REVIEW

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Atria: A comprehensive evaluation with echocardiography

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Abstract

Left and right atria have gained interest from scientific community. Two or three- dimensional echocardiographic methods have been implemented for better understanding of atrial functions in both healthy persons and patients with various diseases. Atrial volume could be calculated from 2D or 3D images. Volumetric data and derived parameters could be used for determining atrial phasic functions. Nowadays, atrial deformation imaging with 2D-TDI, 2D-speckle tracking imaging or with recently introduced 3D speckle tracking is possible. All those methods have some advantages and disadvantages, which define their clinical value in the future.

Key Words: left atrium, right atrium, functional evaluation, echocardiography

Introduction

Both atria are not mere passive chambers lying between their venous openings and respective ventricles. They are interdependently connected to the ventricles for ensuring best cardiac performance. Phasic changes in the atria provide optimal support for left or right ventricular filling. In addition to their mechanical role, the atria release atrial natriuretic peptide in response to stretching. It has potent diuretic, natriuretic and vasorelaxant effects (1).

During ventricular systole, each atrium has reservoir function when both atrioventricular (AV) valves are in closed position. They receive venous flow from the pulmonary veins. Atrial filling by pulmonary vein flow is affected by ventricular contraction, the descent of ventricular base, systemic and pulmonary venous systolic pressure, and atrial properties (ie, relaxation and chamber stiffness). Conduit function of atria begins with early diastole and blood passively flows from atrium to ventricle. Ventricular relaxation, compliance and stiffness as well as ventricular early diastolic pressures are major determinants of conduit function. Late diastolic atrial contractility pumps remaining blood (20-30% of cardiac stroke volume) actively into the ventricles. The atrial pressure-volume relationship consists of two loops: the A loop representing atrial pump function and the V loop representing atrial reservoir function (Fig. 1). Factors affecting each phase are shown in Table 1.

Atrial reservoir and booster functions increase with exercise, whereas conduit function is not (2). Enhancement of reservoir function supports ventricular filling by creating higher AV pressure gradient favoring diastolic flow, and also, by increasing atrial pump through an increase in its preload.

Any pressure and/or volume loading conditions such as atrial fibrillation (AF), ischemic heart disease, heart failure, valvular disease, hypertension and diabetes lead to atrial remodeling. Atrial remodeling is caused by electrical, mechanical, and metabolic stressors in a time-dependent way (3). It can be structural, functional, and electrical (4). Longer duration of stressors (> 5 weeks) may cause irreversible atrial damage (apoptosis and fibrosis) (3). While structural remodeling is manifested by atrial dilatation, functional remodeling results in decreased function with or without a change in atrial size. Atrial arrhythmias, especially AF, are the hallmarks of electrical remodeling (Fig. 2) (5).

In this review, our aim is to provide better understanding of left and right atrial structural and functional evaluation by focusing on echocardiography.

Left atrium

Anatomy

Left atrium (LA) is a posteriorly localized cardiac chamber. Right atrial (RA) localization is anterior and inferior to left atrium (6). Major anatomic parts of left atrium are:

-Left atrial appendage (LAA) is smaller compared to right atrial appendage and shows various forms such as cauliflower,

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Table 1. Factors affecting atrial functions

Atrial function	Factors affecting the function
Reservoir	Atrial compliance during ventricular systole Atrial contractility and relaxation Descent of left ventricular base Ventricular end-systolic volume
Conduit	Atrial compliance Ventricular compliance Ventricular relaxation
Booster Pump	Atrial contractility Atrial pre-load (venous return) Atrial after-load (ventricular end-diastolic pressure) Ventricular systolic reserve

