Original Article

Determinants Of Left Atrial Size And Volume And Cardiovascular Diseases

Mohammad Gouda Mohammad, Ashraf AlSeed Dwedar, Ahmed Reda Abdelrahman Marwad, Islam Ghanem Ahmed

Cardiology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt.
Corresponding author: Ahmed Reda Abdelrahman Marwad
Email : ahmedmarwad007@gmail.com
DOI: 10.47750/pnr.2023.14.02.162

Abstract

Background: Left atrial (LA) enlargement has been considered as a parameter of diastolic burden and a predictor of common cardiovascular outcomes such as atrial fibrillation, stroke, congestive heart failure, and cardiovascular death. It has been shown that advancing age alone does not independently contribute to left atrial enlargement, and the impact of gender on left atrial volume can largely be accounted for as the differences in body surface area between men and women. Therefore, enlargement of the left atrium reflects remodeling associated with pathophysiologic processes

Keywords: of left atrial size and volume

INTRODUCTION

Left atrial (LA) enlargement has been considered as a parameter of diastolic burden and a predictor of common cardiovascular outcomes such as atrial fibrillation, stroke, congestive heart failure, and cardiovascular death. It has been shown that advancing age alone does not independently contribute to left atrial enlargement, and the impact of gender on left atrial volume can largely be accounted for as the differences in body surface area between men and women. Therefore, enlargement of the left atrium reflects remodeling associated with pathophysiologic processes **(1).**

There is strong evidence that left atrial (LA) enlargement, as determined by echocardiography, is a robust predictor of cardiovascular outcomes. Recently, it has been shown that left atrial volume provides a more accurate measure of left atrial size than conventional M-mode left atrial dimension **(1)**.

To optimize the usage of left atrial volume for risk stratification, an understanding of the physiologic determinants of left atrial size and the methods for accurate quantitation is important. Recent guidelines from the American Society of Echocardiography provide clarification as to which of the multiple methods for left atrial volume quantitation that should be used in clinical practice **(2)**.

Such a standardized approach for left atrial volume assessment will be crucial for reproducible measures and communication of left atrial size between laboratories. Herein, we present an overview of left atrial size and function, and describe the physiologic determinants and clinical implications of left atrial enlargement.

- ***Anatomy***

The left atrium is located in the mediastinum, oriented leftward and posterior to the right atrium (RA). Left atrium structure is characterized by a pulmonary venous component, a lateral fingerlike appendage, an inferior vestibular component, which surrounds the mitral valve orifice, and a prominent body that shares the septum with the right atrium. The pulmonary venous component with venous orifices at each corner is located posteriorly and superiorly, and directly confluent with the body. The walls of the left atrium can be described as superior (roof), posterior (infero-posterior), left lateral, septal, and anterior. The majority of the atrium is relatively smooth, while the appendage is rough with pectinate muscles. The walls are composed of one or more overlapping layers of differently aligned myocardial fibers, with marked regional variations in thickness. Circular fibers are more or less parallel to the atrioventricular valve plane, while longitudinal fibers run nearly perpendicularly. Oblique fibers are those inclined between the two major axes **(3)**.

- ***Structure***

The left atrium is located superior to the left ventricle, posterolateral to the right atrium, posterior to the aortic root, and anterior to the esophagus. The left atrium receives the pulmonary veins, has an appendage, and directs blood into the left ventricle through the mitral valve. With conventional two-dimensional (2D) transthoracic echocardiography, the left atrium should be visualized from the parasternal, apical, and subcostal views. Although, inherent to the limitations of 2D imaging, no single view completely characterizes the shape and size of the left atrium. So, it is recommended that multiple views from standard imaging planes be obtained to more completely visualize the left atrium with careful attention to focus on the structure of interest, optimize endocardial border definition, and avoid foreshortening. Quantification of left atrial size by transthoracic echocardiography has advanced from M-mode and 2D linear measurements to 2D and three-dimensional (3D) volumes. Compared with linear measures, volumes more accurately quantify left atrial size and perform better as prognostic markers **(3)**.

Left atrial volumes obtained with 3D imaging are similar to those obtained from cardiac computed tomography (CT) or magnetic resonance imaging (MRI). Although, the lack of widespread clinical availability, standardization, and normative data from 3D echocardiography has led the American Society of Echocardiography to currently recommend 2D left atrial volumetric assessment by transthoracic echocardiography **(4)**.

