion of the curve (low intracavity pressure phase) there is a large increase in volume to a small increase in pressure, while the end portion (higher intracavity pressure phase), a small volume increase promotes a large pressure increase[22]. The slope of a line from point x to v relates to atrial rigidity[20].

LA Conduit Function

Once the mitral valve opens, the blood stored in the LA during the reservoir phase flows quickly to the LV, making up the descending portion of loop **V**. The blood from the pulmonary veins concomitantly enters the LA without substantially changing intra-atrial volume, since the blood virtually flows into the LV through the open mitral valve. This volume is not attributed to the reservoir function or atrial contraction and characterizes the LA conduit function[24-26]. This phase ends before atrial contraction.

LA Booster Pump Function

LA booster pump contraction or function contributes significantly and effectively to cardiac output, especially in patients with heart diseases, when in sinus rhythm[12].

Note that the atrial systolic function measurement evaluated by volumetric chamber measurements depends on multiple factors, including atrial contraction time, vagal stimulation, magnitude of venous return (preload) and LV end-diastolic pressure (afterload) and cannot, therefore, be used strictly as an index of LA inotropic state[24,26].

The contribution of LA to LV filling depends fundamentally on the diastolic properties of this chamber[27]. In individuals with normal diastolic function, the relative contribution of reservoir, conduit and booster pump functions is approximately 40%, 35% and 25%, respectively[28].

With abnormal LV relaxation, the contribution of reservoir and booster pump functions increases and conduit function decreases[27,28].

However, as the LV filling pressure increases progressively with diastolic dysfunction worsening, the LA acts predominantly as a conduit[27,28].

Methods of Evaluation of Left Atrial Function

LA compliance is an important determinant of reservoir function (late phase) and can be analyzed by the pressure-volume ratio. As described above, in clinical practice it is not