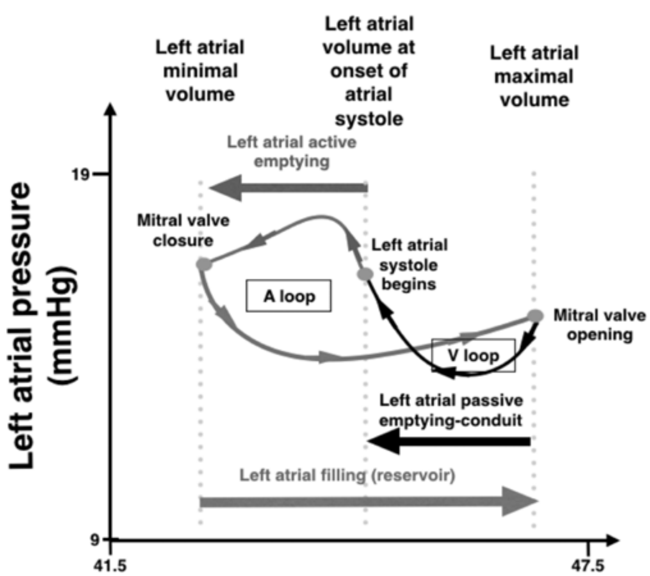

Figure 1. Left atrial pressure to volume loop curves

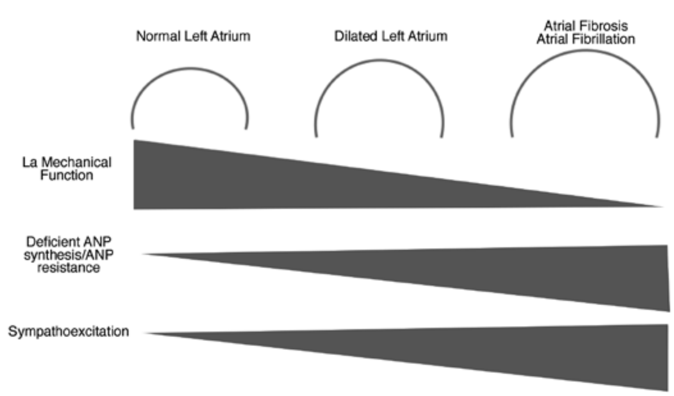

Figure 2. Changes in left atrial structural, mechanical and electrical properties with left atrial dilatation

(Modified from reference 5)

windsock, cactus and chicken wing (7). The shape of LAA has direct effect on embolic risk in patients with AF (8).

-Interatrial septal component is especially related to aorta and transverse pericardial sac at its anterior part. Fossa ovalis as a true anatomic septum is another important structure in this part of left atrium.

-Pulmonary veins are directly opened to venous portion. Left pulmonary veins are superiorly localized compared to right pulmonary veins.

-The vestibule is an outlet portion of left atrium surrounding mitral valve orifice. Coronary sinus is in close contact with the posterior vestibular wall (9).

Left atrial size and phasic function

Increased left atrial size is a marker reflecting left ventricular diastolic dysfunction (4). That is an early step in a cascade of events ending with left atrial failure (Fig. 2) (5). Enlargement of left atrium is a predictor of both all-cause mortality (10, 11) and future cardiovascular events such as AF (12).

It is also a marker for worse prognosis in patients with heart failure (preserved or reduced ejection fraction) (13), valvular heart disease (14) and diabetes (15).

Echocardiography, cardiac computed tomography (cCT) and cardiac magnetic resonance (cMR) could be used for assessment of atrial size and function. Echocardiography is by far the most commonly used imaging technique because of its availability, versatility, safety and cost. It is associated with high temporal and spatial resolution. Transthoracic echocardiography (TTE) should be used for determining atrial size because transesophageal echocardiographic (TEE) views cannot show entire left atrium.

LA diameter

TTE M-mode or two-dimensional (2D) based parasternal long-axis antero-posterior (AP) diameter at end-systole has traditionally been used linear dimension reflecting left atrial size. An increased AP diameter is a risk factor for incident AF (16, 17), stroke, and death (18). An AP diameter ≥55 mm also has prognostic value in patients with mitral regurgitation (19).