Characterization of left atrial size by transesophageal echocardiography is limited to semiquantitative assessment, because the entire left atrium usually does not fit within the image. Even though, transesophageal echocardiography is superior to transthoracic echocardiography for imaging of the left atrial appendage, interatrial septum, and pulmonary veins. Quantification of 2D left atrial volume is performed from the transthoracic apical four- and two-chamber views. In each of these views, the left atrial endocardial borders are traced at end ventricular systole just before mitral valve opening when the left atrium is at its maximal size. A modified Simpson's (method of disks) biplane volume can then be calculated **(4)**.

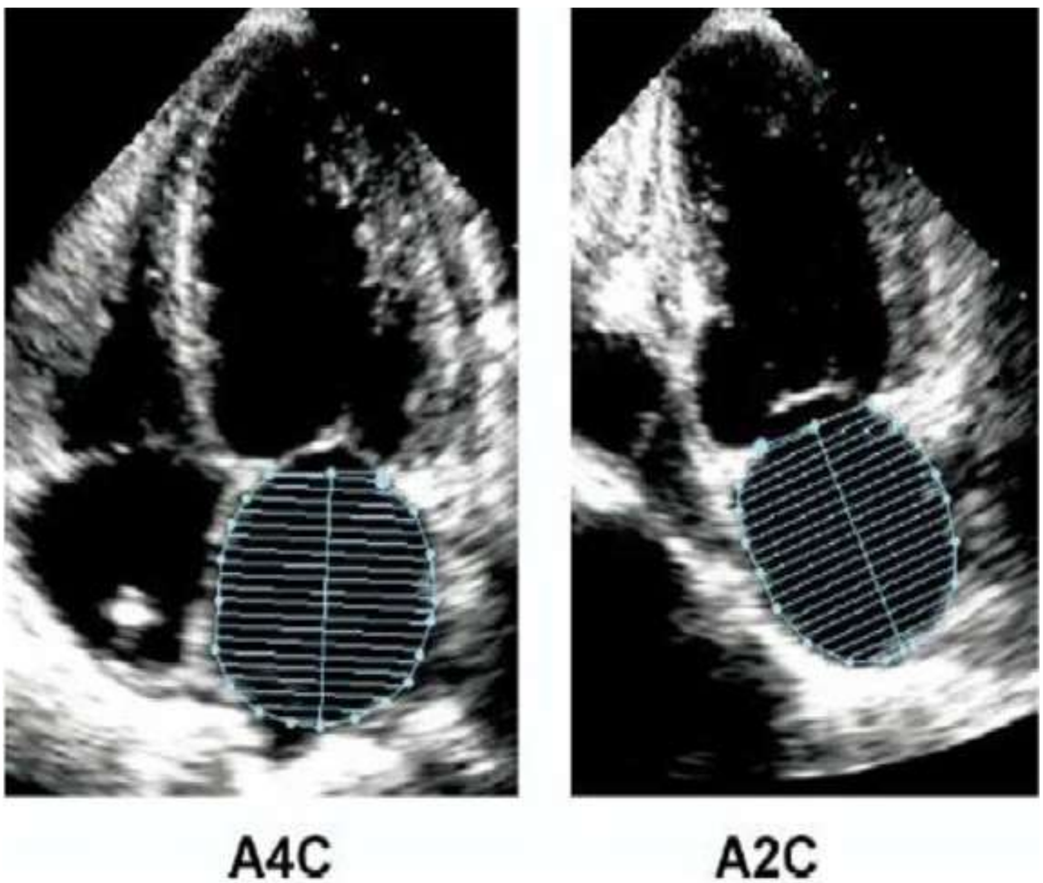

Figure 1: Biplane method of disks **(4)**.

Alternatively, the area (cm2) and lengths (cm) of the left atrium can be measured in each view with volume calculated as (0.85 × Area4c × Area2c)/length, where the shorter length of the major axis from the four- or two-chamber view is used **(5)**.