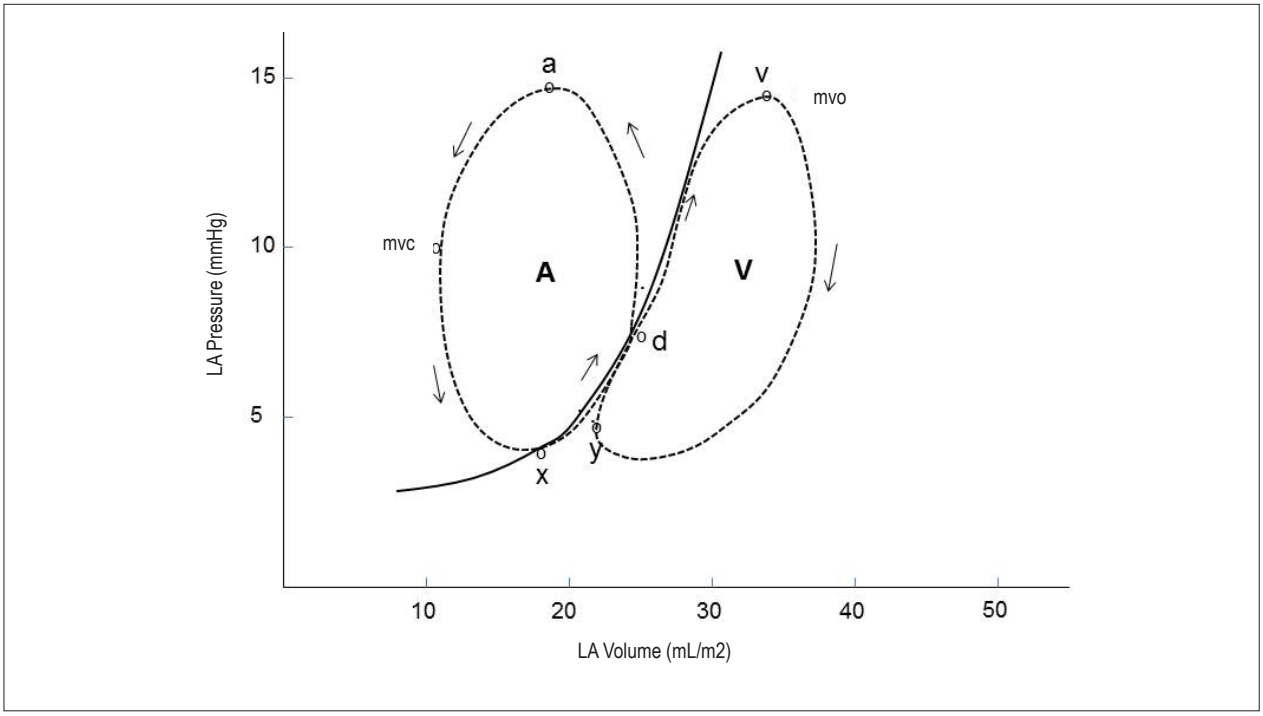

Figure 2 - *Left atrial pressure-volume ratio in the cardiac cycle. With atrial contraction, pressure (LAP) increases and volume (LAV) decreases, making up loop A. As the mitral valve closes (mvc), ventricular systole begins, LAP decreases and LAV increases. From descent x to point v, LAV and LAP increase rapidly, making up the ascending portion of loop V. As the mitral valve opens (mvo), LAV and LAP quickly fall to descent y, making up the descending portion of loop V, completing the cycle at point d. See text.*

analyzed for methodological limitations. Some information of the basic LA functions can be obtained by analyzing the flow of pulmonary veins using Doppler echocardiography and atrial volume variation analysis throughout the cardiac cycle[17,25,26].

1. Pulmonary veins flow

It is strictly linked to LA and LV hemodynamic conditions and viscoelastic properties. It can be used to assess left atrial function.

S Wave

Transesophageal Echocardiography (TEE) shows a two-phase systolic wave in 73% of the cases with one initial peak (S1) and a late peak (S2)[13,29] (Figure 3). It should be noted that the two-phase systolic wave is best observed when the records are taken on the left superior pulmonary vein. The same does not occur when the approach is from the right upper pulmonary vein, especially when performed by transthoracic echocardiography (TTE).

Although it has not been directly demonstrated that the S1 wave is related to atrial relaxation, some evidence points to this association: 1) Wave S1 and reverse A wave (ARev) - The reverse A wave stems from the retrograde flow through the pulmonary veins after atrial contraction — these disappear in patients with atrial fibrillation; both reappear gradually after cardioversion to sinus rhythm, 2) Wave ARev is closely related to S1, 3) Wave S1 occurs simultaneously with the beginning of descent **x** of LA pressure curve[19,29].

The morphology of the S wave is variable and depends on the technique used (TTE or TEE). Usually, when the transthoracic approach is used, a single S wave is most commonly obtained (Figure 4). Smallhorn[30], in a study involving 41 normal children, showed this morphology in 63% and the two-phase pattern in 36%. On the other hand, the S wave morphology may change with load conditions, becoming two-phase in 63% of cases with reduction of pre-load[2].

The initial S wave acceleration phase coincides with the **x** descent (active atrial relaxation) and the deceleration phase matches the initial ascent phase until wave **v** (atrial filling). Hence, the magnitude and the velocity-time integral of the initial S wave, the acceleration and deceleration times, as well as their rates may provide insights on the left atrial function, particularly the reservoir function[19,27,31].

Effect of Volume Sample Position in the Pulmonary Vein

Although up to a depth of 2.5 cm into the pulmonary vein there is no difference in the velocities recorded, the quality of the pattern worsens progressively as the

