INTRODUCTION

The quantification of cardiac chamber size and function is the cornerstone of cardiac imaging, with echocardiography being the most commonly used noninvasive modality because of its unique ability to provide real-time images of the beating heart, combined with its availability and portability [1]

Nowadays, by new echocardiographic techniques, such as strain (S), Doppler, speckle tracking, and 3D echocardiography, we are able to recognize early atrial dysfunction, before clinical manifestations and earlier than standard echocardiographic parameters [2]

Atrial size and function can be assessed with echocardiography, cardiac computed tomography (CCT), and cardiac magnetic resonance (CMR). Although echocardiography is best suited for these tasks because of its availability, safety, versatility, and ability to image in real time with high temporal and spatial resolution, CCT and CMR are complementary in specific clinical instances [3]

AIM OF THE WORK

To evaluate the effect of diabetes mellitus on left atrial volumes and functions by using real-time three dimensional echocardiography in a population of patients free of symptomatic cardiovascular disease as compared to normal subjects.

Chapter 1

LEFT ATRIAL ANATOMY

Being the most posteriorly situated cardiac chamber, it is only separated from the esophagus by the fibrous pericardium.The left atrial body possesses a venous component which receives the pulmonary veins and a vestibule which surrounds the mitral orifice and it has a blind-ending pouch-like appendage. It shares the septum with the right atrium [(4)]

The pulmonary veins enter the posterior part of the left atrial body with the orifices of left veins located more superiorly than the right veins.The walls of the left atrium are muscular and can be described as superior, posterior, left lateral, septal (or medial), and anterior, with the addition of postero-inferior wall(Fig.1) [(5)]

Excluding the atrial appendage, the walls of the left atrium are fairly smooth on the endocardial aspect although of non-uniform thickness [(6)]

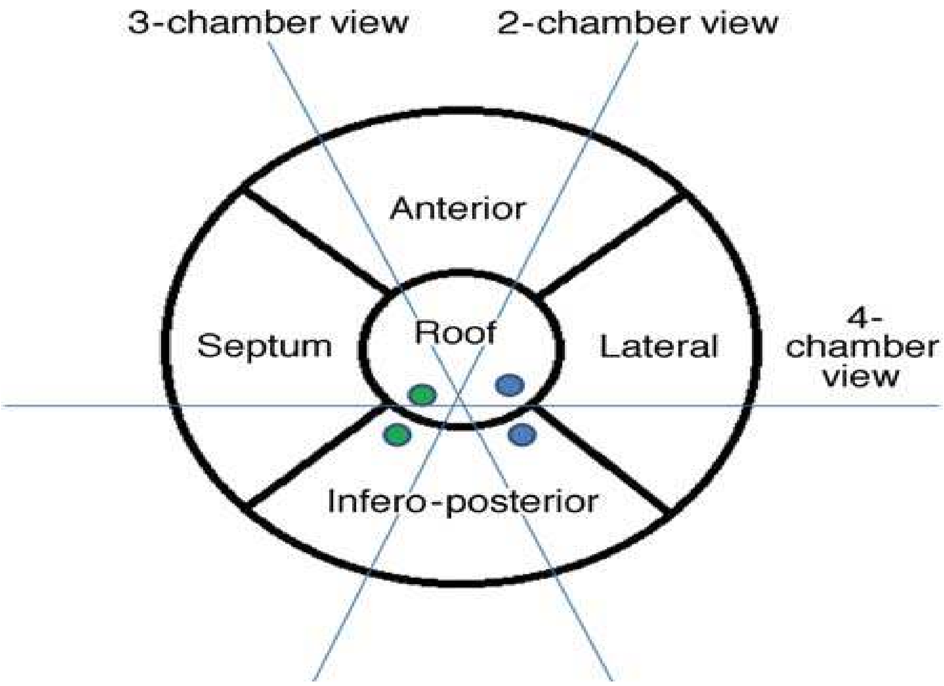


Figure (1): Proposal of a five-segment model for left atrial segmentation by trans-thoracic two-dimensional echocardiography The apical four-chamber view cuts the heart obliquely from the apex of the left ventricle. Conventionally, the inter-atrial septum is situated medially and the lateral wall on the opposite side, inferiorly the mitral annulus and superiorly the roof. The anterior and infero-posterior walls can be visualized in the apical two-chamber view. Only the infero-posterior wall can be observed, facing the aorta, in a three-chamber view. The green and blue solid dots represent right and left pulmonary veins (upper and lower), respectively (5)