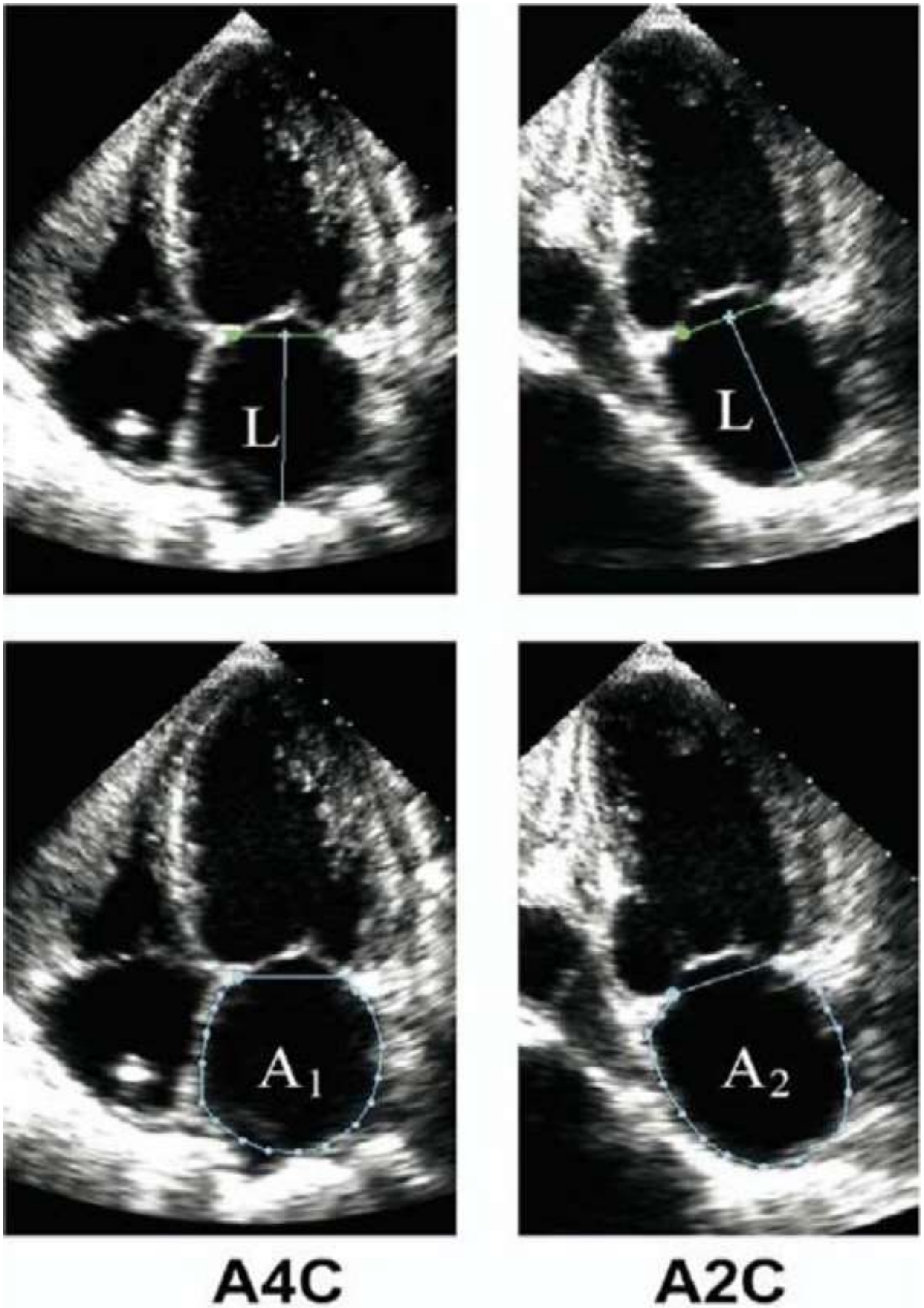

Figure 2: Area-length technique **(6)**.

With either the biplane Simpson's or area-length method, it is recommended that left atrial volume be indexed to body surface area to account for gender differences, with the upper limit of normal for both men and women being less than 34 mL/m2 **(4)**.

If volumetric assessment from the apical views cannot be obtained, then the 2D linear anterior-posterior length from the parasternal long-axis view can be used to size the left atrium. This measure is the distance between the posterior edge of the aortic root and the posterior wall of the left atrium, timed at the end of ventricular systole in the cardiac cycle **(4)**.

Left atrial size is a barometer for left-sided filling pressures, with enlargement typically correlating with chronically elevated left ventricular end-diastolic pressure, and/or pulmonary capillary wedge pressure. **(5)**.

Therefore, left atrial enlargement (>34 mL/m2) is a central component of the algorithm for the echocardiographic assessment of left ventricular filling pressures and diastolic dysfunction **(7)**.

