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REVIEW

The Evaluation of the Heart Failure Patient by Echocardiography: Time to go beyond the Ejection Fraction

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Abstract

Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood. The echocardiogram is the single most performed and useful study in these patients. This article reviews the role of the echocardiogram in the evaluation of the heart failure patient, without focusing on the left ventricle. The discussion includes the use of the echocardiogram in the assessment of the right ventricle and diastolic function and in detecting hemodynamic and morphologic changes in heart failure over a period of time. In addition, we highlight some of the limitations of echocardiography in the assessment of these patients.

Keywords: right ventricle; diastolic dysfunction; echocardiography; Doppler; heart failure

Introduction

There are approximately 5.7 million people in the United States who have a diagnosis of heart failure. The echocardiogram is the single most performed study in these patients. Quantification of the left ventricular (LV) chamber size and thickness, the evaluation for wall motion abnormalities, and the assessment of LV systolic function are important aspects of the echocardiogram and should be performed on every patient. However, the overall assessment of the heart function goes beyond measuring the ejection fraction and analysis of the left ventricle. This article reviews the role of the echocardiogram in the evaluation of the heart failure patient, without focusing on the left ventricle.

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Right Ventricular Size and Function

The right ventricle is sometimes referred to as "the forgotten ventricle" as more attention is focused on the left ventricle. The right ventricle is a complex structure which cannot be completely visualized in any single echocardiographic imaging window, thereby making its assessment more difficult than that of the left ventricle. The right ventricle plays an essential role in the morbidity and mortality of patients presenting with signs and symptoms of cardiac disease and noncardiac disorders that affect the heart [1, 2]. Important information can be garnered

by one paying careful attention to its size, structure, function, and associated hemodynamics [3].

The American Society of Echocardiography (ASE) has recommended that in all reported echocardiographic studies, the right heart should be examined with multiple acoustic windows, and the report should represent an assessment based on qualitative and quantitative parameters [4]. These parameters should include right ventricular (RV) size, right atrial (RA) size, and RV systolic function. In the assessment of RV systolic function, at least one of the following should be included: fractional area change (FAC), tricuspid annular plane systolic excursion (TAPSE), and RV index of myocardial performance, which is an index of global RV performance (RV index of myocardial performance is not discussed in this article). Estimation of the systolic pulmonary artery pressure (SPAP), which also includes estimation of the RA pressure on the basis of inferior vena cava (IVC) size and collapse, should also be documented. In many conditions, additional measurements such as pulmonary artery diastolic pressure (PADP) are indicated. The reference values for these recommended measurements are displayed in Table 1.

If three-dimensional (3D) echocardiography is available, use of it for measurements of RV volumes should be attempted as 3D imaging makes it easier to define the endocardial border, thereby enhancing morphologic information. Normal values for indexed RV area and volume for men and women are included in Table 1. There are some limitations to 3D echocardiographic imaging. Three-dimensional (3D) echocardiographic values of RV volumes need to be established in larger groups of subjects as reference values are limited by lack of published data [5]. The routine clinical use of 3D echocardiography is limited by the need for excellent-quality transthoracic data sets for accurate analysis. The technique can be used only in patients with stable sinus rhythm, since several beats are need for the recording. In addition, intraobserver and interobserver variability is still a limitation. Cardiac magnetic resonance imaging is an alternative imaging modality to consider when one is evaluating the right ventricle as it provides a unique opportunity to image the right ventricle in motion and in three dimensions without some of the limitations of echocardiography [6].

Measuring Right Ventricular Dimension

RV dimension is best estimated at end diastole, from a focused apical four-chamber view [7]. An image demonstrating the maximum RV diameter without foreshortening it should be used. It can be acquired

Table 1 Normal Measurements for Right Ventricular (RV) Chamber Size.

Parameters	Normal range	
RV basal diameter (mm)	25–41	
RV mid diameter (mm)	19–35	
RV longitudinal diameter (mm)	59–83	
RVOT1, PLAX diameter (mm)	20–33	
RVOT2, PSAX proximal diameter (mm)	21–35	
RVOT3, PSAX distal diameter (mm)	17–27	
RV wall thickness (mm)	1–5	
Parameters	**Men, normal range**	**Women, normal range**
RVOT EDA (cm^2)	10–24	8–20
RV EDA indexed to BSA (cm^2/m^2)	5–12.6	4.5–11.5
RV ESA (cm^2)	3–15	3–11
RV ESA indexed to BSA (cm^2/m^2)	2.0–7.4	1.6–6.4
RV EDV indexed to BSA (mL/m^2)	35–87	32–74
RV ESV indexed to BSA (mL/m^2)	10–44	8–36

BSA, body surface area; EDA, end-diastolic area; ESA, end-systolic area; PLAX, parasternal long-axis view; PSAX, parasternal short-axis view; RVOT, RV outflow tract.

by one ensuring that the crux and apex of the heart are in view as in Figure 1. The conventional apical four-chamber view focusing on the left ventricle results in considerable variability in how the right side of the heart is imaged. RV linear dimensions and areas may vary widely in the same patient with minor rotations in transducer position. An RV diameter greater than 41 mm at the base and greater then 38 mm at the mid level indicates RV dilatation. Similarly, a longitudinal dimension greater than 86 mm indicates RV enlargement. Qualitatively, the right ventricle should appear smaller than the left ventricle, usually no more than two thirds the size of the left ventricle in the standard apical view. RV liner measurements can also be measured from the parasternal long-axis and short-axis view as outlined in Figure 2.

The right ventricle dilates in response to chronic volume and/or pressure overload and with RV failure [8, 9]. Many heart failure patients will develop RV volume and pressure overload over a period of time. In general, the right ventricle adapts better to volume overload than to pressure overload. The right ventricle may tolerate volume overload for a long time without a significant decrease in RV systolic function. In contrast to volume-overload states, moderate to severe acquired pulmonary arterial hypertension often leads to RV failure [10]. Pressure overload of the right ventricle also may lead to RV ischemia, which may further aggravate