Measuring LA Size

Quantifying LA size is difficult, in part because of the left atrium's complex geometry and intricate fiber orientation and the variable contributions of its appendage and pulmonary veins (7)

LA size is most often measured using M-mode and 2-dimensional echocardiography (2DE) [8]

LA size is measured at the end-ventricular systole when the LA chamber is at its greatest dimension, in long-axis view (anterior-posterior diameter) and in the 4-chamber view (longitudinal and transverse diameters (Table 1).[8]

Among these measurements, maximal left atrial volume (LAV) indexed to body surface area (LAVi) is most strongly associated with cardiovascular disease and is the most sensitive in predicting cardiovascular outcomes and providing uniform and accurate risk stratification. [9]

The normal left atrial volume index (LAVi) using echocardiography is [22 ± 6 ml/m2]. [10]

The American Society of Echocardiography considers LA enlargement as LAV >28 ml/m2. However, for the purpose of identifying LV diastolic dysfunction, LAV cut point >34 ml/m2 should be present. [11]

Inaccuracies owing to geometric assumptions and foreshortening of the LA cavity with 2D biplane volume methods are less with real-time 3-dimensional (3D) echocardiography (RT3DE) which has been shown to accurately and reproducibly estimate LAV and yielded comparable results to CMR. [12]

Table (1): Showing recommendations for the echo-cardiographic assessment of LA size. [1]

Parameter and method	Echocardiographic imaging	Advantages	Limitations
Internal linear dimensions. The anteroposterior diameter of the left atrium can be measured in the parasternal long-axis view perpendicular to the aortic root long axis, and measured at the level of the aortic sinuses by using the leading-edge to leading-edge convention.	M-mode tracing 	• Reproducible • High temporal resolution • Wealth of published data	Single dimension not representative of actual LA size (particularly in dilated atria)
	2D-guided linear measurements 	• Facilitates orientation perpendicular to LA posterior wall	• Lower frame rates than in M-mode • Single dimension only
Area. Measured in four-chamber apical view, at end-systole, on the frame just prior to mitral valve opening by tracing the LA inner border, excluding the area under the mitral valve annulus and the inlet of the pulmonary veins.	2D images 	• More representative of actual LA size than anteroposterior diameter only	• Need for a dedicated view to avoid LA foreshortening • Assumes a symmetric shape of the atrium

Assessing LA Functions

LA function can be assessed echocardiographically using:

- Volumetric analysis
- Spectral Doppler of transmitral, pulmonary venous and LA appendage flow
- Tissue Doppler and deformation analysis (strain [ε] and strain rate [SR] imaging) of the LA body. [13]

Volumetric methods:

Three basic functions of the LA can be derived:

1. ***LA reservoir function:***

- LA total emptying volume= LAVmax – LAVmin
- LA total emptying fraction = (LAVmax –LAVmin) /LAVmax.

2. ***LA conduit function:***

- LA passive emptying volume = LAVmax – LAVpreA
- LA passive emptying fraction= (LAVmax – LAVpreA) /LAVmax
- Conduit Volume= stroke volume – total emptying volume.

3. ***LA booster pump function:***

- LA active emptying volume = LAVpreA − LAVmin
- LA active emptying fraction = (LAVpreA − LAVmin) /LAVpreA (Fig. 2) [(14)].