Even though, left atrial enlargement also happens in the setting of mitral valve disease, atrial fibrillation, and intracardiac shunts,

such that the presence of these conditions must be considered when assessing left ventricular filling pressures and diastolic function. Left atrial enlargement has been consistently demonstrated to be a powerful predictor of adverse cardiovascular outcomes, including incident atrial fibrillation, stroke, heart failure, and death **(5)**.
Importantly, the prognostic information carried in left atrial size is independent of clinical factors, left ventricular size, and ejection fraction.

TABLE (1): Quantification of Left Atrial Size by 2D Transthoracic Echocardiography **(4)**.

		Normal	**Mild**	**Moderate**	**Severe**
Volume index (mL/m2)	Men	16 to <34	34 to <41	41 to ≤48	>48
	Women	16 to <34	34 to <41	41 to ≤48	>48
A-P diameter (cm)	Men	3.0 to <4.0	4.0 to <4.6	4.6 to <5.2	≥5.2
	Women	2.7–3.8	3.8 to <4.2	4.2 to <4.7	≥4.7

- ***Function***

While not commonly clinically reported on transthoracic echocardiography, quantification of left atrial function from conventional 2D and Doppler imaging as well as speckle tracking and 3D echocardiography is garnering increased attention. Atrial function is typically described in three phases: reservoir, conduit, and pump **(8)**.

The atrial reservoir phase corresponds to ventricular systole (atrial relaxation) when the mitral valve is closed and the left atrium expands due to venous return and descent of the mitral annulus towards the left ventricular apex.

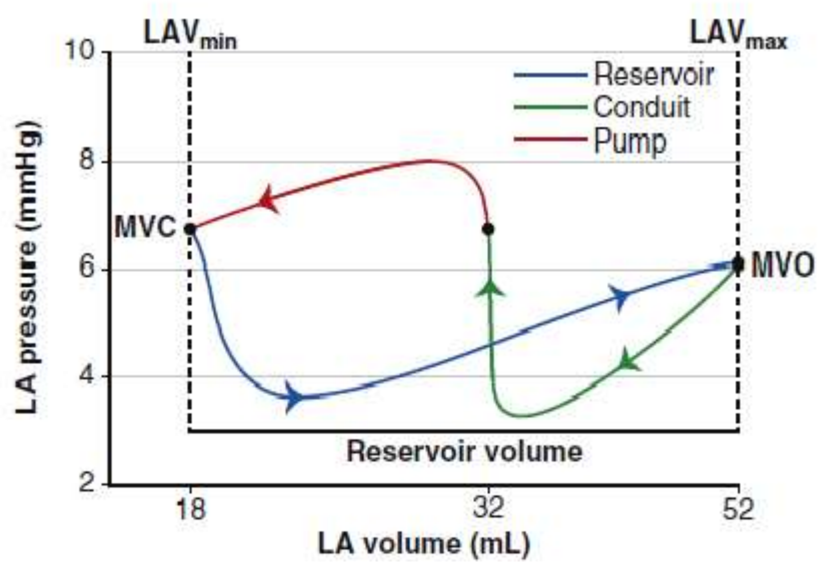

Figure 3: Left atrial phasic function according to the pressure-volume relationship. The reservoir phase corresponds to ventricular systole when the mitral valve is closed, allowing the atrium to fill with blood. The conduit phase begins with mitral valve opening and corresponds to early ventricular diastole. The pump phase follows atrial contraction in late diastole. *LA*, left atrium; *LAV*, left atrium volume; *MVC*, mitral valve closure; *MVO*, mitral valve opening. **(9)**.

The conduit (passive emptying) phase starts with ventricular diastole when the mitral valve opens and blood flows through the atrium into the ventricle. The pump (active emptying) phase coincides with atrial contraction and is completed with the onset of ventricular systole, when the reservoir phase starts again. Overall left atrial function (emptying fraction) can be quantified from the largest and smallest left atrial volumes **(9)**.
Using 2D or 3D volumetric measurements, overall and phasic atrial function can be calculated with the following formulas:
Overall, by emptying fraction: (LA max vol − LA min vol)/LA max vol Conduit by passive emptying fraction: (LA max vol − LA pre-A vol)/ LA max vol. Pump by active emptying fraction: (LA pre-A vol − LA min vol)/LA pre-A vol. Reservoir by

expansion index: (LA max vol − LA min vol)/LA min vol. Blood flow Doppler can also be used to assess left atrial function. Early diastolic blood flow (conduit phase) from the left atrium into the left ventricle can be measured with pulse wave spectral Doppler at the tips of the mitral valve leaflets as the E wave. From this same Doppler tracing, atrial pump function can be quantified from the A wave peak velocity and velocity time integral, which coincides with the electrocardiographic P wave and atrial contraction **(10)**.