Unfortunately, LA is a three-dimensional structure, and hence, one-dimensional measurement of AP diameter could not reflect true left atrial size. Indeed, AP diameter measurement underestimates true left atrial volume (LAV) (20) Recent guideline about chamber quantification recommended that AP linear dimension should not be used as the sole measure of LA size (21).

LA area

Left atrial area can be calculated from apical 4- and 2-chamber views but again superseded by left atrial volume measurement.

Reference values for AP diameter and LA area are shown in Table 2 (22).

LA functional assessment by pulsed wave Doppler

Both pulse-wave (PW) mitral (E and A waves) and pulmonary vein waves (S, D and A waves) are used for evaluation of left ventricular filling pressures. Those waves are also show valuable information about LA phasic functions (Table 3-5) (23-25).

Left atrial ejection force (26) and kinetic energy (LAKE) (27) are calculated from PW data and reflect atrial function but their use is not recommended at this time, which is probably related to lack of robust data and time-consuming calculation from multiple parameters (21).

Table 2. Reference values for AP diameter and left atrial area (22)

Parameters	Mean (SD)	2SD range
LA diameter-PLAX, mm	33.6 (4.3)	26.7-41
LA area, cm^2 Ap4Ch	16.5 (3.2)	11.5-21.9
LA area, cm^2 Ap2Ch	17.5 (3.1)	12.7-23.1

*AP-antero-posterior, Ap2Ch- apical 2 -chamber view, Ap4Ch - apical 4- chamber view, SD-standard deviation, PLAX- parasternal long-axis

Table 3. PW Doppler parameters and left atrial phasic functions (23)

LA function	Transmitral flow	Pulmonary venous flow	Composite indexes
Reservoir		S velocity and VTI	
Conduit	E velocity, E/A ratio	D velocity and VTI	
Booster function	A velocity, E/A ratio	PVa	Ejection force, LAKE

A - atrial contractility filling phase, E- early diastolic filling, LA - left atrium, LAKE-LA kinetic energy, PW - pulse-wave, PVa - pulmonary vein A wave, VTI - velocity time integral

Table 4. Normal values for mitral inflow normal PW Doppler parameters (24)

Parameters	Age groups, years		
	20-40	40-60	>60
E velocity, cm/sec	0.82 (0.16)	0.75 (0.17)	0.70 (0.16)
A velocity, cm/sec	0.50 (0.13)	0.62 (0.15)	0.74 (0.16)
E/A ratio	1.71 (0.50)	1.24 (0.19)	0.98 (0.29)

Data are presented as Mean (SD)

A - atrial contractility filling phase, E- early diastolic filling, PW - pulse wave

Table 5. Reference values for PW Doppler pulmonary vein flow parameters (25)

	Age groups, years			
	16-20	21-40	41-60	>60
PV S/D ratio	0.82 (0.18)	0.98 (0.32)	1.21 (0.2)	1.39 (0.47)
PV Ar, cm/sec	16 (10)	21 (8)	23 (3)	25 (9)
PV Ar duration	66 (39)	96 (33)	112 (15)	112 (15)

Data are presented as Mean (SD)

Ar - reversal flow during atrial contraction, PW - pulse wave PV - pulmonary vein, S/D - systolic/diastolic

LA volume

Ellipsoid model, disk summation and area- length methods can be used for LAV measurement (28). All three methods require good image quality with clear LA border, exclusion of LAA and pulmonary vein orifices from the measurement, and end-systolic timing.

Volumes by the ellipsoid method were consistently smaller than other two methods. The mean LA volume indexed to body surface area was 27(12) ml/m^2 for ellipsoid method, 37(16) ml/m^2 for area-length method, and 34(14) ml/m^2 for Simpson's method (29). Relative inaccuracy of ellipsoid method has led to Simpson's disk summation method as preferred volume measurement tool (21).

Area-length method can be used as an alternative. Apical four- and two- chamber views are needed for better volumetric calculation but single-plane measurements could be used in case of insufficient biplane planimetry. Measured LA volumes are maximal LA volume (end-systolic volume) just before the opening of the mitral valve at end-systole, (ECG: at the end of the T wave), the minimal LA volume at end-diastole when the mitral valve is closed (ECG: at the beginning of QRS) and just before atrial systole (ECG: at the beginning of P wave) (Fig. 3).