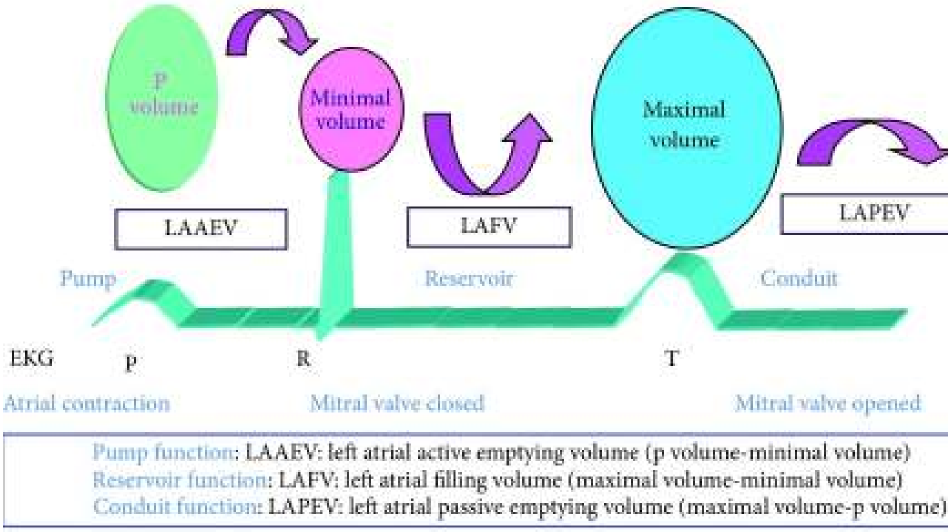


Figure (2): Three different atrial volumes during cardiac cycles. [15]

In normal LA function, the mean total LA emptying volume is 13.5±4.3 ml/m2 (representing 37±13% of LV stroke volume), the fractional emptying of the LA is 65±9%, and the conduit volume is 23±8 ml/m2. [16]

Conventional echocardiography allows measurement of all LA volumes:

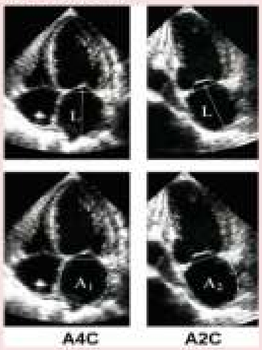
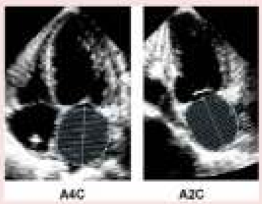
LA passive volumes consist of:

- Pre-atrial contraction volume (V_{preA}), measured at the onset of the P-wave on an electrocardiogram (ECG). [17]
- Minimal LA volume (V_{min}), measured at the closure of the mitral valve in end-diastole (Table 2). [18]
- Maximal LA volume (V_{max}), measured just before the opening of the mitral valve in end-systole (Table 2). [18]

LA active volumes are:

- LA reservoir volume (Vmax - Vmin)
- LA conduit volume (LV total stroke volume-LA reservoir volume)
- LA passive emptying volume (Vmax –VpreA)
- LA contractile volume (VpreA- Vmin). [19]

Table (2): Showing recommendations for the echo-cardiographic assessment of LA volume. [1]

Parameter and method	Echocardiographic imaging	Advantages	Limitations
Volume. 2D volumetric measurements are based on tracings of the blood-tissue interface on apical four- and two-chamber views. At the mitral valve level, the contour is closed by connecting the two opposite sections of the mitral annulus with a straight line. Endocardial tracing should exclude atrial appendage and pulmonary veins. LA length L is defined as the shortest of the two long axes measured in the apical two- and four-chamber views (to provide reliable calculations the two lengths should not differ more than 5 mm). Volumes can be computed by using the area-length approximation: $\frac{8}{3\pi}\left[\frac{(A_1 \cdot A_2)}{L}\right]$ where A1 and A2 are the corresponding LA areas. Alternatively LA volume can be calculated using the disk summation technique by adding the volume of a stack of cylinders of height h and area calculated by orthogonal minor and major transverse axes (D1 and D2) assuming an oval shape: $\pi/4(h)\sum(D1)(D2)$ 3D data sets are usually obtained from the apical approach using a multibeat full-volume acquisition	2DE Area-length technique  Biplane method of disks  	• Enables accurate assessment of the asymmetric remodeling of the left atrium • More robust predictor of cardiovascular events than linear or area measurements	• Geometric assumptions about LA shape • Few accumulated data on normal population • Single plane volume calculations are inaccurate since they are based on the assumption that A1 = A2
	3D data sets 	• No geometrical assumption about LA shape • More accurate when compared to 2D measurements	• Dependent on adequate image quality • Lower temporal resolution • Limited data on normal values • Patient's cooperation required

Spectral Doppler

As 2D echocardiography is limited by the use of geometric models and by possible errors due to foreshortening, it may underestimate LA volume compared with cardiac magnetic resonance, while Doppler assessment of LA function and/or the use of the LA ejection force are indirect parameters for LA function assessment. [20]

By pulsed Doppler we can also measure pulmonary venous flow. The sample volume is placed into pulmonary veins (commonly right upper vein) from the apical four chamber view (Fig. 3). We can measure:

