The concepts for the assessment of left ventricular (LV) diastolic function were established in the cardiac catheterization laboratory and necessitate the use of high fidelity pressure and conductance catheters. The most recent [1] set of criteria (Figure 1) for diagnosing diastolic heart failure (DHF) include the presence of increased LV filling pressures (mean wedge pressure >12 mmHg, or LV end diastolic pressure >16 mmHg), prolonged time constant of LV relaxation (tau >48 ms), and increased LV stiffness (b >0.27). While the above measurements are determined invasively, a noninvasive approach is feasible and can be of value. This article will discuss the application of echocardiography (Table 1) to drawing conclusions about LV diastolic function.

Mitral Inflow

Mitral inflow remains the cornerstone among existing echocardiographic methods. Flow is recorded by Pulsed-wave (PW) Doppler using a 1-2 mm sample volume placed at the level of the annulus then at the mitral valve leaflets tips. Adjustment of gain and filter is essential to having clear signals from which velocity and time measurements are obtained [2]. At the level of tips, peak early (E) diastolic and late (A) diastolic velocities are measured as well as the deceleration time (DT) of E velocity. In addition, isovolumetric relaxation time (IVRT) can be recorded by continuous wave (CW) Doppler by placing the sample volume midway between LV outflow tract and mitral leaflets. With normal LV relaxation, predominant flow across the valve occurs in early diastole (E/A ratio >1); DT is <200 ms; and IVRT is <80 ms. However the values are age dependent, and in individuals older than 60 years of age, the E/A ratio is usually <1, whereas DT (>200 ms) and IVRT (>90 ms) are prolonged.

With impaired LV relaxation and normal filling pressures, an impaired relaxation pattern is observed which can be identical to that observed in healthy octogenarians. However if left atrial pressure is increased (which frequently occurs as a compensatory mechanism that maintains LV filling and stroke volume), the E/A ratio increases, and DT as well as IVRT shorten (pseudonormal filling). When E/A ratio is ≥2, and/or
DT <160 ms, LV filling pattern is described as restrictive [3]. Importantly, this pattern is predictive of clinical events in patients with heart failure and acute myocardial infarction. This is particularly true when this restrictive LV filling pattern persists despite adequate medical therapy [4, 5].

It should be noted that measurements of IVRT and peak acceleration rate of mitral diastolic velocity are still predictive of filling pressure in the setting of atrial fibrillation [6] even when LVEF is normal. On the other hand, DT (Figure 2) is accurate only in patients with depressed EF [6, 7]. Because of variations in cycle length, measurements are most accurate when obtained from 10 cardiac cycles, but reasonable accuracy can be achieved with 3–5 cardiac cycles or a single measurement provided the cycle chosen has an RR interval that matches the average heart rate during the echocardiographic examination [6].

**Pulmonary Venous Flow**

Pulmonary venous flow is recorded using PW Doppler in the apical 4-chamber view. A 1-2 mm sample volume is placed in the right upper pulmonary vein, guided by color Doppler. Pulmonary venous flow signals can be enhanced by intravenous contrast, which should be kept in mind should contrast be needed for other reasons as for endocardial border detection.

Forward flow into the left atrium occurs in systole (S) and diastole (D), with reverse flow into pulmonary veins during LA contraction (Ar) as shown in Figure 3. In normal young subjects, D velocity is higher than S velocity, and Ar duration is shorter than mitral A duration (measured at the level of the mitral annulus).

With diastolic dysfunction, S/D ratio is usually >1, and Ar velocity is increased to >35 cm/s. Specifically, when LV end diastolic pressure is increased, Ar duration is prolonged and is more than 30 ms longer than mitral A duration [8-10]. With a further increase in LV filling pressures, namely mean LA pressure, S/D ratio is <1, and the proportion of LA filling during systole is <40% [11]. In patients with atrial fibrillation, the deceleration time of D velocity (≤220 ms) can be used to predict LV filling pressures [12].

**Flow Propagation Velocity (Vp)**

Vp is acquired by color M-mode in the apical 4-chamber view (Figure 4). The M-mode cursor is

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![Fig. 2. Deceleration time in atrial fibrillation](image)

Correlation between LV filling pressures and deceleration time (DT) in atrial fibrillation. The relation in patients with EF <45% is shown with a solid line and closed circles. The relation in patients with EF ≥45% is shown as an interrupted line and open circles. Modified after reference 6.

![Fig. 3. Pulmonary vein velocity](image)

Pulmonary Venous flow pattern in elderly patients. The top panel represents the normal flow from a subject with normal left atrial pressure and normal LV end diastolic pressure (LVEDP). The middle panel is obtained from a patient with increased LV end diastolic pressure but normal mean left atrial pressure. Notice the increased amplitude and duration of atrial (A) velocity signal. The lower panel is obtained from a patient with increased left atrial pressure as well. Notice that the ratio of systolic (S) to diastolic (D) velocities is <1 and the increased amplitude and duration of atrial (A) velocity signal.
aligned with LV intracavitary flow, and color scale and baseline shift are used as needed to have a clear border. The slope is measured either at color/no color interface [13], or at the border of the first inter aliasing velocity [14]. Studies have shown that Vp is significantly related to the time constant of LV relaxation and minimal pressure [15, 16], and the ratio of mitral E to Vp is used to predict LV filling pressures in patients in sinus rhythm [14] and atrial fibrillation [6].