Left atrial volume is directly affected by gender. Indexing according to body size area overcomes this restriction and should always be used when reporting LAV. The upper normal limit for 2D echocardiographic LAV index (LAVi) is 34 mL/m^2 for both genders (Table 6) (21). LAVi is an independent predictor of adverse cardiovascular events including stroke, heart failure, myocardial infarction and AF (30).

Apart from LAVi, minimal LAV measured at the end-diastole has capacity to predict an increased pulmonary wedge pressure if it is more than 40 ml (31).

Geometric assumptions and difficulty in obtaining correct LA alignment restrict accuracy of 2D TTE volumetric measurements. LA diameter, area or volume values are relatively crude evaluation for an active heart chamber. Functional parameters may be better suited for more in-depth analysis of atria and may provide a framework for examining atria in both healthy and disease conditions. Indeed, LA phasic changes occur earlier in disease process and could provide early diagnosis compared

Table 6. 2D echo left atrial volume index (LAVi) (ml/m^2): normal range and partition cut-offs (for both sexes) (21)

Normal Range	Mildly Abnormal	Moderately Abnormal	Severely Abnormal
16-34	35-41	42-48	>48

to LA enlargement (32). Volume-based calculation or tissue Doppler/deformation imaging could be used for this purpose (Table 7-8).

Increasing age comes with decreasing conduit function but pronounced active pump function of LA (35). LA reservoir function did not vary with age or sex (35). In early stage of left ventricular dysfunction (mild degree of increased left ventricular filling pressures) LA reservoir and conduit functions decrease with an increase in booster pump function. Advancement of left ventricular diastolic dysfunction causes impairment in all phases of LA function (36, 37).

LA emptying fraction (LAEF) has been shown to be an independent predictor of mortality and incident AF (38, 39). Patients with both LAEF < 49% and LAVi >38 ml/m^2 are at the highest risk of events (39).

Left atrial function index (LAFI) is dependent on LA conduit function and independent of cardiac rhythm disturbances (40). LAFI >16.57 is a strong predictor of long-term survival in patients with heart failure with reduced ejection fraction (33).

Table 7. Volume-derived indexes of left atrial functional assessment (23, 33)

LA global function Left atrial functional index (LAFI)= (LAEF × left ventricular outflow tract-velocity time integral [LVOT-VTI])/LAVimin
LA reservoir function: LA total emptying volume: LAVmax -LAVmin LA emptying fraction (LAEF) : LAVmax -LAVmin / LAVmax [normal values:70(9)]
LA conduit function LA passive emptying volume: LAVmax -LAVpreA LA passive emptying fraction (Passive EF): LAVmax -LAVpreA / LAVmax [normal values:44(12)] Conduit Volume= Stroke volume - Total emptying volume
LA booster pump function LA active emptying volume: LAVpreA -LAVmin LA active emptying fraction (Active EF): LAVpreA -LAVmin / LAVpreA [normal values:47(12)]

A - atrial contractility, EF - emptying fraction LA - left atrium, LAV - left atrial volume

LA tissue Doppler velocities (TDI)

TDI records high amplitude low frequency atrial wall velocities. Examination should be performed at end-expiration with sample volume on the atrial side of the mitral annulus at the basal inter-atrial septum from the apical four-chamber view.

Peak ventricular systolic velocity (S´), peak early diastolic velocity (E´) and peak atrial contractility (A´) could be recorded. E´ velocity decreases with aging but A´ shows no change. A´ velocity has direct relationship with atrial function (41, 42). In patients with various cardiac diseases, A´ wave velocity lower than 4 cm/s points to a higher cardiac mortality (43).

Tissue Doppler velocities (Table 9) have important restrictions: measurement error due to angle dependency, and the effects of cardiac motion and tethering.