1. Peak systolic (S) velocity
2. Peak anterograde diastolic (D) velocity
3. Peak retrograde diastolic (Ar) velocity
4. Its duration during LA contraction. [21]

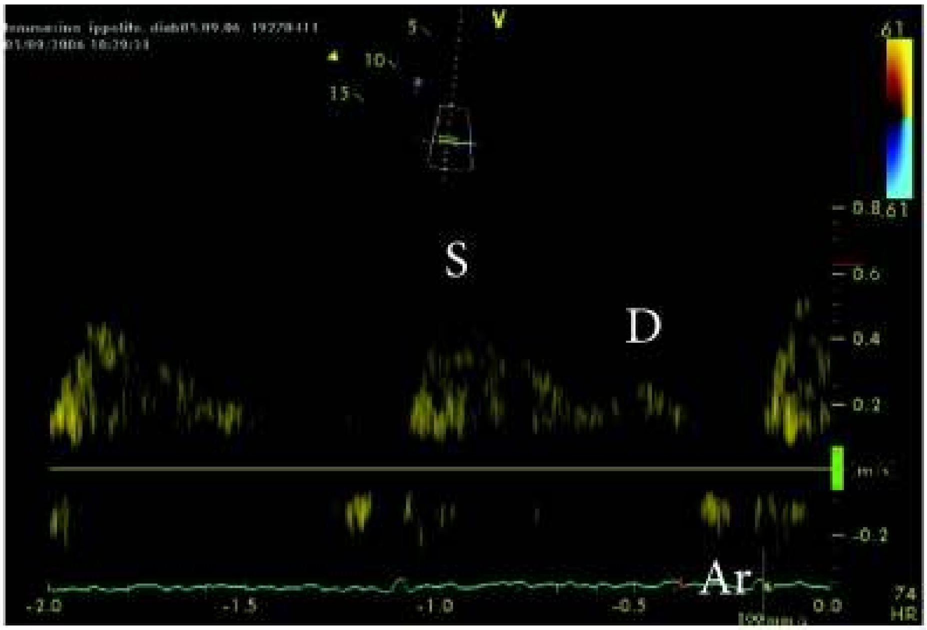


Figure (3): Pulmonary venous flow velocity by pulsed Doppler. (15)

The atrial reversal velocity has been used as measurement of left atrial function. (22)

Tissue Doppler

Pulsed-wave and color tissue Doppler of atrial contraction (A') provide regional and global (when several sites are averaged) snapshots of atrial systolic function. Tissue velocities during ventricular systole (S') and early diastole (E') correspond to reservoir and conduit function, respectively (Fig. 4). However, tissue Doppler velocities are subject to error because of angle dependency and the effects of cardiac motion and tethering and have been superseded by deformation analysis. (23)

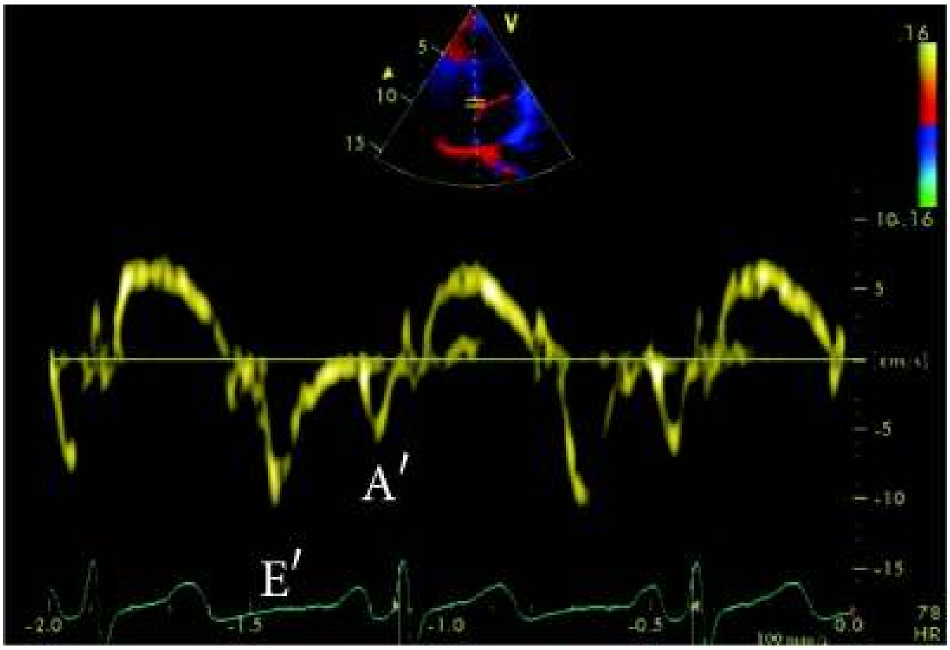


Figure (4): Tissue Doppler imaging of medial annulus. [15]