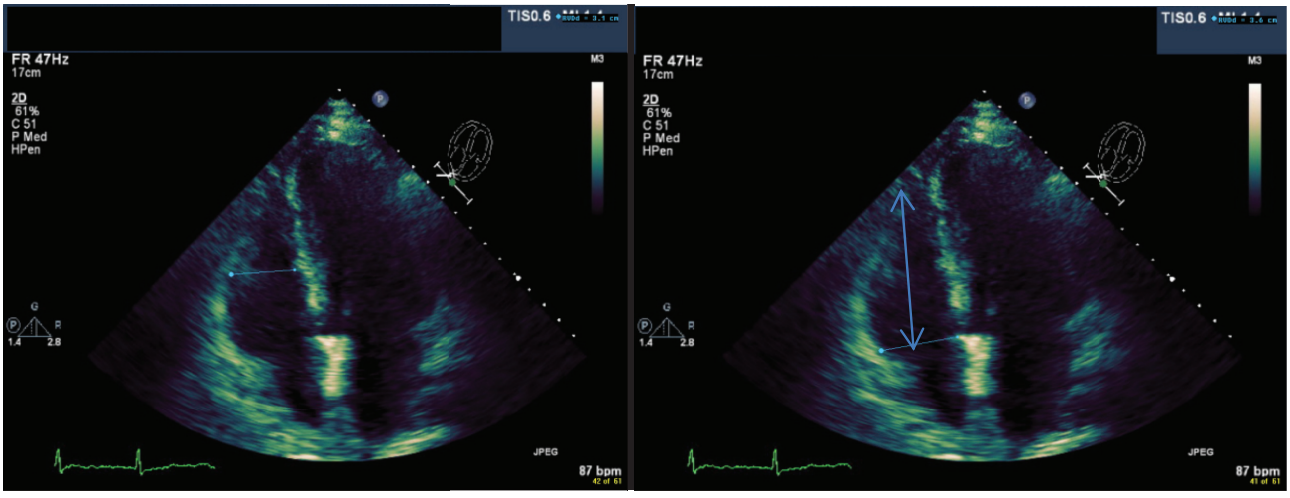

Figure 1 Measurement of Right Ventricular (RV) Diameter in the Apical Four-chamber View.
RV diameter measurement at the mid level (left). RV measurement at the base and longitudinal (right).

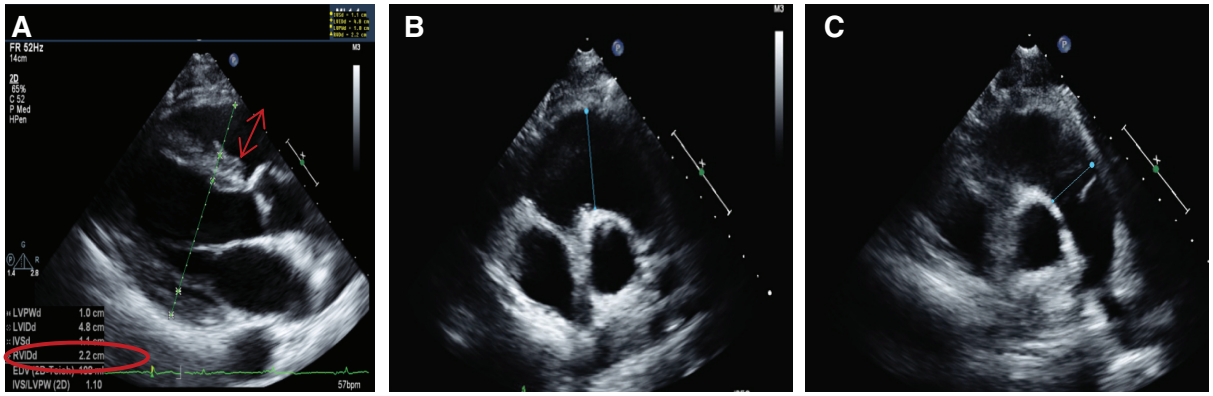

Figure 2 Measurement of Right Ventricular (RV) Diameter in the Parasternal Views.
Left: Parasternal long-axis view, RV outflow tract 1. Middle: Parasternal short-axis view, RV outflow tract 2. Right: Parasternal short-axis view, RV outflow tract 3.

ventricular dysfunction. Indexed RV end-diastolic diameter has been identified as a predictor of survival in patients with heart failure [9].

Quantitative Assessment of Right Ventricular Systolic Function

Per the ASE guidelines, there should be at least one attempt to quantitatively assess the RV systolic function in all echo report. The following are some of the quantitative methods suggested.

Tricuspid Annular Plane Systolic Excursion

TAPSE is easily obtainable and is a measure of RV longitudinal function. RV muscle fiber orientation results in contraction that occurs predominantly along the longitudinal plane. The measurement is taken from the lateral tricuspid annulus in two-dimensional (2D) M-mode and requires a good standard apical four-chamber window (Figure 3). The cursor is placed at the junction of the tricuspid valve plane and the free wall of the right ventricle. The data are averaged over five beats. The normal value for TAPSE is 17 mm or greater [11] and has shown good correlation with other measures used to estimate RV global systolic function, such as the radionuclide-derived RV ejection fraction, the 2D RV FAC, and the biplane Simpson 2D RV ejection fraction. There are three practical limitations that should be considered with regard to TAPSE. Some reference values are based on values obtained from normal individuals without a history of heart disease. The values are not indexed to body surface area or height, and therefore patients at either extreme may be misclassified as having values outside the reference ranges. Finally, it assumes that the displacement of this lateral annular segment in the apical four-chamber view is representative of the function of the entire right ventricle, an assumption that is not valid in some disease states or when there are regional RV wall motion abnormalities.

Two-Dimensional Fractional Area Change

An alternative method for assessing RV function is to use the FAC. The FAC is a surrogate of the RV ejection fraction.

The RV FAC is calculated as follows (Figure 4): (RV diastolic area – RV systolic area)/RV diastolic area.

The RV diastolic and systolic areas are traced in the apical four-chamber view. To ensure as accurate a measurement as possible, the entire right ventricle should be in the field of view during both systole and diastole, including the apex and the lateral wall. Trabeculations should be excluded when one is tracing the RV area. An RV FAC of 35% or greater is considered normal [7]. Measurement of the RV FAC has been studied in certain groups; for example, a typical LV assist device (LVAD) candidate has an RV FAC between 20% and 30%. Patients with an