LA 2D deformation analysis

Myocardial deformation imaging encompasses TDI or 2D-based (speckle tracking) methods. TDI, as previously mentioned, has

Table 8. Tissue Doppler/deformation imaging parameters for functional evaluation (34)

LA function	Tissue Velocity	Strain ε	Strain rate
Reservoir	S´	εs (total)	SR-S´
Conduit	E´	εe, εpos	SR-E´
Booster pump	A´	εa, εneg	SR-A´

ε-strain, A´- peak atrial contractility velocity E´- peak early diastolic velocity, neg- negative, pos- positive, S´- peak ventricular systolic velocity, SR- strain rate

Table 9. Normal values for tissue Doppler based parameters (26)

	Age groups, years		
	20-40	40-60	>60
	Mean (SD)	Mean (SD)	Mean (SD)
Septal E´, cm/sec	12.1 (2.5)	9.8 (2.6)	7.6 (2.3)
Septal A´, cm/sec	8.5 (1.7)	9.8 (2.0)	10.5 (1.7)
Lateral E´, cm/sec	16.4 (3.4)	12.5 (3.0)	9.6 (2.8)
Lateral A´, cm/sec	8.2 (2.2)	9.4 (2.6)	10.6 (2.9)

A´ -peak atrial contractility velocity, E´- peak early diastolic velocity

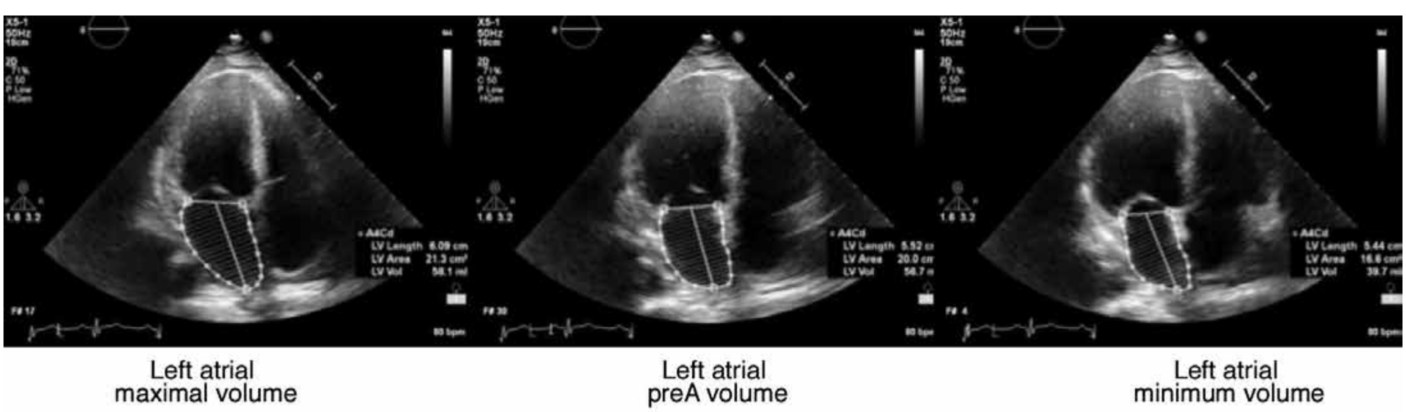

Figure 3. 2D- echocardiographic measurement of left atrial volumes: apical 4- chamber view

angle dependence and signal to noise ratio sometimes could be problematic. Therefore, 2D methods with speckle tracking (2D STE) has gained acceptance in many echocardiography laboratories.

2D STE is an angle independent imaging method but needs good image quality and relatively high frame rate (50-70 frame/sec) for accurate tracking. 2D STE is used for determination of strain and strain rate (SR) values from 6-12 segments (apical 4-3-2-chamber views)

Two reference points on ECG could be selected for left atrial deformation imaging: onset of QRS complex or P wave. If the QRS complex is marked as reference point, peak positive longitudinal atrial strain corresponds to reservoir function. Early and late diastolic strain waves (εe and εa, respectively) point to atrial conduit and booster pump functions. In contrast, if P wave is selected, first negative peak ε (εneg) represents the atrial booster pump function, positive peak ε (εpos) corresponds to conduit function, and their sum (εtotal) represents reservoir function (Fig. 4) (44).