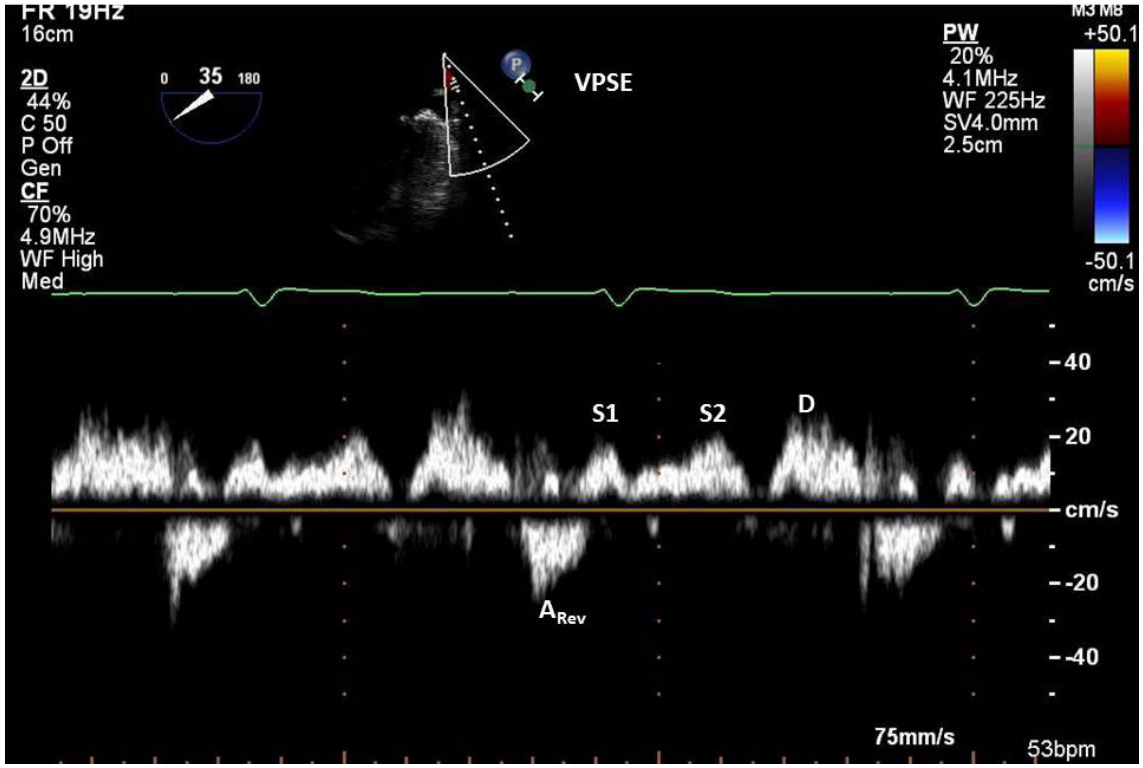

Figure 3 - *Left Upper Pulmonary Vein Flow (LUPV) obtained by transesophageal echocardiography, highlighting the systolic waves S1 and S2, diastolic wave D and post-atrial contraction wave A_{Rev}.*

volume-sample deepens into the vein. It is recommended to place it 0.5 to 1.0 cm from the orifice in order to obtain a stable pattern[13].

The choice of the pulmonary vein is also important. The S wave velocity is generally higher in the left upper pulmonary vein than in the right, both in transthoracic echocardiography and in the transesophageal echocardiography. However, using the transthoracic approach, the right upper pulmonary vein flow is more parallel to the ultrasound beam, and is therefore the most widely used[13].

The S2 wave is related to LV ejection. Therefore, it is related to the mitral annulus caudal displacement[13,20], or to the increased pressure in the pulmonary veins, probably by propagation of right ventricular systolic pressure[32,33].

The S wave is very unstable and becomes two-phase with changes in LA load conditions and myocardial dysfunction[9,34]. It should therefore be interpreted judiciously.

D wave

Once the mitral valve is opened, there is rapid LV filling and LA pressure drop, which determines the antegrade flow through the pulmonary veins. During much of the cardiac cycle phase, the pulmonary veins flow moves freely into the LV since the LA works merely as a conduit. The D wave, which is recorded at this phase, has peak velocity and deceleration time similar to the mitral flow. The same determinants influence it: left atrial pressure, left ventricular relaxation and viscoelastic myocardial properties[2].

Some authors use the D wave as an index of the LA conductive function[24].

The beginning of mitral annulus contraction after ventricular contraction coincides with the beginning of mitral flow D and E waves[33].

Reverse A Wave

The atrial contraction determines flow in two directions: antegrade flow through the mitral valve (A wave) and retrograde flow through the pulmonary veins (ARev wave). Ventricular filling with atrial contraction basically depends on the intraventricular pressure at the time of atrial contraction, as well as other factors such as LV compliance and atrial contractility. Analyzing the behavior of both flows helps better understanding of the mechanisms involved in ventricular filling. Hence, where there is decrease in LV compliance, there is greater LA pressure increase with atrial contraction, which consequently increases the ARev wave. With an increased ventricular compliance, a reverse situation occurs in the behavior of ARev and A waves[2].