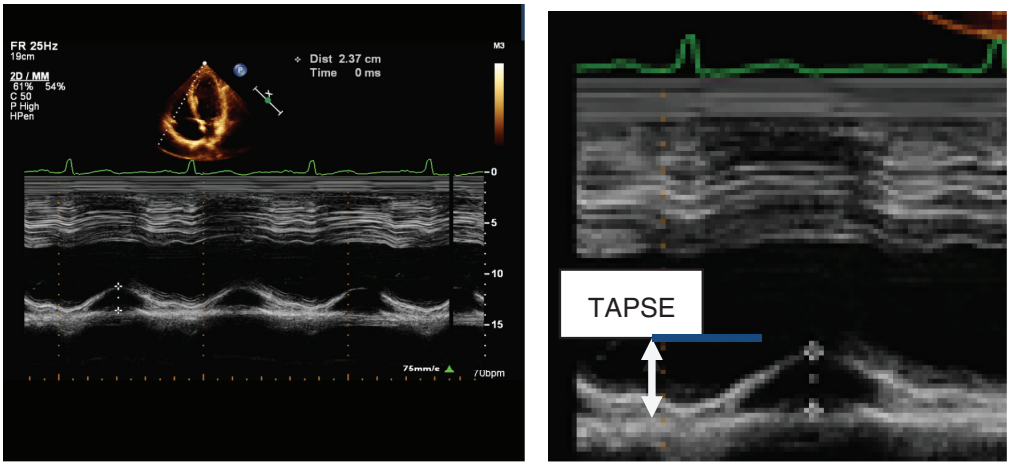

Figure 3 Tricuspid Annular Plane Systolic Excursion (TAPSE) M-mode Recording in a Patient with Preserved Right Ventricular Function.

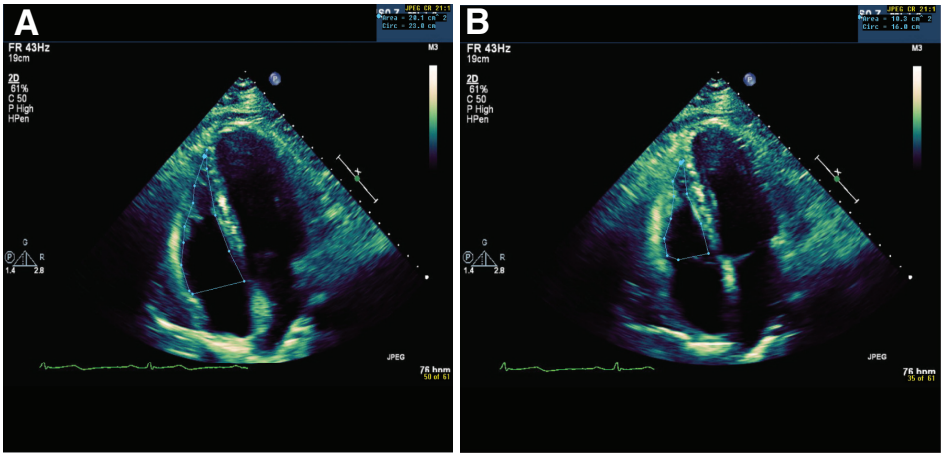

Figure 4 Fractional Area Change (FAC).
Here, the FAC is (20.1 cm^2 – 10.3 cm^2)/20.1 cm^2 = 49%. The endocardial border is traced in the apical four-chamber view from the tricuspid annulus along the free wall to the apex, then back to the annulus, along the interventricular septum at end diastole (A) and end systole (B).

RV FAC less than 20% are at risk of RV failure with the initiation of LVAD therapy [12].

Peak Tricuspid Annular Systolic Velocity

A quick and reliable method of measuring RV systolic function is by measuring the peak tricuspid annular systolic velocity (*S′*). This is achieved by tissue Doppler imaging (Figure 5). Tissue Doppler imaging is superior to blood flow Doppler imaging as it directly reflects myocardial function and is less subjected to preload changes. Similarly to TAPSE, it does not take into account RV outflow tract contraction and septal contribution to RV ejection. *S′* less than 10 cm/s indicates RV systolic dysfunction. *S′* has been shown to correlate well with other measures of global RV systolic function, regardless of pulmonary artery pressure [13].

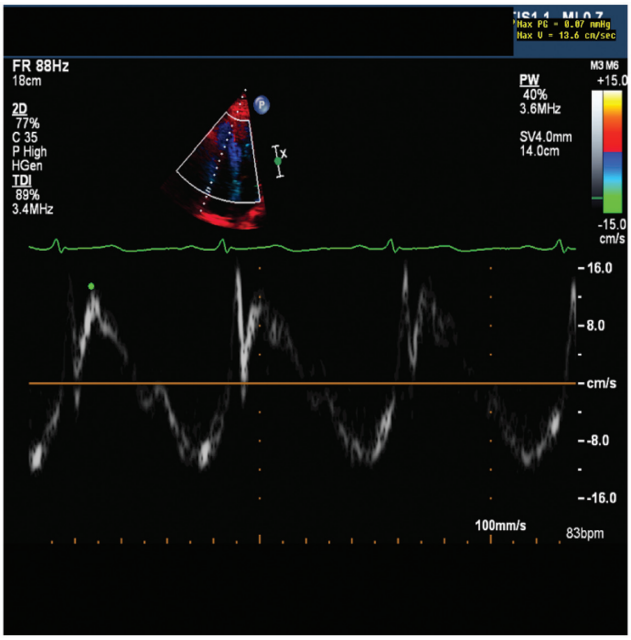

Figure 5 Peak Tricuspid Annular Systolic Velocity, *S′*.
S′ = 13.6 cm/s. Measured by tissue Doppler imaging from the lateral annulus of the tricuspid valve. The basal segment and the annulus should be aligned with the Doppler cursor to avoid errors when one is performing this measurement.

Estimation of Pulmonary Artery Systolic Pressure

The estimation of pulmonary artery systolic pressure (PASP) via echocardiography is important in the treatment of any patient with heart failure. This entails one measuring the peak tricuspid regurgitant jet velocity using the simplified Bernoulli equation and combining the measurement with the estimated RA pressure measurement. One can estimate the RA pressure by determining the diameter of the IVC and its inspiratory collapsibility (Figure 6). The PASP is equivalent to the RV systolic pressure in the absence of a gradient across the pulmonic valve or RV outflow tract.