Lower peak longitudinal strain values is associated with possibility of having permanent AF (45), worse prognosis after acute myocardial infarction (46), and higher grade mitral regurgitation (47).

An interesting research area for deformation imaging is the determination of atrial fibrosis. This task could be accomplished with cMR (48) but echocardiographic methods can be used for obtaining data indirectly reflecting the presence of fibrosis. Peak positive longitudinal strain (Table 10) (50) reflects left atrial stretching capacity during reservoir phase, and hence, directly related to atrial compliance which adversely affected by fibrosis (49). There is a negative correlation between peak atrial longitudinal strain and degree of atrial fibrosis in patients with AF (51) and mitral regurgitation (52).

Table 10. Grading of 2D speckle tracking (STE) peak atrial longitudinal strain (50)

Normal	Mildly Abnormal	Moderately Abnormal	Severely Abnormal
>40%	30-<40%	23-<30%	<23%

Left atrial deformation analysis brings some difficulties compared to left ventricular speckle tracking. Left atrium is positioned at far field of echocardiographic window, and hence, image quality is relatively poor with low signal-to-noise ratio. Motion of some speckles out of image plane causes error in strain and strain rate calculations. Thin walled left atrium also could lead to more variability on different software vendors. Left atrium specific software packages with clear reference and time points are needed. 2D STE based left atrial functional imaging may have a future if above-mentioned restrictions to be solved.

LA volume - strain analysis based on three dimensional data

Three-dimensional (3D) echocardiographic left atrial volume calculation shows better correlation with cCT and magnetic resonance compared to 2D volumes (53, 54). 3D volume analysis does not require any geometric assumption. Regrettably, it is dependent on image quality and has lower temporal resolution. Pyramidal 3D datasets including LA volumes can be obtained with wide-angle mode from apical 4-chamber view. Offline analysis with a dedicated software is required for final analysis which takes 4-5 min for each atrium (55).

Three LA volumes as in 2D volumetric data could be calculated: LAVmax, LAVmin and LAV pre A (Fig. 5) (56). There is a paucity of data about 3D left atrial volume in both healthy subjects and patients with various diseases (Table 11) (55). From 3D speckle data several global or segmental unidirectional strain parameters could be calculated including radial (RS), longitudinal (LS) and circumferential strains (CS). (57). More complex multidirectional variables such as area strain (AS) and 3D strains could also be determined (57).