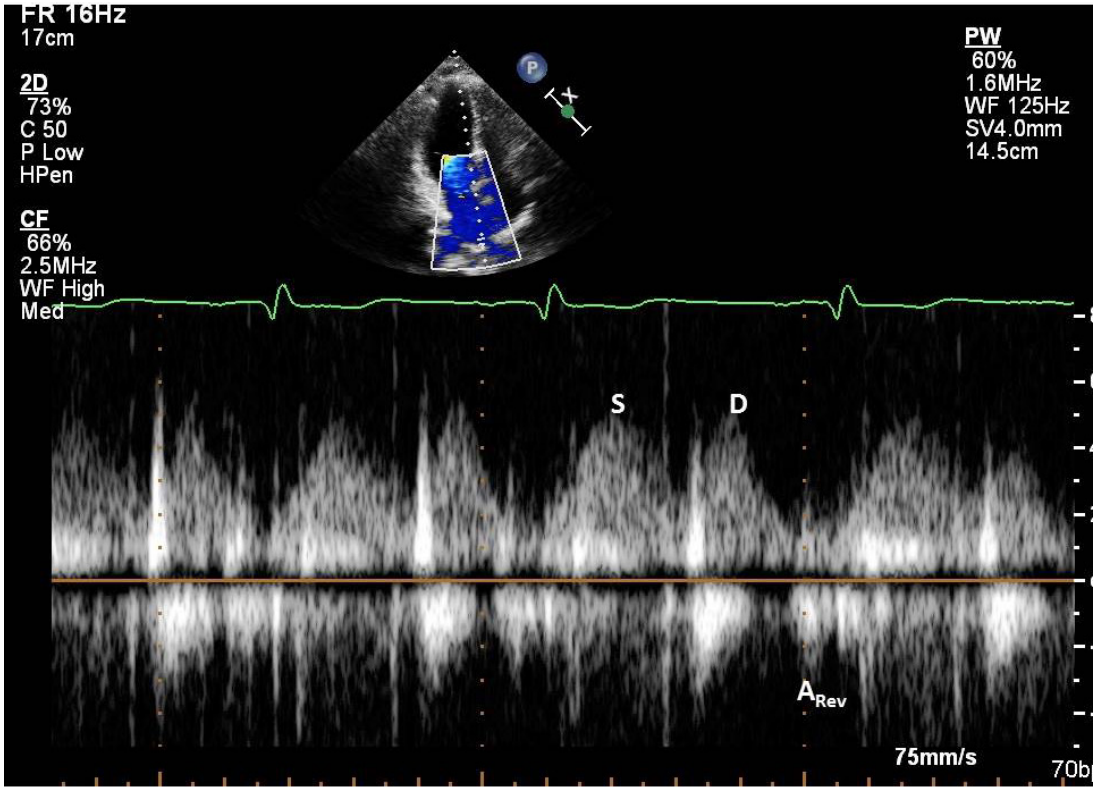

Figure 4 - *Right pulmonary vein flow obtained by transthoracic echocardiography, with record of waves S, D and A_{Rev}.*

One of the difficulties in the study of the ARev wave is recording it on conventional transthoracic Doppler echocardiography. In this approach, it is possible to record it in only 37% of patients in sinus rhythm, as opposed to the TEE, which allows identifying it in most cases[13].

Relationship of Pulmonary Veins Flow with LA Pressure

When the LA pressure is normal, the S wave (peak velocity and velocity integral over time) is usually greater than the D wave. Where there is an increased LA pressure, this relationship is reversed, with flow occurring predominantly during diastole. The systolic antegrade flow is mainly determined by atrial relaxation, LV systolic function (suction effect by annulus caudal displacement), left ventricular relaxation, mitral regurgitation and left atrial compliance and pressure[35].

2. LA Volumetric Evaluation

To analyze and measure LA volume, the main diagnostic techniques used are: echocardiography, magnetic resonance imaging, computed tomography. However, both two-dimensional and three-dimensional echocardiographies are the most simple and inexpensive techniques, and currently represent the method of choice for this evaluation, despite the possible limitations of ultrasound.

When two-dimensional echocardiography is used, it is recommended to measure the volume using the area-length method, or Simpson's modified 2 and 4-chamber view[36]. The real-time three-dimensional echocardiography (RT3DE) is a more recent non-invasive imaging technique, which enables directly measuring LA volumes throughout the cardiac cycle without the need for geometric models with an excellent time resolution[37]. It allows evaluating, with high accuracy, the LA volume and function, and has been studied, for this purpose, in many clinical situations[38-40].

