Left atrium function assessment by echocardiography – physiological and clinical implications

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Abstract

Left atrium enlargement is a pathophysiological response to volume and pressure overload associated with a wide range of cardiovascular disorders leading to left ventricle systolic and diastolic dysfunction. Physiological factors contribute to significant differences in left atrium size in normal individuals. Moreover, left atrium enlargement was shown to have a significant prognostic value for cardiovascular events such as heart failure, atrial fibrillation or stroke, and increased cardiovascular and all-cause mortality rates. Current imaging techniques such as two- and three dimensional echocardiography, cardiac magnetic resonance imaging and multi-detector computed tomography allow a detailed assessment of the left atrium. The current paper aims to offer an overview of two-dimensional echocardiography parameters which provide data concerning left atrium dimensions and phasic functions and may lead to a better understanding of left atrium physiology and pathology.

Keywords: left atrium, two-dimensional echocardiography, dimensions, diastolic function

Left atrium (LA) structure and function assessment by echocardiography has gained interest lately and several quite recent studies were focused particularly on the LA and the changes it is submitted to in a wide range of pathologies. LA impairment has already been shown to emerge with advancing age [1,2], heart failure [3,4] and other cardiovascular disorders such as hypertension [5], atrial fibrillation [6], or hypertrophic cardiomyopathy [7]. Moreover, LA enlargement was proved to be associated with an increased risk of developing chronic atrial fibrillation [8] and stroke [9], as well as with higher cardiovascular and all cause mortality rates, particularly in men and in the presence of associated cardiovascular risk factors (high body mass index, smoking, advanced age or diabetes mellitus) [10,11].

Left atrium anatomy and physiology

The LA has a complex morphology, which may render echocardiographic assessment difficult, due to the oblique position of the interatrial septum and the long and narrow LA appendage [12]; current echocardiographic techniques, which allow surface and volume assessment, assume spherical, cube or ellipsoid models for the LA that are not entirely accurate and may lead to error [13]. Moreover, the four pulmonary veins enter the LA via the posterior wall and are frequently inaccessible for venous flow evaluation by Doppler [12].

LA performance is based on four basic mechanical functions: the *reservoir* function; the *conduit* function; the *active contractile pump* function; and the *suction force* [14]. The latter is not described by most authors, as it is considered the early stage of the reservoir phase.

As a reservoir, the LA receives blood from the pulmonary veins during ventricular systole; the mitral annulus and valve descend as a consequence of longitudinal shortening during ventricular contraction, leading to an increase in LA volume and a decrease in pressure due

to active relaxation of the atrium, which allow atrial filling; incoming blood flow from the pulmonary veins triggers a further increase in both volume and pressure; in early diastole, the atrium serves as a conduit allowing the blood to flow passively into the left ventricle (LV), thus leading to increasing ventricular pressure until it equals intraatrial pressure (the diastazis phase); therefore, the conduit phase is highly dependent on left ventricle (LV) relaxation [15]; in late diastole, the atrium behaves as a pump, as pressure rises due to active atrial contraction, and pushes the blood through the mitral valve, contributing with 15% to 30% to LV filling [16,17]. Consequently, both intraatrial volume and pressure decrease. The LA booster pump function depends on preload, afterload and contractility [18]. The suction force describes atrial filling in the first phase of LV systole and, like the reservoir function, is dependent on atrium relaxation and atrial chamber stiffness [19], but also on the LV systolic function [20]. Invasive assessment of left chambers pressures by left cardiac catheterisation has proved that LA function is best described by an exponential pressure-volume relationship during the reservoir and conduit phases and a counter clockwise pressure-volume loop during atrial contraction and suction [21].

Pathophysiology

The LA is highly susceptible to various acute or chronic stress factors, as alterations in both preload and afterload lead to atrial remodeling [6,21], previously shown to be correlated with global cardiac remodeling [22].

The elevated preload due to mitral regurgitation is known to be associated with LA enlargement [23], as is increased afterload, which is mostly determined by the LV's elastic properties and downstream pressure and increases with aggravated diastolic dysfunction and elevated filling pressures [24]. LA physiology and physiopathology is highly dependent on LV function, as the atrium is exposed to intraventricular pressure, particularly during diastole. As a consequence, any change in intraventricular pressure or volume is reflected on LA function.