Spectral continuous-wave Doppler signal of tricuspid regurgitation corresponding to the right

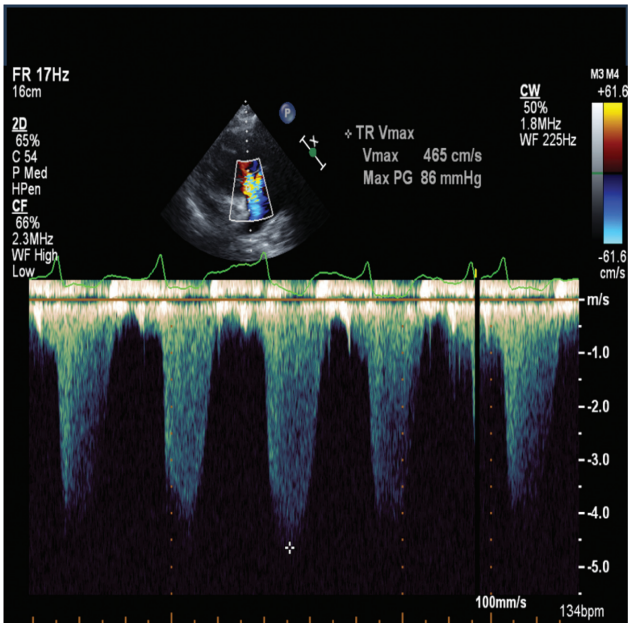

Figure 6 Doppler Echocardiographic Determination of Pulmonary Artery Systolic Pressure (PASP).

ventricular (RV)–right atrial (RA) pressure gradient. PASP was calculated as RV systolic pressure = $4V^2$ + RA pressure, where V is the peak velocity (in meters per second) of the tricuspid valve regurgitant jet, and RA pressure is estimated from the inferior vena cava diameter and respiratory changes. In this example, PASP is estimated as 86 + central venous pressure, or 101 mmHg, if RA pressure is assumed to be 15 mmHg.

The ASE recommends that the PASP should be estimated and reported in all subjects with reliable tricuspid regurgitant jets [7]. It is advised to obtain tricuspid regurgitation signals from several windows as velocity measurements are angle dependent. The signal with the highest velocity should be used in the calculation. If the signal is weak, it may be enhanced with agitated saline or blood-saline contrast. Careful attention of where the peak signal is measured should be confirmed by the echocardiographer to avoid overestimation of the spectral envelope, which would overestimate the PASP. There is the potential for error in the measurement of the estimated PASP in patients with severe tricuspid regurgitation. The tricuspid regurgitation spectral Doppler envelope may be cut off early (called the "V wave cut-off sign") because of an early equalization of RV and RA pressures, which would underestimate the PASP calculated with the simplified Bernoulli equation.

In practice, when one is assessing pulmonary hemodynamics via echocardiography, PASP is more commonly measured and reported than are the mean pulmonary artery pressure and PADP. Normal resting PASP corresponds to a peak tricuspid regurgitation gradient of 2.8 m/s or less to 2.9 m/s or a peak systolic pressure of 35 or 36 mmHg, assuming a RA pressure of 3 (0–5) mmHg [14]. It is recommended that further evaluation of patients with dyspnea without a known cause should be performed if the estimated RV systolic pressure is greater than 40 mmHg [15].

Estimating the Right Atrial Pressure

The subcostal view allows imaging and measurement of the IVC and assessment of the inspiratory collapsibility. According to the ASE guidelines [7], the diameter of the IVC should be measured just proximal to the entrance of hepatic veins at the end of expiration. The entrance of the hepatic vein usually lies approximately 0.5–3.0 cm proximal to the ostium of the right atrium. For simplicity and uniformity of reporting, the ASE also recommends that specific values of RA pressure, rather than ranges, should be used in the determination of SPAP. If the diameter of the IVC is less than 2.1 cm and collapses by more than 50% with a sniff, the RA pressure is then estimated to be normal and should be recorded as 3 mmHg (range 0–5 mmHg). If the diameter of the IVC is greater than or equal to 2.1 cm and collapses by more than 50% with a sniff, this suggests a high RA pressure of 15 mmHg (range 10–20 mm Hg). In scenarios where the IVC diameter and collapse do not fit this paradigm, an intermediate value of 8 mmHg (range 5–10 mmHg) may be used or, preferably, other indices of RA pressure should be integrated to downgrade or upgrade the pressure to the normal, lower or higher value of RA pressure. If the IVC is greater than 2.1 cm in diameter and does not collapse at all with sniff, an RA pressure of 20 mmHg can be assigned. In normal young athletes, the IVC may be dilated in the presence of normal RA pressure. In addition, the IVC is commonly dilated and may not collapse in patients on ventilators. Caution should be exercised in these cases and others in an effort to not overestimate the RA pressure. Although a distended IVC usually denotes elevated RA pressures, in patients with

otherwise normal examination results, reassessment of the IVC size and collapsibility in the left lateral position may be useful to avoid overestimation of the RA pressure.

Estimation of Pulmonary Artery Diastolic Pressure

PADP can be estimated from the end-diastolic pulmonary regurgitation velocity and the estimated RA pressure. This is done by use of the simplified Bernoulli equation to quantify the pulmonary artery to RV gradient, PADP = 4 × (end-diastolic pulmonary regurgitant velocity)^2 + RA pressure. The PADP increases disproportionately in pulmonary hypertension, causing a higher pressure gradient and, subsequently, an increased end diastolic regurgitant velocity. Ristow et al. found [16] that an increase in the pulmonary regurgitation end-diastolic pressure gradient of more than 5 mmHg was associated with RV systolic dysfunction, diastolic dysfunction, higher New York Heart Association functional class, lower metabolic equivalents achieved on treadmill testing, and elevated brain natriuretic peptide concentration.

Mean Pulmonary Artery Pressure

One can estimate the mean pulmonary artery pressure by measuring the pulmonary artery acceleration time (AT) using the Mahan formula, by using the peak early PR velocity, or one can derive it from the systolic and diastolic pulmonary pressures. It is recommended to use more than one method when one is estimating the mean pulmonary artery pressure:

Method 1, Mahan formula: mean pulmonary artery pressure = 79 – (0.45 × AT). In patients with ATs less than 120 ms, the following formula for the mean pulmonary artery pressure should be used instead [17]: mean pulmonary artery pressure = 90 – (0.62× AT). AT is measured by pulsed wave (PW) Doppler echocardiography of the pulmonary artery in systole.

Method 2, peak early PR velocity [18]: 4 × (early PR velocity)^2 + estimated RA pressure (Figure 7B).

Method 3, systolic and diastolic pulmonary pressures. Once systolic and diastolic pressures are known, the mean pulmonary artery pressure may be estimated by the standard formula: mean pulmonary artery pressure = 1/3(SPAP) + 2/3(PADP).