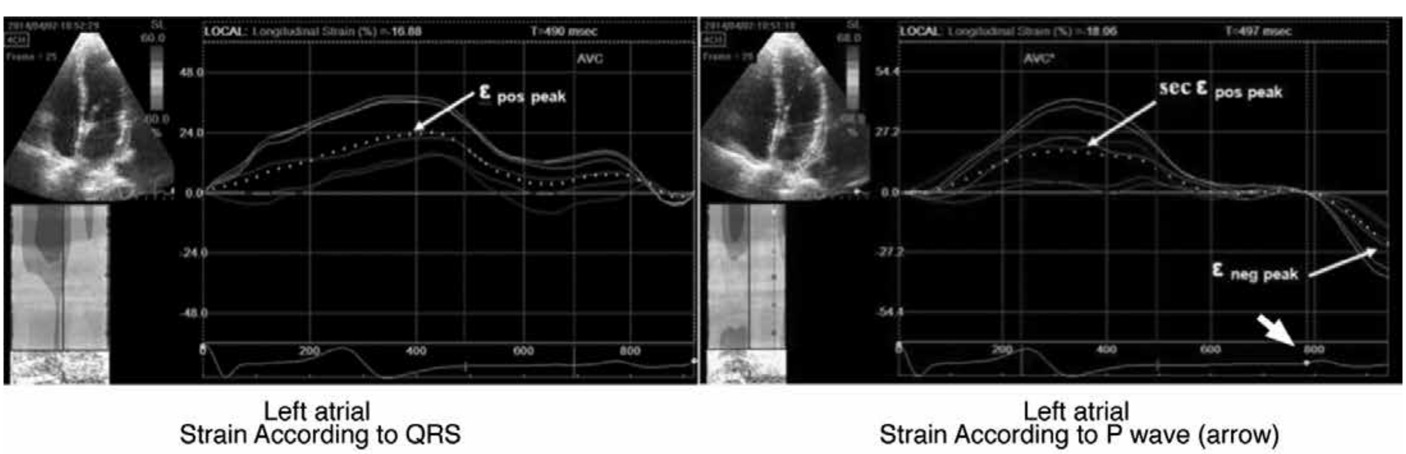

Figure 4. 2D -echocardiographic left atrial strain measurement

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Right atrium

Right ventricle, once forgotten chamber, has been gained attention from medical community but research about right atrium has been very scarce.

Right ventricular filling is provided by right atrium with its reservoir, conduit and booster pump functions. RA reservoir function predominates right ventricular filling under normal conditions with increased ventricular pressures favoring conduit function (58).

In chronic RV pressure overload, the RV diastolic function is impaired but systolic function may be preserved. RA compensated that with enhanced contractility and distensibility (59). A chronic volume overload state such as tricuspid

Anatomy

Right atrium has major anatomic landmarks as follows:

- Anteriorly located appendage

- Crista terminalis: A muscle bundle passes from vena cava superior to vena cava inferior at right atrial anteromedial wall.

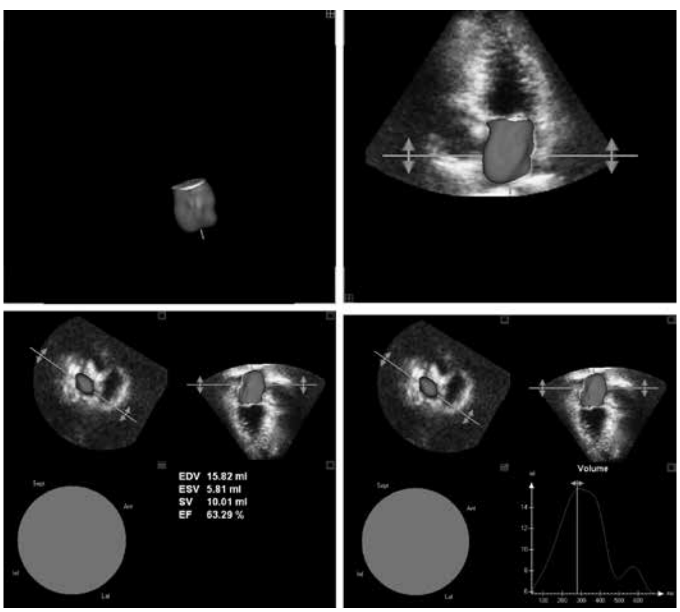

Figure 5. 2D-echocardiographic left atrial volume measurement

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Table 11. 3D left atrial volumes: normal reference ranges (95% confidence intervals) (55)

RT3DE	Males (n=75)	Females (n=84)	Total study group (n=159)
LAVi max, ml/m^2	15-42	15-39	15-41
LAVi min, ml/m^2	6-20	5-18	5-19
LAEF, %	46-77	44-80	45-79

3D - 3- dimensional, LAEF - left atrial emptying fraction, LAVi - left atrial volume index, RT3DE - real time 3-dimensional echocardiography

Crista terminalis is a boundary between venous portion and appendage.

- Cavotricuspid isthmus: An endocardial region delineated anteriorly by the annular attachment of septal and lateral tricuspid leaflets, posteriorly by the vena cava inferior rim and the Eustachian valve, laterally by the crista terminalis, and medially by the coronary sinus.