Deformation analysis (ε and SR imaging)

Strain and SR represent the magnitude and rate, respectively, of myocardial deformation, they can be assessed using either tissue Doppler velocities (tissue Doppler imaging [TDI]) or 2DE techniques (2D speckle-tracking echocardiography [STE]). Both have been used successfully to assess LA global and regional function (Fig. 5 and 6). [24]

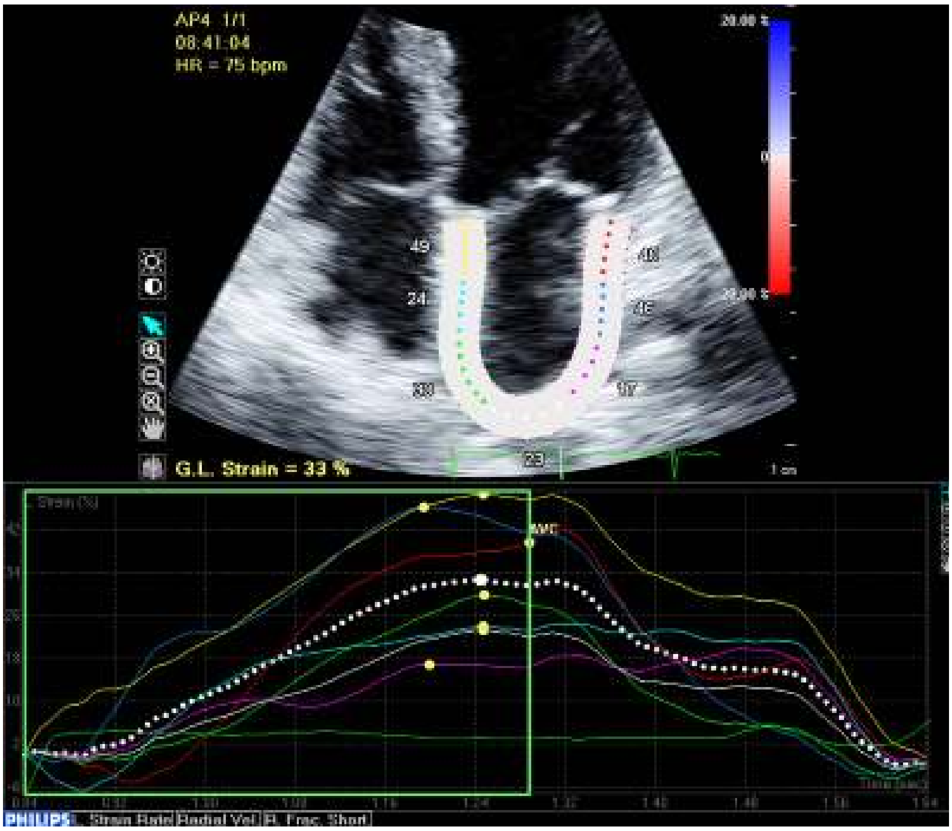


Figure (5): Regional strains are denoted by the colored lines and global longitudinal (G.L.) strain by the white dotted line. The closed circles on each regional strain-time curve identify peak strain. AP4 =apical 4-chamber; AV = aortic valve; AVC = aortic valve closure; HR = heart rate; STE = speckle-tracking echocardiography. (25)

Figure (6): Strain curves for the inferior (purple) and anterior (yellow) segments are shown. (25)

Although temporal resolution is excellent and ideal 2D image quality is not necessary, TDI is highly angle dependent, and signal-to-noise ratios may be problematic. In contrast, 2D STE analyzes myocardial motion by frame-by-frame tracking of natural acoustic markers that are generated from interactions between ultrasound and myocardial tissue within a user-defined region of interest, without angle dependency. Frame rates of about 50 to 70 frames/s are needed to avoid speckle decorrelation, and good image quality is needed for accurate tracking. (26)