Diastolic Function

It is important to assess LV diastolic function in all echocardiographic studies as diastolic dysfunction develops quite early in many cardiac diseases and

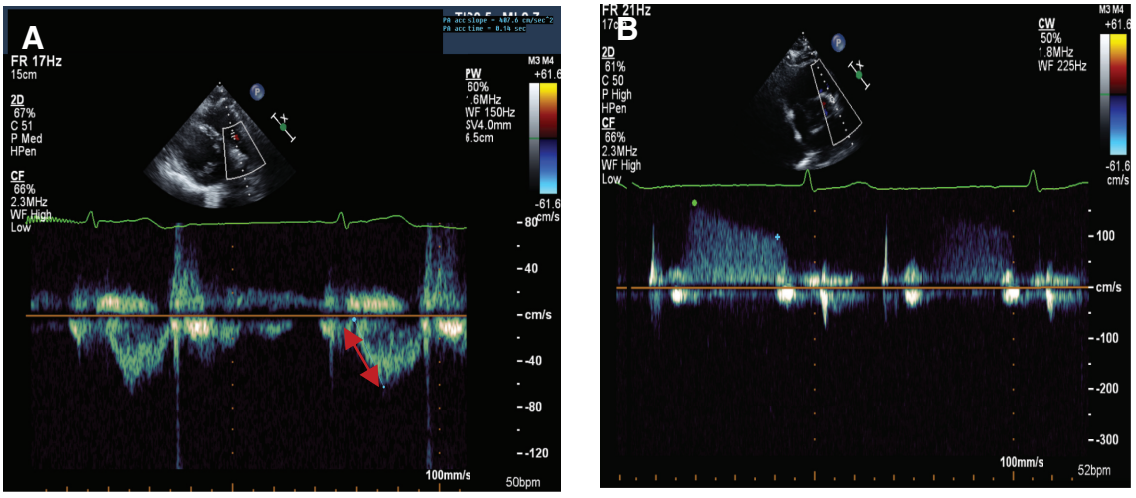

Figure 7 Measurement of Mean Pulmonary Artery Pressure by Means of Acceleration Time (AT) and Early PR Velocity. (A) The shorter the AT (measured from the onset of the Q wave on electrocardiography to the onset of peak pulmonary flow velocity), the higher the pulmonary vascular resistance and the pulmonary artery pressure. If the heart rate is in the range from 60 to less than 100 beats/min, the normal AT is more than 130 ms. (B) Image illustrating peak early PR velocity.

causes an elevation of LV filling pressures. Echocardiographic measurements of diastolic function can yield important prognostic information [19–28].

Among all patients with heart failure, diastolic heart failure or heart failure with preserved ejection fraction is as prevalent as systolic heart failure or heart failure with reduced ejection fraction [29, 30]. In patients with heart failure with preserved ejection fraction, the LV ejection fraction is normal or near normal but higher filling pressures are needed to obtain a normal end-diastolic volume of the left ventricle. Heart failure with preserved ejection fraction is increasing in prevalence with the aging of the population, and morbidity and mortality rates are comparable to those of heart failure with reduced ejection fraction [31–33]. Women are more often affected than men, especially patients with long-standing hypertension. Diastole in the cardiac cycle should not be regarded as a secondary process as it is as important as systole. Diastolic dysfunction tends to be chronic and can progress. It can be short term, as in the case of an acute myocardial infarction. Several techniques can be used to assess diastolic function, but echocardiography is the technique of choice.

There are many methods by which diastolic function can be assessed by echocardiography. This section focuses on the importance of mitral inflow, the changes with the Valsalva maneuver, pulmonary venous flow, tissue Doppler annular early and late diastolic velocities (tissue Doppler imaging), and isovolumic relaxation time (IVRT). Other means of assessing diastolic dysfunction including color M-mode flow propagation velocity, deformation measurements, LV untwisting, and diastolic stress test are beyond the scope of this article and further reading from the ASE guidelines is recommended.

Normal Diastolic Function and Mechanisms of Diastolic Dysfunction

Normal diastolic function is the complete and efficient filling of the left ventricle at physiologic pressures. Diastole starts at aortic valve closure and includes LV pressure fall, rapid filling, diastasis, and atrial contraction. The following terms will be useful as they are universally used in describing diastolic function:

E wave: This is early LV diastolic filling. Following isovolumic relaxation, the mitral valve opens and most of LV filling occurs in the first third of diastole, during rapid early filling. This is due to elastic recoil and active relaxation of the left ventricle. It is measured by PW Doppler echocardiography.

A wave: Atrial systole contributes only a relatively small amount of LV filling. Therefore, the peak A wave velocity is less than that of the E wave in an individual with normal function.

Deceleration time: This is the interval from the peak of the E wave velocity to its extrapolation to the baseline. To evaluate E and A waves and the deceleration time, the PW Doppler sample volume is placed at the mitral valve leaflet tips in the apical four-chamber view, and is then measured over at least three consecutive cardiac cycles (five in atrial fibrillation).

E′ or e′: As the left ventricle expands to accommodate the inflow of blood, there is a simultaneously brisk motion of the mitral annulus. This process is recorded with tissue Doppler imaging. Only a minute amount of filling occurs in diastasis (mid diastole), the duration of which is dependent on heart rate. Mid diastole significantly shortens or even disappears with increasing heart rate.

IVRT: This is the interval from aortic valve closure to mitral valve opening. It provides information on LA pressure and rate of early active LV relaxation. In general, it parallels the deceleration time. When relaxation is prolonged, mitral valve opening is delayed and IVRT is increased. Conversely, whenever LA pressure is elevated, mitral valve opening will occur earlier and IVRT will be shortened.

Pulmonary venous flow: The pulmonary vein systolic component (PVs) to pulmonary vein diastolic component (PVd) ratio is measured by PW Doppler echocardiography. Changes in the PVs/PVd ratio correlate with the stages of diastolic dysfunction. Further details regarding acquisition, obtaining measurements, normal values, clinical applications, and its limitations are discussed in more detail later.

Pulmonary venous flow: A – Ar is also measured by PW Doppler echocardiography. The difference in the duration of the two waves reflects LV filling pressure; where the retrograde pulmonary venous A wave duration (Ar) is typically shorter than the mitral A wave duration.

Further Understanding of Diastolic Dysfunction

The mitral E-wave velocity is related directly to the LA pressure and inversely to LV relaxation. In patients who have systolic heart failure, increased filling pressure (high LA pressure) and reduced LV relaxation coexist, so the E-wave velocity alone correlates poorly with mean LA pressure. One can more accurately estimate LA pressure (surrogate of mean wedge pressure) by correcting the E-wave velocity for any abnormal LV relaxation. The peak early diastolic mitral annular velocity (E') on tissue Doppler imaging has been validated as measures of LV relaxation and has been combined with E-wave velocity to estimate pulmonary capillary wedge pressure [34]. Early diastolic motion of the mitral annulus is influenced by the motion of longitudinally oriented myocardial fibers. The lengthening of these fibers in diastole results in mitral annular descent toward a relatively fixed apex. The velocity of early mitral annular (E') descent reflects LV relaxation and is independent of LA pressure. As the E-wave velocity is determined by the LV relaxation and LA pressure, correction of the E-wave velocity for LV relaxation is paramount. To obtain E' and A' tissue velocities, images are recorded from the apical four-chamber view with the sample volume placed 1–2 cm within the mitral annulus; septal then lateral or vice versa. The ASE recommends use of the average E' velocity obtained from the septal and lateral sides of the mitral annulus for the prediction of LV filling pressures [35].