Pulse wave spectral Doppler of the pulmonary veins can also reveal an A wave, which can be used to characterize atrial contractile function.

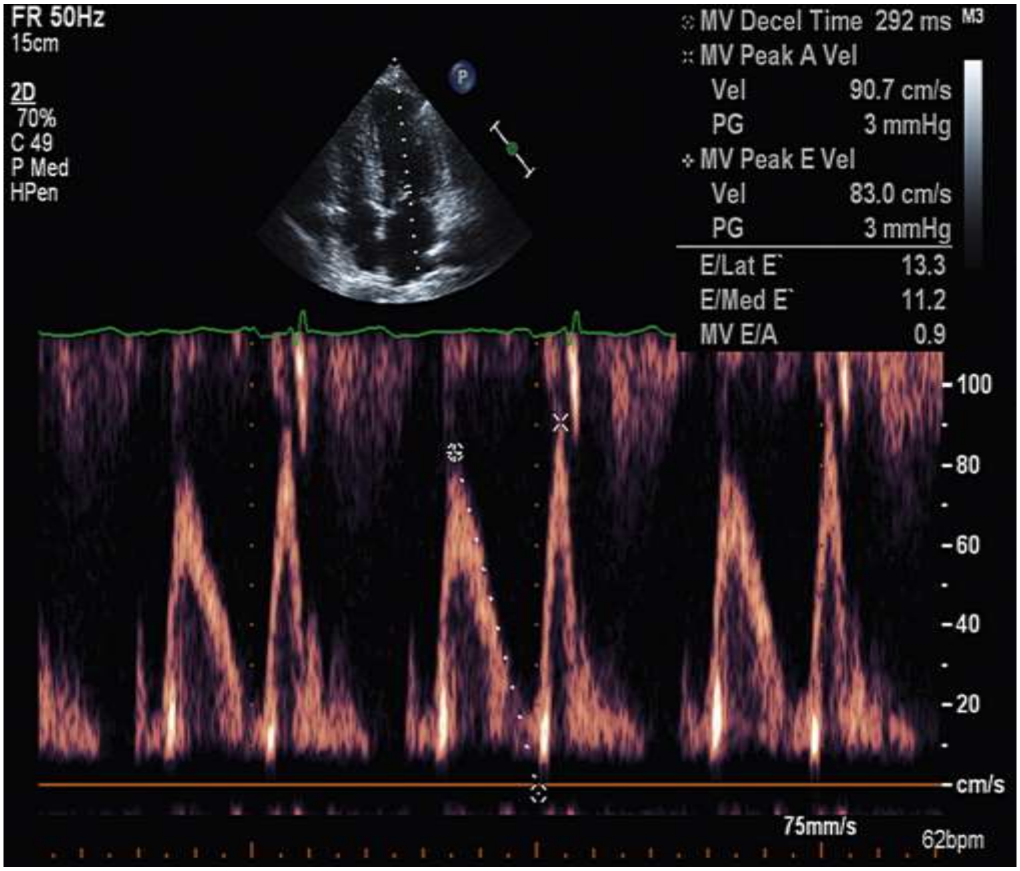

Figure 4: Trans mitral spectral Doppler demonstrating left ventricular inflow. The E and A waves are measures of atrial conduit and pump function, respectively **(10)**.

In contrast to blood flow Doppler, which is developed by pressure gradients between two chambers, pulse wave tissue Doppler of the mitral annulus provides information regarding the mechanical properties of the myocardium. The late diastolic A prime velocity of the mitral annular tissue Doppler signal is also a measure of left atrial contraction **(11)**.

In atrial fibrillation, the spectral Doppler and tissue Doppler A waves are absent. Assessing left atrial function has informed understanding of thromboembolic risk in atrial fibrillation. Using Doppler imaging, electromechanical dissociation of the left atrium has been demonstrated to occur following electrical cardioversion of atrial fibrillation to sinus rhythm **(10)**.