Unlike the two-dimensional echocardiography, whereby the LA volume is estimated from geometric models, with the RT3DE, it is possible to digitally reconstruct the LA over a single cardiac cycle, and measuring the volume using this technique is less operator-dependent[41]. Furthermore, the volume variation curve throughout the cardiac cycle, digitally generated, allows selecting the volume at any point of the curve or the cardiac cycle phase (Figure 5). Hence, the RT3DE is the ideal method to assess LA volume and is comparable to nuclear magnetic resonance imaging[42], with a small interobserver variability[43], which is lower than in the resonance imaging[44].

Regardless of the method used to evaluate the basic LA functions, the volume measurement should be performed before the mitral valve opening (maximum volume), before the electrocardiography P wave (pre-atrial contraction volume) and after atrial contraction, immediately after the mitral valve closing (minimum volume).

With these measures, it is possible to derive some variables related to different phases of atrial function (Table 1).

3. Other Left Atrial Function Evaluation Methods

Atrial Ejection Force

It represents the force exerted by the LA to accelerate blood to the LV during atrial systole applying Newton's second law of motion, and represents an alternative for noninvasive evaluation of atrial systolic function, combining two-dimensional echocardiography data and mitral flow A wave[45]. Although it is attractive, its usefulness has been questioned due to the influence of load conditions, age, and undocumented reproducibility[27,46].

Tissue Doppler, Strain and Speckle Tracking

This technique allows characterizing the myocardial motion velocity, with the advantage of being relatively independent of load conditions. With the volume-sample in the mitral annulus, the LV systolic velocity (s' wave), diastole start velocity (e' wave) and velocity during atrial contraction (a' wave) are derived. Some studies highlight a good correlation between the a' wave and left atrial function[47-49].

Two newer techniques, using the tissue Doppler imaging and speckle tracking assess the atrial myocardial strain and

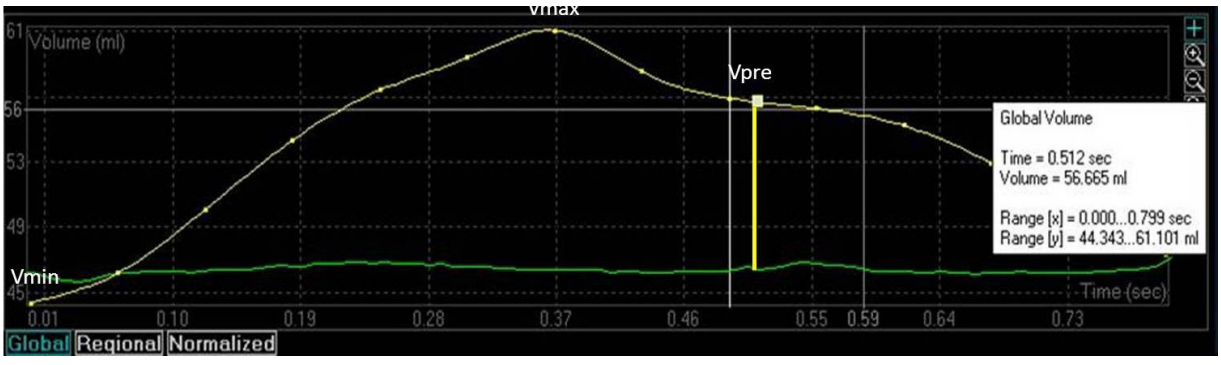

Figure 5 - *Left atrial volume variation curve during a cardiac cycle on three-dimensional echocardiography. Vmax: maximum left atrial volume Vmin: minimum left atrial volume Vpre: left atrial volume before atrial contraction.*

strain rate . Both have the advantage of being independent of heart swing and are promising methodologies in the investigation of atrial function[11,46].

Aspects of Clinical Importance

The inclusion of echocardiographic variables in risk assessment and prognosis of cardiovascular diseases has been of great value. LV ejection fraction, ventricular hypertrophy, diastolic dysfunction parameters, LA volume, among others, are frequently used variables[8]. On the other hand, parameters of left atrial function, such as prognostic factor in cardiovascular diseases, are still discussed and little used, although their importance is recognized in various clinical situations.