Normal Parameters

E/A ratio: Normal 1.1–1.5

Deceleration time: 160–240 ms. May be lower in the young.

E/E' ratio: normal. A septal E/E' ratio of less than 8 is associated with normal LV filling pressures [36].

IVRT: 76 ± 13 ms (>40 years); 69 ± 12 ms (<40 years)

Pulmonary vein A wave flow reversal: <25 cm/s

PVs2 ≥ PVd (PVs2 may be lower than PVd in the young)

No anatomic abnormalities

Stages of Diastolic Dysfunction

Diastolic dysfunction progresses as a continuum from a mild (grade 1) stage to a more advanced stage, eventually becoming irreversible (grade 4) if the underlying disease process is left untreated. Not all patients progress from one grade to another linearly along the pathway. In many cases, reversal to a lower grade can be achieved with optimization of medical treatment, such as weight loss, good blood pressure control, or use of diuretic therapy to decrease preload. These stages have certain pathophysiologic characteristics, which are summarized below (Figures 8 and 9).

Abnormal Function

Three patterns or stages indicate abnormal diastolic filling. In addition, there is fourth stage, which has the same pattern as stage III but is termed "irreversible restrictive."

Stage I: Impaired Early Left Ventricular Relaxation

Reduced LV filling in early diastole.

Significance: Impaired (slow) early LV relaxation.

Signs and symptoms: None at rest.

Functional status: Mild impairment.

Left atrium: Usually normal dimension (may be hypercontractile).

Mitral flow velocity during atrial systole is increased. The auscultatory equivalent is S4.

Filling pressure, E/E' ratio: usually normal at rest.

PW Doppler findings:

E/A ratio less than 1.0 (A wave is now larger through a combination of increased atrial preload and a more forceful atrial contraction)

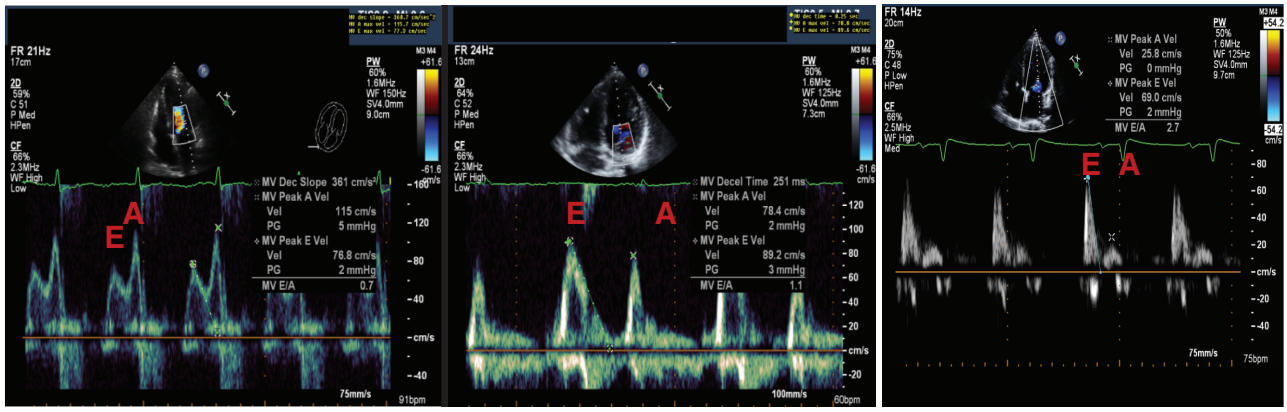

Figure 8 Transmitral Inflow Doppler Spectral Patterns.
Left: Grade 1 diastolic dysfunction. The *E*/*A* ratio is reversed on the mitral inflow echocardiogram. Middle: Grade 2, diastolic dysfunction (similar to a normal transmitral inflow pattern). Frequently, there is a mid-diastolic flow due to significant impairment of myocardial relaxation. With the Valsalva maneuver, *E* and *A* velocities both decrease in combination and increase in deceleration time if this recording is truly normal. Right: Grade 3 diastolic dysfunction. Restrictive filling pattern with a short deceleration time less than 160 ms.

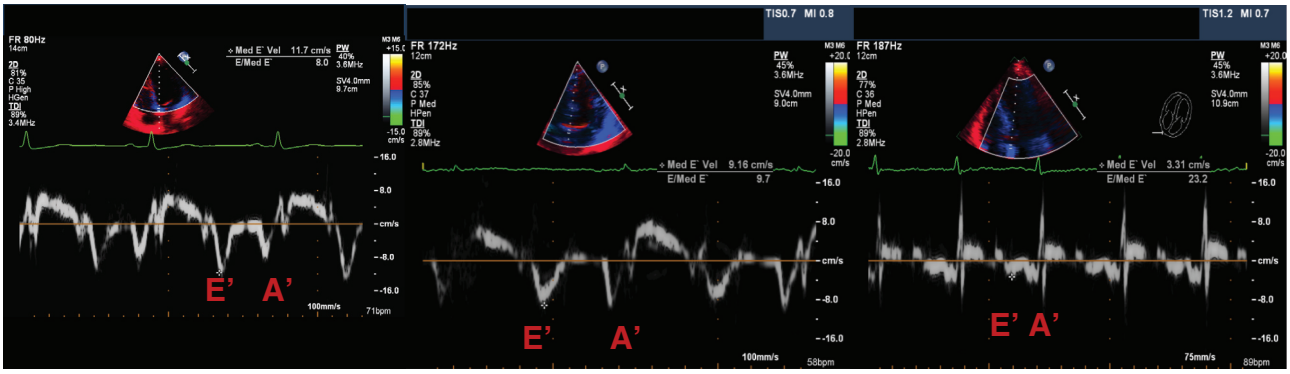

Figure 9 Mitral Annulus Tissue Doppler Imaging Patterns, where *E′* is the Early Annulus Velocity and *A′* the is Late Annulus Velocity.
Left: Normal tissue Doppler imaging. *E′* is greater than *A′* in a normal pattern. In all abnormal patterns, *A′* is greater than *E′*. Middle: Pattern usually seen with grade 1 or 2 diastolic dysfunction. Right: Low *E′* and *A′* velocity in a patient with grade 3 diastolic dysfunction. *E′* is usually reduced to less than 7 cm/s and even as low as 5 cm/s or less.