Similarly, patients with amyloidosis may have markedly reduced atrial contractile function although electrocardiographic sinus rhythm **(12)**.

Spectral Doppler has also been used to interrogate blood flow velocities in the left atrial appendage during transesophageal echocardiography, with values below 34 cm/s associated with greater risk of atrial fibrillation recurrence and stroke. Recently, speckle tracking echocardiography has been applied to study left atrial function. Patients with a history of paroxysmal atrial fibrillation but sinus rhythm during echocardiography have impaired left atrial function, suggesting a more chronic atrial myopathy. Furthermore, although the correlation between left atrial size and function, recent studies demonstrate that left atrial function can be impaired even in the absence of left atrial enlargement. In small studies, functional impairments of the left atrium appear to offer additional prognostic information beyond left atrial size for the prediction of adverse cardiovascular outcomes **(13)**.

- ***Determinants of left atrial size***

1. Left ventricular filling pressures: The increase in left atrial volume is a reflection of elevated left ventricular filling pressures in the absence of congenital heart disease, mitral valve or primary atrial pathology. In a non-compliant left ventricle, as the left atrium is exposed to the pressures of the left ventricle during diastole, left atrial pressure rises to maintain adequate left ventricle filling. It is the increase in left atrial wall tension which leads to chamber dilatation. Left atrial volume is therefore an expression of the chronicity of exposure to abnormal filling pressures. Thus, left atrial volume reflects an average of left ventricular filling pressures over time. It is thus useful for monitoring long-term

hemodynamic control **(5)**.

2. Anthropometry and age: left atrium size should be indexed to body surface area as body size is a major determinant of left atrial size. It is the variation in body size which accounts for gender difference in left atrial size. The left atrial volume index (LAVI) is independent of age from childhood onwards. The age related left atrial enlargement is a reflection of the pathophysiologic changes that accompany advancing age rather than a consequence of chronologic aging **(14)**.
3. Atrial fibrillation: It is difficult to establish a causal relationship between atrial fibrillation and left atrium volume. Structural alterations in left atrium, may be related to the underlying pathophysiology or solely to the arrhythmia itself. Data from experimental animal studies do lend evidence to the fact that atrial arrhythmias induce structural remodeling **(15)**.
4. Volume overload: Chronic volume overload associated with large shunts, valvular regurgitation and high output states including athletic heart can contribute to left atrial enlargement. However myocardial relaxation physiology is usually normal as compared to abnormal myocyte relaxation seen in pressure overload situations **(16)**.

➢ ***Prediction of Cardiovascular Outcomes***

Atrial fibrillation (AF) is a serious cardiac arrhythmia associated with increased morbidity and mortality. Data from the Framingham and Cardiovascular Health Study have incriminated an increased anteroposterior left atrium diameter as the harbinger of AF. It has been confirmed that left atrial volume represents a superior measure over left atrium diameter for predicting outcomes inclusive of AF. The prognostic information provided is incremental to clinical risk factors. Increased LA volume is also a predictor of stroke and death. An indexed LA volume of ≥32 ml/m2 is associated with an increased risk of stroke independent of age and other clinical risk factors for cerebrovascular disease. An increased LA volume is also the predictor of first stroke in elderly who are in sinus rhythm and without any history of ischemic neurological events, AF or valvular heart disease **(17)**.

LA volume is the barometer of LV filing pressure and reflects the burden of diastolic dysfunction. Because a large number of individuals with LV dysfunction are in a pre-clinical phase of the disease, methods to quantify the risk of progression to symptomatic heart failure would be clinically useful. LA volume ≥ 32 ml/m2 is associated with increased incidence of heart failure

which is independent of age, myocardial infarction, diabetes mellitus, hypertension, LV hypertrophy and mitral inflow velocities. Even in subjects with a normal ejection fraction, an increment in LA volume is observed from baseline to the diagnosis of heart failure **(18)**.

Left atrial volume index (LAVI) is a predictor of survival after acute myocardial infarction. An exponential increase in mortality with increasing left atrial volume has been documented. Moreover, the prognostic information is incremental to clinical data and standard echocardiographic measures of left ventricle systolic and diastolic function **(19)**.