However Vp is load dependent [17] and has a stronger relation with LV end systolic volume than with the time constant of LV relaxation [18]. Accordingly, caution should be exercised with Vp when drawing inferences about LV diastolic function in patients with normal LV volumes and EF [19].

**Tissue Doppler of the mitral annulus**

PW Doppler is utilized to record mitral annulus velocities in apical views [20]. A sample volume (<5 mm) is placed at the septal and lateral sites of the mitral annulus, and the recording is obtained at a sweep speed of 50-100 mm/s. Early diastolic velocity (e’) has been studied the most in research studies and enjoys high feasibility and reproducibility. It declines with age similar to other Doppler measurements, and age appropriate values should be used when drawing inferences about LV relaxation using e’. It also has a significant relationship with beta-adrenergic receptor density [21], the extent of interstitial fibrosis [21], and local cytokine levels [22]. Animal [23] and human [24-26] studies have shown that e’ relates significantly and inversely with tau. An increase in preload leads to an increase in e’ when LV relaxation is normal (Figure 5), but has minimal effects when LV relaxation is impaired [23]. For clinical application, the average of septal and lateral e’ velocities (Figure 6) is essential in the presence of regional dysfunction [27, 28] whereas lateral e’ has been reported as the more accurate signal in patients with normal EF [28, 29]. The ratio of mitral E velocity to annular e’ velocity corrects for the effect of LV relaxation on mitral E velocity and can be used to estimate LV filling pressures [26, 30]. This approach (Figure 7) can be applied to patients with normal or depressed EF [26, 28-31], sinus tachycardia [31], atrial fibrillation [32], pulmonary hypertension [33], and hypertrophic cardiomyopathy [34]. In general, a septal ratio >15, a lateral ratio >12, and an average ratio >13 are predictive of increased filling pressures whereas an E/e’ <8 for any of the above ratios occurs in patients with normal filling pressures [28].

**Other Tissue Doppler measurements**

With impaired LV relaxation, e’ velocity is reduced and delayed. This was observed in animal models with coronary artery disease [27, 35] and pacing induced heart failure [36]. Furthermore, e’ is delayed.
such that it occurs after mitral inflow (Figure 8). In animal and human studies, the time interval $T_{E-e'}$ related well with invasive indices of LV relaxation [35, 36] and has been used to estimate LV filling pressures in patients with normal and depressed EF [35], those with mitral valve disease [37], and patients where $E/e'$ ratio was equivocal [38]. It has also been used to identify patients with restrictive cardiomyopathy from those with constrictive pericarditis [39].

Late diastolic mitral annular (a') velocity has also been applied to evaluate LV diastolic function. It is affected by left atrial dP/dt and late LV diastolic pressure [23]. Clinical studies have shown that a' velocity relates significantly with LV end diastolic pressure and predicts outcome in patients with heart failure due to reduced EF [40]. More recently, the lateral $e'/a'$ ratio reportedly identified patients with diastolic heart failure as determined by high fidelity LV pressure/volume measurements [29].

**Fig. 6.** Doppler recording from a patient with regional dysfunction

Recordings of mitral inflow (left), tissue Doppler (TD) velocities at the septal side of the mitral annulus (middle), and lateral side of the mitral annulus (right) from a patient with depressed EF and anteroseptal myocardial infarction. Notice that while septal Ea velocity is reduced (5 cm/s), lateral Ea is normal (12 cm/s). In this case, a more accurate assessment of LV relaxation and filling pressures can be reached by using the average value of Ea at 8.5 cm/s. E stands for peak mitral early diastolic velocity; A, peak mitral late diastolic velocity; Ea, for mitral annulus early diastolic velocity; Aa, mitral annulus late diastolic velocity. Reproduced with permission from reference 28.

**Fig. 7.** Prediction of PCWP in patients with EF <45% and ≥45%

Relation between mean wedge pressure (PCWP) and E/Ea ratio in patients with EF <45% (left) and patients with EF ≥45% (right). Reproduced with permission from reference 31.
Fig. 8. $T_{EE}$ in animal model of Cx. constriction

Recording of mitral inflow and TD mitral annulus velocities at septal side of mitral annulus at baseline (left) and after circumflex coronary artery constriction (right). Notice the near simultaneous onset of mitral E and annular Ea at baseline and the delayed onset of Ea after circumflex constriction. Abbreviations as in figure 6. Reproduced with permission from reference 35.