Deceleration time longer than 240 ms

IVRT longer than 90 ms

Pulmonary vein atrial (PVa) velocity less than 25 cm/s

PVs2 >> PVd

Stage II: Pseudonormalization

Significance: Suggests impaired (slow) early LV relaxation with decreased LV compliance.

Signs and symptoms: Exertional dyspnea.

Functional status: May have moderate impairment.

*Left atrium: Enlarged and hypocontractile.[1]

**E′* is usually less than 7 cm/s.

*Filling pressures, septal *E*/*E′*: may be increased. A ratio greater than 15 is associated with increased filling pressures [36].

PW Doppler findings:

E/*A* ratio 1.0–1.5

Deceleration time 160–240 ms

[1] An asterisk indicates echocardiographic features which can differentiate normal from pseudonormal.

IVRT 76 ± 13 ms (>40 years), 69 ± 12 ms (< 40 years)

*PVa velocity greater than 25 cm/s; may be large

*PVs2 < PVd

At stage II, the effects of impaired early LV relaxation on early diastolic filling are now opposed by the elevated left atrial (LA) pressure, and the early diastolic transmitral pressure gradient and mitral flow velocity pattern return to normal. This stage is referred to as "pseudonormalization," indicating that although the mitral inflow pattern appears normal, LV filling pressures are elevated. In addition, in many patients, LV end-diastolic filling pressure is elevated and there is 2D echocardiographic evidence of structural heart disease such as an increase in LA size, decreased ejection fraction, or LV hypertrophy. A decrease in preload such as that resulting from the patient performing the Valsalva maneuver may be able to unmask the underlying impaired LV relaxation in patients with true stage II diastolic dysfunction.

Stage III: "Restrictive" Filling Pattern (Reversible)

Significance: Severe decrease in LV compliance and impaired (slow) early LV relaxation

Signs and symptoms: Dyspnea on minimal exertion

Functional status: Marked impairment

Left atrium: Enlarged and hypocontractile

Filling pressures, E/E': Markedly increased

PW Doppler findings:

E/A ratio greater than 2.

Deceleration time less than 160 ms.

IVRT less than 60 ms.

PVa velocity 35 cm/s or greater. This occurs because pulmonary venous flow during systole is greatly reduced compared with diastolic flow (variable, depending on atrial systolic function).

PVs2 << PVd.

Ar- A greater than 30 ms. Retrograde pulmonary venous A-wave duration (Ar) is typically longer than the mitral A-wave duration, consistent with elevated filling pressures.

Mitral annulus E' is reduced to less than 7 cm/s and may even be as low as 5 cm/s or less.

E/E' is usually greater than 15.

Stage III represents a severe decrease in LV chamber compliance as there is further deterioration in diastolic function. Diastolic filling pressures are elevated. Patients are markedly symptomatic and demonstrate a severely reduced functional capacity. Despite the presence of impaired LV relaxation, the markedly elevated LA pressure results in a high velocity of early diastolic filling, which stops abruptly because of an abnormally rapid rise in ventricular pressure and atrial dysfunction. In some patients, this stage may be reversible. The stage could revert to impaired LV relaxation or the pseudonormalization stage by any intervention which lowers the LA pressure and reduces the LA-LV pressure gradient such as preload reduction with diuresis. As expected, there is 2D echocardiographic evidence of structural heart disease.

Stage IV: "Restrictive" Filling Pattern (Irreversible)

The diastolic pattern can become irreversible, but technically speaking with the advent of the continuous-flow LVADs and their improvement in systolic and diastolic function [37, 38], this pattern could become reversible after some time. This is due to the impact of continuous-flow LVADs on myocardial unloading and remodeling improving hemodynamics over a period of time [39–41].

In the grade 4 pattern, preload reduction or Valsalva maneuver no longer leads to an improvement in the filling pattern. Volume management in these patients is difficult as maintaining a balance between volume overload and hypoperfusion provides a challenge that is tedious for even the most seasoned clinician. If the restrictive filling pattern does not change with the Valsalva maneuver, reversibility cannot be excluded because the Valsalva maneuver may not be adequate or filling pressure may be too high to be altered by the maneuver.

Pulmonary Venous Flow Patterns

Measurement of the pulmonary vein flow velocity is performed in the apical four-chamber view with PW Doppler echocardiography. It aids in the assessment of LV diastolic function [42]. It is recorded at the junction of the pulmonary veins and left atrium with color flow imaging being useful for the proper location of the sample volume in the right upper pulmonary vein. A 2 to 3-mm sample volume is placed about 5 mm into the pulmonary vein and superior angulation is often required for optimal recording of the spectral waveforms. Measurements should be taken over three consecutive cycles at the end of expiration.

Measurements

Pulmonary venous flow consists of three main components: a peak systolic anterograde (PVs) wave, a peak anterograde diastolic (PVd) velocity and the peak retrograde wave (Ar) in late diastole, corresponding to atrial systole. The ratio of the peak anterograde velocities in systole and diastole is reported as the PVs/PVd ratio (the normal value is greater than 1). There are two systolic velocities (PVs1 and PVs2), which are most noticeable when there is a prolonged PR interval as in the case of bradycardia or first-degree atrioventricular block. In such cases, PVs2 should be used to compute the ratio of peak systolic to peak diastolic velocity [43, 44]. A decrease in LA compliance and an increase in LA pressure decrease the PVs velocity and increase the PVd velocity, resulting in a PVs/PVd ratio less than 1. Shortening of the deceleration time of the PVd velocity to less than 150 ms occurs as pulmonary capillary wedge pressure increases [45]. The peak velocity and duration of the pulmonary vein atrial flow reversal increase with higher LV end-diastolic pressure [46]. For patients in atrial fibrillation, there is blunting of the PVs wave (as PVs1 becomes lost and PVs2 is usually smaller than that of the PVd wave) and absence of the Ar velocity.

Normal Values and Clinical Applications

Pulmonary venous inflow velocities (Figure 10) are influenced by age. Normal young subjects younger than 40 years usually have prominent PVd velocities, reflecting their mitral E waves.