Diastolic heart failure in particular was shown to have a strong impact on LA function [25-27]. When LV diastolic dysfunction occurs, LA pressure increases in order to overwhelm intraventricular pressure and provide adequate LV filling [28]. The rise in pressure leads to increased LA wall tension and is associated with atrial enlargement, thus implying that the LA, as the LV, is submitted to the Frank-Starling law [29].

In their study on patients with heart failure and preserved ejection fraction, Pritchett et al have shown that left atrium volume indexed to body surface (LAVI) increased considerably with aggravated diastolic dysfunction [27]. Kurt et al obtained similar results, also showing that in patients with grade I diastolic dysfunction the pump function became more expressed, to compensate for the decreased reservoir and conduit functions, impaired by the rise in diastolic LV pressures [25]. However, with even higher degrees of diastolic dysfunction, atrial contractility decreases and therefore the contribution of the LA pump to LV filling is lower [30]. By contrast, in patients with atrial fibrillation, in which the pump function is completely absent, the LA adapts by reservoir and conduit function enhancement [31].

Moreover, LA enlargement and increased intratrial pressure trigger the secretion and storage of atrial natriuretic peptides [32,33] which leads to natriuresis and vasodilatation, as well as the inhibition of the sympathetic and renin-angiotensin-aldosterone systems [24], thus contributing to the restoration of hemodynamic balance at the cost of LA remodeling by extensive interstitial fibrosis and myocyte hypertrophy [34]. Moreover, the high rate of cell depolarisation in all types of tachycardia and particularly in atrial fibrillation triggers atrial enlargement, leading to the development of tachycardiomyopathies [6].

Left atrium size assessment

Left atrium diameter

The complex LA physiology, as well as the pathological implications, has raised the need for a more extensive echocardiographic examination. The first parameter to be used for LA assessment was the LA antero-posterior (AP) diameter measured in the parasternal long axis view at LV end-systole by using either B-mode (fig 1) or M-mode; M-mode measurements are performed from the leading edge of the anterior LA wall to the leading edge of the posterior wall (fig 2). Current guidelines endorsed by the American Society of Echocardiography recommend the use this parameter to describe LA enlargement as mild (41–46 mm in men or 39–42 mm in women), moderate (47–51 mm in men or 43–46 mm in women) or severe (≥52 mm in men or ≥47 mm in women) [35]. AP diameter measurement is easily obtained and does not require high-quality equipment or exceptional skills, but its accuracy is reduced; LA enlargement is predominant in the superior-inferior or medial-lateral axis, due to the fact that the LA is positioned between the aortic root and the tracheal bifurcation [36]. Despite this major impediment, data from the Framingham Heart Study suggested that an incremental enlargement by 5 mm of the LA AP diameter was associated with high risk (39%) of develop-
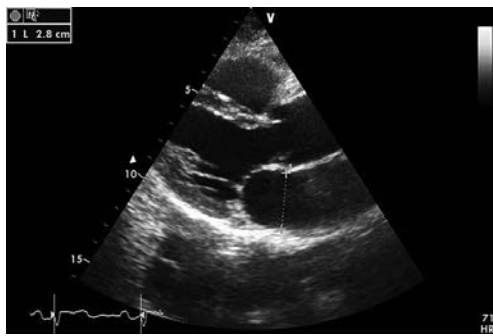
Fig 1. Measurement of left atrium antero-posterior diameter by B-mode echocardiography from the parastenal long axis view.
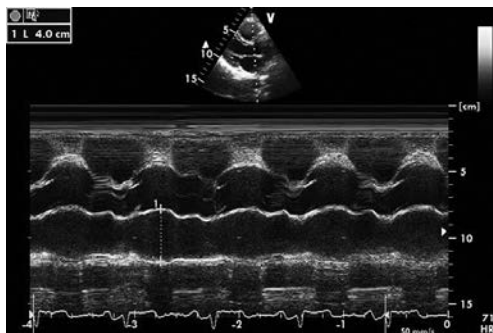

Fig 2. Measurement of left atrium antero-posterior diameter by M-mode echocardiography from the parastenal long axis view. Chamber dimensions are slightly overestimated, as cursor alignment is suboptimal due to patient's echocardiographic view.

ing atrial fibrillation during follow-up [37]. In addition to that, the Cardiovascular Health Study reported that the risk for developing atrial fibrillation was four times bigger in patients with a LA AP diameter >50 mm [38].