There is evidence that left atrial volume index (LAVI) ≤ 28 ml/m2 is strongly predictive of normal stress echocardiogram. Although a robust data in this perspective is awaited, it holds promise to provide a simple means of identifying patients with low ischemic risk. LA volume is intimately related to LV mass/hypertrophy, systolic and diastolic dysfunction. The incremental value of each parameter for the prediction of death is expected to diminish when considering others. But LAVI derives its importance in providing incremental value in predicting mortality **(20)**

REFERENCES

1. **Lester SJ, Ryan EW, Schiller NB et al (1999):** Best method in clinical practice and in research studies to determine left atrial size. Am J Cardiol.; 84:829 –32.
2. **Lang RM, Bierig M, Devereux RB, et al (2005):** Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr;18: 1440–63.
3. **W. A. McAlpine, (1975):** Heart and Coronary Arteries: An Anatomical Atlas for Clinical Diagnosis, Radiological Investigation, and Surgical Treatment, Springer, Berlin, Germany.
4. **Lang RM, Badano LP, Mor-Avi V., et al. (2015):** Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Journal of the American Society of Echocardiography, 28, 1–39. e14.
5. **Tsang TS, Barnes ME, Gersh BJ, et al. (2002):** Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. The American Journal of Cardiology, 90, 1284–1289.
6. **Nistri S, Galderisi M, Ballo P, et al. (2011):** Determinants of echocardiographic left atrial volume: implications for normalcy. European Journal of Echocardiography, 12, 826–833.
7. **Nagueh SF, Appleton CP, Gillebert TC, et al. (2009):** Recommendations for the evaluation of left ventricular diastolic function by echocardiography. Journal of the American Society of Echocardiography, 22, 107–133.
8. **Pagel PS, Kehl F, Gare M, et al. (2003):** Mechanical function of the left atrium: new insights based on analysis of pressure-volume relations and Doppler **echocardiography. Anesthesiology, 98, 975–994.**
9. **Abhayaratna WP, Fatema K, Barnes ME, et al. (2008):** Left atrial reservoir function as a potent marker for first atrial fibrillation or flutter in persons ≥ 65 years of age. The American Journal of Cardiology, 101, 1626–1629.
10. **Manning WJ, Silverman DI, Katz SE, et al. (1994):** Impaired left atrial mechanical function after cardioversion: relation to the duration of atrial fibrillation. Journal of the American College of Cardiology, 23, 1535–1540.
11. **Thomas L, Levett K, Boyd A, et al. (2003):** Changes in regional left atrial function with aging: evaluation by Doppler tissue imaging. European Journal of Echocardiography, 4, 92–100.
12. **Dubrey S, Pollak A, Skinner M, et al. (1995):** Atrial thrombi occurring during sinus rhythm in cardiac amyloidosis: evidence for atrial electromechanical dissociation. British Heart Journal, 74, 541–544.
13. **Yasuda R, Murata M, Roberts R, et al. (2015):** Left atrial strain is a powerful predictor of atrial fibrillation recurrence after catheter ablation:

study of a heterogeneous population with sinus rhythm or atrial fibrillation. European Heart Journal Cardiovascular Imaging, 16, 1008–1014.

14. **Pearlman JD, Triulzi MO, King ME, et al. (1990):** Left atrial dimensions in growth and development: normal limits for two-dimensional echocardiography. J Am Coll Cardiol.;16:1168 74.
15. **Allessie M, Ausma J, Schotten U. (2002):** Electrical, contractile and structural remodeling during atrial fibrillation. Cardiovasc Res ;54:230 46.
16. **Hoogsteen J, Hoogeveen A, Schaffers H, et al. (2003):** Left atrial and ventricular dimensions in highly trained cyclists. Int J Cardiovasc Imaging 2003;19:2117.
17. **Barnes ME, Miyasaka Y, Seward JB, et al. (2004):** Left atrial volume in the prediction of first ischemic stroke in an elderly cohort without atrial fibrillation. Mayo Clin Proc ;79:1008 14.
18. **Gottdiener JS, Kitzman DW, Aurigemma GP, et al. (2006):** Left atrial volume, geometry, and function in systolic and diastolic heart failure of persons ≥ 65 years of age (the Cardiovascular Health Study). Am J Cardiol 2006;97:83 9.
19. **Moller JE, Hillis GS, Oh JK, et al. (2003):** Left atrial volume: a powerful predictor of survival after acute myocardial infarction. Circulation; 107: 2207-12.
20. **Alsaileek AA, Osranek M, Fatema K et al. (2006):** Predictive value of normal left atrial volume in stress echocardiography. J Am Coll Cardiol.; 47: 1024-28.