- Interatrial septum and foramen ovale regurgitation significantly reduces the RA reservoir phase mechanics (60).

Right atrial size and phasic function

Enlarged RA has prognostic importance in pulmonary hypertension, systolic heart failure, Eisenmenger syndrome and pulmonary embolism (61-65). RA size and function could be evaluated by similar 2D-echocardiographic methods as LA. Linear dimensions, volumetric methods and deformation imaging could be selected according to local expertise and availability.

RA linear dimensions, area and volume

RA volume instead of linear dimensions recommended for RA size evaluation (21). Major and minor axis linear dimensions taken from Apical 4-chamber view are shown in Table 12 (22). RA volumes are affected by gender and are smaller than LA volumes because of monoplane calculation compared to biplane LA volume determination (21).

RA 2D deformation analysis

Apical 4-chamber view should be used for speckle tracking based deformation imaging. Strain and strain rate calculation and derived parameters are same as for LA. If P wave on ECG was taken for reference point, following parameters could be measured: first negative peak ε (εneg) represents the atrial booster pump function, positive peak ε (εpos) corresponds to conduit function, and their sum (εtotal) represents reservoir function (66). In contrast, peak positive longitudinal atrial strain, early and late diastolic strain waves (εe and εa, respectively) are recorded according to QRS complex on ECG reference point (67). These correspond to reservoir, conduit, and booster pump

Table 12. Reference values for RA dimensions, area and volume index according to gender: Apical 4-chamber view measurement (22)

	Women	Men
Indexed RA minor axis dimension, mm/m^2	20.2 (3.0)	19.8 (2.8)
Indexed RA major axis dimension, mm/m^2	26.1 (3.2)	24.8 (2.5)
Indexed RA area, cm^2/m^2	7.8 (1.6)	8.3 (1.4)
2D RA volume index. ml/m^2 (Simpson)	19.0 (1.2)	22.5 (6.5)

*Data are presented as Mean (SD)

2D - 2-dimensional, RA - right atrial

functions respectively. There are no standardized cut-off values for right atrial strain but Padeletti et al. reported RA total strain value of 49 (13)% and RA strain during late diastole 18(6.38)% (67). Reported mean (SD) values for P wave based analysis were: total RA strain 44 (10)%, peak positive RA strain 27(9)% and peak negative strain -17(4)% (66). A decreased peak RA systolic strain was independently predictive of clinical outcomes in PAH (68).

RA volume - strain analysis based on three dimensional data

RA assessment with 3D echocardiography is a feasible and reproducible technique (66). Morenao et al showed that 3D RA volume values were higher than 2D volume values with poor correlation and agreement between two methods (69). Aune et al. (55) provided normal reference values for 3D RA volumes (Table 13) (55).

Future Directions

Echocardiographic examination of both atria underwent an evolutionary process from simple anteroposterior diameter measurement to sophisticated 3D volume strain analysis. Each step in this long way adds invaluable information to current understanding. 3D analysis holds promise for the future but many obstacles exist such as poor image quality and exclusion of some anatomic structures from the analysis. Right or left atrium specific software capable of feasible, accurate and reproducible analysis certainly required. 2D and 3D volumetric and speckle-based deformation imaging data have to be standardized with clear cut-off values. Combining data reflecting structural and functional properties of atrium (ie: volume and strain data) may provide early diagnosis of atrial problems.

That information could be used for effective treatment, or at least, for preventing or delaying disease processes.

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Table 13. 3D right atrial volumes: normal reference ranges (95% confidence intervals) (55)

RT3DE	Males (n=75)	Females (n=84)	Total study group (n=159)
RAVi max, ml/m^2	18-50	17-41	18-47
RAVi min, ml/m^2	7-22	5-18	5-20
RAEF, %	46-74	48-83	46-80

3D - 3- dimensional, RAEF - right atrial emptying fraction, RAVi - right atrial volume index, RT3DE - real time 3 -dimensional echocardiography

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