Left atrium area and volume

Nowadays, area and volume measurements are preferred for assessing LA dimensions, as they were shown to correlate better with an increased risk for cardiovascular events [39,40]. Several methods may be used to derive LA volumes such as the cube method, the area-length method, the ellipsoid method or Simpson's modified rule, with the latter being preferred by most physicians, as it relies on fewer geometrical assumptions when compared to the previous methods, particularly the ellipsoid method [41,42].

Several studies have shown that LA dimensions may be influenced by non-pathological factors such as age, gender, or body mass index, although the results are controversial. In a study by Prittchett et al, LA volume (LAV) increased with aging was only associated with the presence of heart disease and was not statistically sig-

nificant in healthy subjects [40]. However, in Pritchett's research, gender differences were highlighted after correction for body size using the body mass index and the body surface area.

Consequently, in recent original research, LA volumes are indexed to body surface for more accurate results, although currently data concerning reference values are still scarce.

Pritchett et al mention a median normal value of LAVI to body surface of 22 ml/m^2 in men and 21 ml/m^2 in women [41], data which is consistent with the findings of Tsang et al [43]. Pending the criteria of the American Society of Echocardiography and Standards Committee and the Chamber Quantification writing group, LAVI values may be used to describe LA enlargement as mild (29–33 mL/m^2), moderate (34–39 mL/m^2) or severe (>40 mL/m^2) [35,41]. Abhayaratna et al mention a LAVI value of ≥34 mL/m^2 to be an independent predictor of death, heart failure, atrial fibrillation and ischemic stroke [44] which is consistent with the findings of Messika-Zeitoun et al who also demonstrated that cardiovascular events were more likely to occur in patients who underwent cardiovascular surgery for mitral regurgitation in the presence of LA enlargement [22]. Rossi et al obtained similar results in their study on patients with dilated cardiomyopathy, proving that increased LAVI was correlated with LV remodeling, LV diastolic dysfunction and more severe mitral regurgitation, and was highly predictive of worse outcomes [45]. Moreover, LA volumes were shown to regress in patients with dilated cardiomyopathy and severely impaired LV systolic function who responded to cardiac resynchronization therapy [46].

However, a complete assessment of the LA size and function may not rely on maximum LAVI alone, as LA dimensions vary widely during the cardiac cycle. An electrocardiogram guided echocardiography allows an accurate quantification of LA functions by measuring LA volumes at different times during the cardiac cycle. Measurements are usually taken as follows:

1. at end-systole, just before the opening of the mitral valve (at the end of the T-wave on the ECG) – the LA maximum volume (LAV$_{max}$) (fig 3);

2. at end-diastole, just before mitral valve closure (at the beginning of the QRS complex on the ECG) – minimum LA volume (LAV$_{min}$) (fig 4);

3. at mid-diastole, just before atrial contraction (at the beginning of the P wave on the ECG) – preA volume (LAV$_{preA}$) (fig 5).

Indexed to body surface, the normal LAV$_{max}$ is 22+6 mL/m^2, LAV$_{min}$ is 11+4 mL/m^2, and LAV$_{preA}$ is 15+5 mL/m^2 [24,47,48].
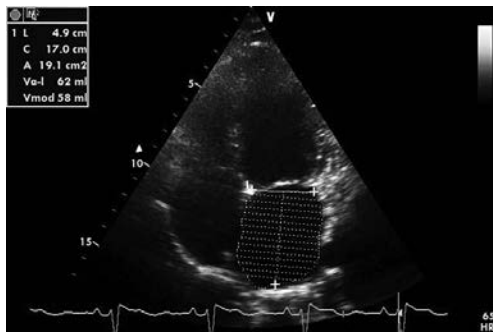
Fig 3. Maximum left atrium volume measured at end-systole using Simpson's modified method from the apical 4-chamber view.
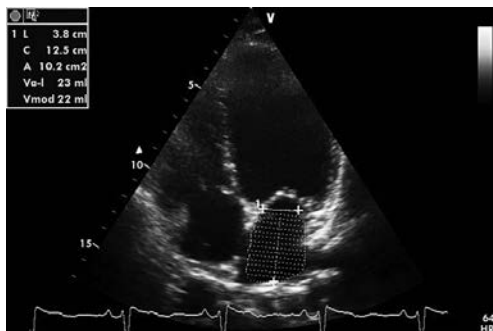