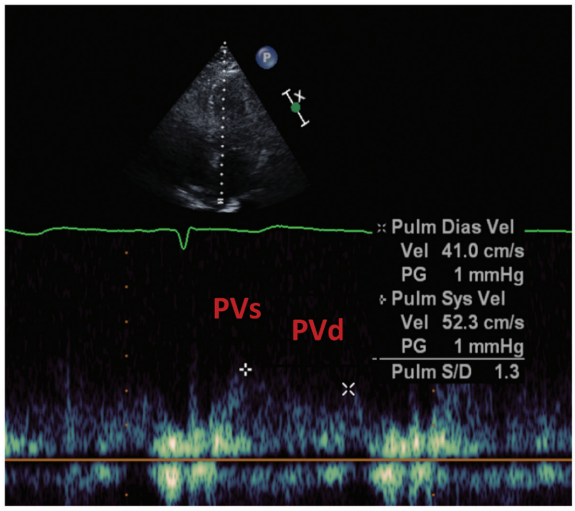

Figure 10 Pulmonary Venous Flow by Doppler Echocardiography, where PVs is Peak Systolic Anterograde Velocity and PVd is Peak Diastolic Anterograde Velocity.

With increasing age, the PVs/PVd ratio increases. In normal subjects, Ar velocities can increase with age but usually do not exceed 35 cm/s. A higher value suggests increased LV end-diastolic pressure [47]. The Ar – A duration difference is useful as it is the only age-independent indication of LV A-wave pressure increase [47]. This increase in LV end-diastolic pressure is the first hemodynamic abnormality seen with diastolic dysfunction.

The Left Atrium

In the assessment of LV diastolic function, measurement of LA size and volume is important (Table 2). As the left atrium remodels and enlarges, in many cases diastolic dysfunction becomes more evident. LA size should be measured at the end of LV systole in the cardiac cycle, when it is at its greatest dimension. The most widely used linear dimension is the LA anteroposterior (AP) measurement in the parasternal long-axis view with M-mode echocardiography or, preferably, 2D echocardiography. Measurement of LA size can provide prognostic information [48–51]. When one is acquiring images to measure LA size and volumes, care should be taken to avoid foreshortening of the left atrium. One corrects the effect of different body surface areas on LV volume with the use of an indexed value

Table 2 Normal Measurements of the Left Atrium.

	Men	Women
AP dimension (cm)	3.0–4.0	2.7–3.8
AP dimension index (cm/m^2)*	1.5–2.3	1.5–2.3

AP, anteroposterior.
*Indexed to body surface area.

by dividing LA volume by the patient's body surface area. The newly recommended upper normal indexed LA volume, regardless of age and sex, is 34 mL/m^2 [4]. An LA volume index of 34 mL/m^2 or greater is an independent predictor of death, heart failure, atrial fibrillation, and ischemic stroke [52]. LA volume reflects the cumulative effects of filling pressures over time. The most accurate measurements are obtained via the apical four-chamber view (Figure 11) and two-chamber view [4].

When one is assessing the LA size, measurement of LA volume is recommended over measurement of LA size as LA volume has been shown to be a better prognostic variable in a variety of cardiac disease states than measurement of LA anteroposterior diameter [53, 54] or LA area. As the biplane disk summation technique incorporates fewer geometric assumptions, it should be the preferred method to measure LA volume in clinical practice. The ASE recommends use of this method [52].

Right Atrial Measurements

The right atrium can be visualized in several views. Its size and function are not as well studied as those of the other chambers. It is commonly enlarged in patients with disorders which cause RV volume and pressure overload and RV failure. For clinical purposes, the visual comparison of RA to LA size in the apical four-chamber view is most commonly used to assess if there is RA enlargement. Several recent studies have provided normal values of RA dimensions for men and women [55, 56]. Measurement of RA volume can be performed, but its value is underestimated with 2D echocardiographic techniques compared with 3D echocardiography [57, 58]. The ASE recommends the single-plane area-length or disk summation techniques in a dedicated apical four-chamber view (Figure 11) when one is assessing RA size and RA volume [4]. The normal ranges for 2D echocardiographic RA volume are 25 ± 7 mL/m^2 in men and 21 ± 6 mL/m^2 in women.

In patients presenting with heart failure symptoms who are found to have a preserved ejection fraction, valvular heart disease, constrictive pericarditis (diastolic pericardial heart failure), and restrictive cardiomyopathy should be considered as well.

Conclusion and Take-Home Message

Heart failure is a complex syndrome characterized by progressive decline in the function of the left ventricle, low exercise tolerance, and increased mortality and morbidity. LV diastolic dysfunction plays a major role in heart failure and in the progression of most cardiac diseases.

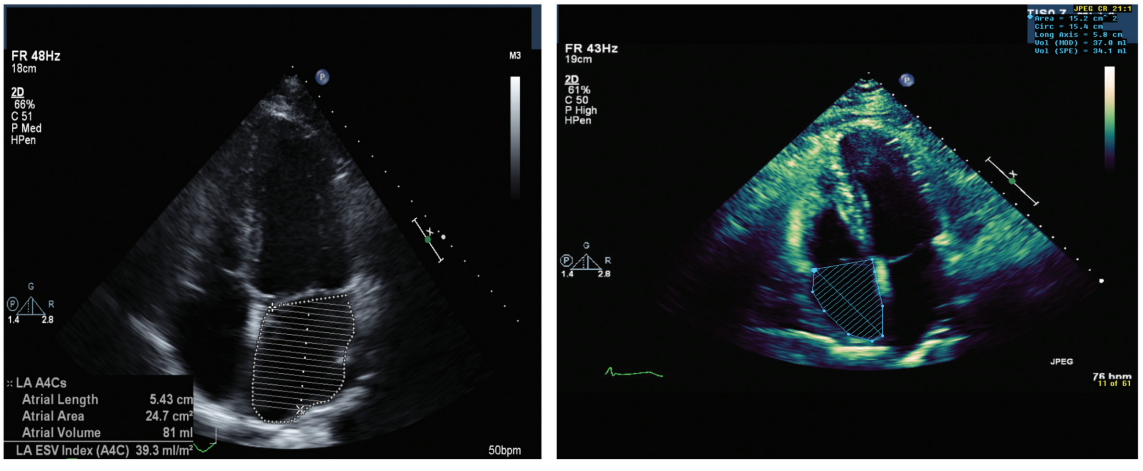

Figure 11 Volume Measurement of the Left Atrium (left) and Right Atrium (right) in the Apical Four-chamber View.

Use of echocardiography to assess diastolic dysfunction in these patients can assist with guiding their medical treatment. In addition, understanding how the right side of the heart functions is crucial. Many of these patients will develop pulmonary hypertension over a period of time; the echocardiogram is a reliable noninvasive tool for this assessment, but it is time to go beyond the LV ejection fraction.

Conflict of interest

The authors declare no conflict of interest.

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