Pathophysiological modifications imposed by cardiovascular diseases change the left atrial function. Hence, in early LV diastolic dysfunction, the contribution of reservoir and booster pump functions for ventricular filling prevails. As ventricular filling pressure increases, when ventricular filling acquires a restrictive pattern, LA works predominantly as a conduit, with declining contribution of the other ventricular filling functions[28,46].

In Heart Failure

Making clinical distinction between asymptomatic individuals with diastolic dysfunction and those with heart failure at an early stage is a major challenge; non-invasive investigation methods available using conventional parameters do not allow a clear distinction of these two clinical conditions. Some evidence of changes in left atrial function or rigidity in patients with heart failure represent an encouragement in that kind of evaluation[38,39,50,51]. In this scenario, two-dimensional echocardiography demonstrated that the physical capacity of patients with idiopathic dilated cardiomyopathy is directly related to LA emptying fraction[52]. A direct relationship between left atrial function and maximum oxygen uptake was observed on cardiopulmonary exercise testing[53].

Table 1

LA Function	Formula
Reservoir function	
Total emptying volume	Vol_{max} - Vol_{min}
Total emptying fraction	(Vol_{max} - Vol_{min})/ Vol_{max}
Conduit function	
Passive emptying volume	Vol_{max} – $Vol_{pre\ A}$
Passive emptying fraction	(Vol_{max} – $Vol_{pre\ A}$)/ Vol_{max}
Conduit volume	VS_{VE} – (Vol_{max} - Vol_{min})
Booster pump function	
Active emptying volume	$Vol_{pre\ A}$ - Vol_{min}
Active emptying fraction	($Vol_{pre\ A}$ - Vol_{min})/ $Vol_{pre\ A}$

Volmax = maximum LA volume immediately before the mitral valve opening; Volpre A = LA volume before eletrocardiography P wave; Volmin = LA volume upon mitral valve closure; VSVE = LV systolic volume

In Systemic Hypertension

In patients with systemic hypertension, in addition to the LV diastolic dysfunction, abnormalities in LA reservoir and conduit functions are described[54,55] and may precede ventricular hypertrophy and LA dilation[56].

In Atrial Fibrillation

Atrial fibrillation (AF) is a condition associated with functional and structural LA abnormalities and is the subject matter of many studies, both from the perspective of management and prevention. The evaluation of LA function may provide additional insights of great clinical importance.

During AF, apart from the LA booster pump function, reservoir and conduit functions are also impaired[46]. After treatment with radiofrequency ablation, the reservoir function usually worsens after the procedure, but with a delayed recovery within eight-month follow-up[27].

The relationship between structural LA remodeling and AF is well established[27,58,59]. Evidence shows that decreased reservoir function is an important predictor for the development of atrial arrhythmias[60].

In Cardiomyopathies

The existence of a myopathic process involving both ventricles and atria is generally accepted. In dilated forms of the disease, LA contractile dysfunction cannot be attributed only to the dilatation of the chamber, or to wall tension[61]. A postmortem anatomical pathological study showed high prevalence of fibrosis in the LA of patients with nonischemic dilated cardiomyopathy[62]. The LA contractile function response is also observed after inotropic stimulation[63].

A more significant impairment of left atrial function has been recently observed in patients with Chagas' cardiomyopathy compared to patients with idiopathic dilated cardiomyopathy, a fact that was attributed to the higher LV filling pressure and greater LA myopathic involvement[64].

In the hypertrophic form of the disease, there is an increased atrial rigidity attributed to an increase in rigidity and/or increased atrial myocardial thickness, responsible for the decrease in reservoir function[31,40,65,66]. In these patients, it was observed that the left atrial function is related to the presence and intensity of heart failure symptoms[66].

Conclusion

The analysis of left atrial function integrated with the left ventricular function may add key insights into the interpretation and understanding of the pathophysiological mechanisms and symptoms of cardiovascular diseases involving, either directly or indirectly, the left chambers of the heart.

Modern equipments allows this investigation, not only because it is easy to allow images and patterns, but also due to the new technologies incorporated into the system, allowing the analysis of refined details of atrial dynamics, adding valuable and accurate information.

Therefore, it is essential to incorporate it in echocardiographic evaluation, as a complement in cardiological investigations, not routinely, but in which where the contribution of LA in cardiac output may be impaired as part of the prevailing hemodynamic condition, or for the purposes of pathophysiological follow-up of cardiovascular diseases.

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