Fig 4. Minimum left atrium volume measured at end-diastole using Simpson's modified method from the apical 4-chamber view.
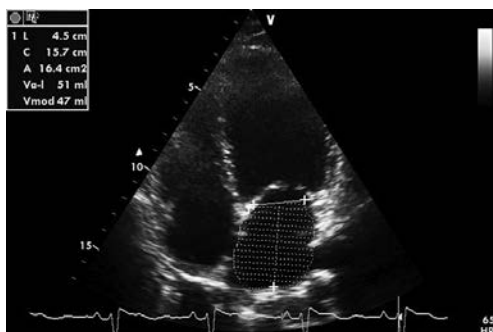

Fig 5. PreA left atrium volume measured in mid-diastole using Simpson's modified method from the apical 4-chamber view.

Left atrium function assessment

Left atrium function assessment using the volumes method

Based on the previously discussed volumetric measurements, several indices corresponding to the three basic functions of the LA can be derived:
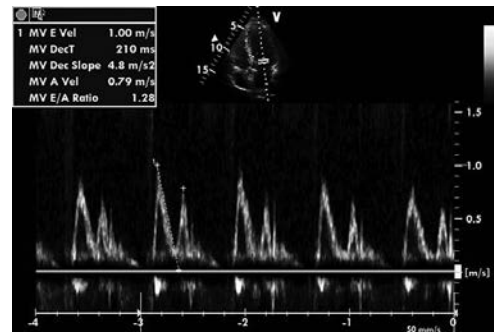
1. LA reservoir function:

Fig 6. Transmitral flow assessment by pulsed wave Doppler.

LA total emptying volume= $LAV_{max} - LAV_{min}$

LA total emptying fraction = $(LAV_{max} - LAV_{min})/LAV_{max}$.

2. LA conduit function:

LA passive emptying volume = $LAV_{max} - LAV_{preA}$

LA passive emptying fraction= $(LAV_{max} - LAV_{preA})/LAV_{max}$

Conduit Volume= stroke volume – total emptying volume.

3. LA booster pump function:

LA active emptying volume = $LAV_{preA} - LAV_{min}$

LA active emptying fraction = $(LAV_{preA} - LAV_{min})/LAV_{preA}$.

In a study of normal LA function, the mean total LA emptying volume was 13.5 ± 4.3 ml/m^2 (representing $37\pm13\%$ of LV stroke volume), the fractional emptying of the LA was $65\pm9\%$, and the conduit volume was 23 ± 8 ml/m^2 [44,49].

Left atrium function assessment by pulsed wave Doppler

Functional assessment of the LA also includes the evaluation of the pulmonary vein and transmitral flow, also used to describe LV diastolic function which was shown to greatly influence LA size and function [24].

The pulmonary vein flow provides information about LA phasic functions; the positive S wave describes blood inflow from the pulmonary veins to the LA during ventricular systole and is, therefore, exponential for the reservoir function which can be characterized using the S wave maximum velocity and velocity time integral [50]. Similarly, the second positive D wave corresponding to venous inflow during the early stage of diastole is related to the conduit function and is described using the peak D-wave velocity and the velocity time integral; the negative A wave describes blood reflow from the LA to the pulmonary veins generated by LA contraction in late diastole, and is exponential for the booster pump function [51]; the E wave of the transmitral flow is also exponential for the conduit function, while the positive A wave provides information about the booster pump function (fig 6).

Left atrium function assessment by tissue Doppler

Tissue Doppler may be particularly useful in terms of describing LV diastolic function and for providing more information about the booster pump function by assessing myocardial motion at the level of the mitral annulus during LA contraction (the A wave). Normal median values have been established at around 10±2 cm/s [52], but their importance is limited due to the fact that myocardial velocities are different across the LA, which is more rigid at mitral annulus level and quite mobile in the superior region.

Left atrium function assessment by strain rate imaging

Newer echocardiographic techniques such as strain rate imaging by either tissue Doppler or speckle tracking overcome the limitations imposed by regional differences in myocardial motion. Strain analysis, including longitudinal and radial strain, as well as deformation speed analysis by strain rate imaging, improved LA function assessment, particularly if speckle tracking is used. This imaging technique allows data gathering from 6 to 12 different segments using the 4, 3 and 2-apical chambers view and is independent of beam alignment.

LA analysis by strain and strain rate imaging is based on both longitudinal and radial strain. However, current techniques do not have a sufficient resolution to measure the radial strain of the thin-walled LA [53]; therefore, LA deformation assessment is only based on longitudinal strain, using the apical 4,3 and 2 chamber-view.

Longitudinal strain is positive during the reservoir period when LA myocardial fibers relax and stretch to adapt to the incoming blood flow, negative during the pump and most of the conduit phase, when the LA is emptying and flat during diastasis, which corresponds to the late phase of the conduit phase [54]. Therefore, measurements taken at end-systole, early and late end-diastole may provide information on the reservoir, conduit and pump functions, but normal values differ, pending on the employed echocardiographic method. In one study, Schneider et al [55] used tissue Doppler to measure maximum longitudinal systolic strain and obtained a normal value of 88±23%, while Cameli et al obtained considerably lower values using speckle tracking: 40±8% in the 4-chamber view, 44±6% in the 2-chamber view and a mean value of 42±6% [56].

Irrespective of the used method, both studies have demonstrated that strain and strain rate imaging are valuable for LA function assessment. Cameli et al compared the E/E' ratio and global peak atrial longitudinal strain (PALS) derived by speckle tracking against pulmonary capillary wedge pressure (PCWP) measured invasively by right catheterization; their study showed that global PALS had a considerably high diagnostic accuracy, providing 100% specificity and 93% specificity for elevated LV filling pressures, while the E/E' ratio correlated poorly with invasively measured PCWP [56].

Schneider et al focused on patients with atrial fibrillation who underwent catheter ablation and managed to prove that systolic, as well as early and late diastolic strain, were considerably lower in patients with persistent atrial fibrillation when compared to both patients with paroxysmal atrial fibrillation and normal subjects. In addition to that, they showed that lower strain and strain rate were associated with a higher rate of atrial fibrillation reoccurrence after catheter ablation. This latter finding may have essential prognostic and therapeutic implications concerning the postprocedure cardioembolic risk and oral anticoagulation therapy [55]. In addition to that, Tops et al showed that increased LA strain was associated with reverse LA remodeling, defined as a decrease in LAV_{max} >15%, in patients who underwent catheter ablation for atrial fibrillation [57]. Moreover, strain and rate imaging by speckle tracking may help identify regional abnormalities in patients with mitral valve regurgitation, particularly in the case of eccentric regurgitation jets [23].

Comparison to other imaging techniques

Despite its obvious advantages, two-dimensional echocardiography has some limitations in assessing LA dimensions, mainly due to difficulty in endocardial border tracing and the fact that it relies on geometrical assumptions which ignore LV and LA geometry differences between individuals. The first impediment may be diminished by using novel technology, namely acoustic quantification, which improves myocardial border tracings, thus reducing errors in LA volume assessment [15].

Recent studies have compared the accuracy of two-dimensional echocardiography in LA and LV volumes measurements against other imaging techniques such as three-dimensional echocardiography, magnetic resonance imaging (MRI) and multi-detector computed tomography (MDCT). LA volumes were shown to be systematically underestimated by two-dimensional echocardiography when compared to MRI or three-dimensional MDCT [58-60]. In fact, MRI is nowadays considered to be the gold standard for LA dimension and function assessment [61-63], as it provides superior high temporal and spatial resolution, as well as high reproducibility. Three-dimensional echocardiography may also be used to assess LA volumes and function, as measurements compare well against MRI [64] and MDCT [65] and were proved to be useful for predicting cardiovascular events [66]. Although LA volumes seem to be slightly underestimated when compared to MRI measurements, LA ejection fractions are similar to those calculated using MRI [67,68].

Conclusions

LA dimensions and function assessment is essential for clinical evaluation and prognostic purposes. Two-dimensional echocardiography may provide extensive data if a standard complex investigation protocol is routinely used and individual variables such as body surface area are taken into account. LA volumes measurement may facilitate atrial remodeling assessment in various pathological conditions, as well as reverse remodeling after medical or more invasive therapy, such as cardiac resynchronization therapy or ablation for atrial fibrillation or flutter. Although previous studies have demonstrated the clinical and prognostic value of LA assessment, further more extensive research could provide a better understanding of pathophysiological mechanisms behind LA enlargement and help predict clinical outcomes in many cardiovascular disorders.

Conflict of interest: none

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