Fig. 9. Global diastolic strain rate

Recordings of mitral annulus velocities at the septal side of the mitral annulus (blue), lateral side of the mitral annulus (red), and global LV strain rate (derived by speckle tracking from 3 apical views shown in violet color) from the same cardiac cycle. Notice the presence of annular recoil away from the apex during this period (negative deflection) and myocardial expansion (positive signal) as reflected in global strain rate curve. AVC stands for aortic valve closure; MVO, mitral valve opening; GSRiv, global diastolic strain rate during the isovolumic relaxation period; GSRf, global diastolic strain rate during early diastole; GSRa, global diastolic strain rate during late diastole; Ea and Aa abbreviations are the same as in figure 6. AVC and MVO mark the isovolumic relaxation period. Reproduced with permission from reference 46.
Deformation Measurements

During systole, LV myocardium is compressed, whereas during diastole expansion occurs. Strain measurements by TD and speckle tracking have been well validated against sonomicrometry and cardiac MR [41, 42], and unlike tissue velocity signals, they are not affected by translation and tethering. Both animal and human studies have shown a promising role for regional systolic compression and expansion at rest with dobutamine for examining segmental function and viability [43-45].

Most recently, we used the rate of deformation (strain rate) during the IVRT period as an index of LV relaxation (Figure 9). We validated this measurement in an animal model and in patients with cardiovascular disease [46]. The ratio of mitral E to global diastolic strain rate during the isovolumic relaxation period was

![Diagram](image_url)

**Fig. 10.** Estimation of LV filling pressures in patients with normal EF

Algorithm for using E/E' ratio and E/GSRiv for the estimation of LV filling pressures in patients with normal EF.

![Charts](image_url)

**Fig. 11.** Representative examples of twist (upper panel) and twisting rate (lower panel) curves from 3 groups: control (left), diastolic heart failure (DHF in middle), and systolic heart failure (SHF in right panel). Notice that while twist and untwisting rate are reduced in the patient with SHF, both are normal in the patient with DHF. Reproduced with permission from reference 50.
more accurate when E/e’ ratio was indeterminate, in patients with normal EF, or with regional dysfunction [46]. Figure 10 presents an algorithm for using the different ratios to estimate LV filling pressures in patients with a normal EF. Additional studies are needed to further evaluate the feasibility of this promising clinical method.

**Untwisting Rate**

During systole, LV rotation takes place with the apex moving in a counterclockwise direction and the base in a clockwise direction. The difference between these oppositely directed movements is LV twist, which can be measured by TD [47] and speckle tracking echocardiography [48, 49]. LV untwisting follows and in normal individuals is complete during the isovolumetric relaxation period. LV twist and untwisting are closely coupled, and LV untwisting rate is mostly affected by LV end systolic volume (ESV) such that LV untwisting rate in an animal study tracked changes in LV vol-

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**Fig. 12. TR and PA systolic pressure**

Use of the tricuspid regurgitation (TR) jet by continuous wave Doppler for the estimation of pulmonary artery systolic pressure. In this case, the peak velocity is 3.8 m/s, corresponding to a pulmonary artery systolic pressure of at least 58 mmHg.

**Fig. 13. PR and PA diastolic pressure**

Use of the pulmonary regurgitation (PR) jet by continuous wave Doppler for the estimation of pulmonary artery diastolic pressure. The pressure is estimated using the end diastolic velocity (arrow). PADP stands for pulmonary artery diastolic pressure; RVEDP, right ventricular end diastolic pressure; and RAP, mean right atrial pressure.

\[
P_{PADP} - RVEDP = 4 \times \left( \text{PR end-diastolic velocity (m/s)} \right)^2
\]

\[
P_{PADP} = 4 \times \left( \text{PR end-diastolic velocity (m/s)} \right)^2 + RVEDP
\]

\[
RVEDP = RAP
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\[
P_{PADP} = 4 \times \left( \text{PR end-diastolic velocity (m/s)} \right)^2 + RAP
\]
umes, rather than the change in time constant of LV relaxation [50]. In human studies (Figure 11), LV untwisting rate was significantly related to LV relaxation in patients with systolic heart failure but not in those with diastolic heart failure [50]. Nevertheless, LV untwisting rate can still provide insight into LV restoring forces that aid LV filling in healthy and diseased patients, though additional studies are needed to solidify its role for routine clinical application.

**Surrogate Markers of LV Diastolic Function**

Patients with pathologic LV hypertrophy (for example, hypertension and aortic stenosis) usually have abnormalities in LV relaxation and/or stiffness and along with clinical findings of pulmonary/systemic congestion can be used to diagnose diastolic heart failure [1]. While the presence of hypertrophy may be specific for this diagnosis, both diastolic dysfunction and heart failure can occur in patients without LV hypertrophy.

Patients with longstanding diastolic dysfunction usually have LA dilatation, and a LA volume index ≥34 ml/m² was shown to predict clinical events in this population [51]. However, LA volume does not track rapid changes in LV filling pressures and can be normal early on in patients with LV diastolic dysfunction.

In the absence of pulmonary disease, an increase in pulmonary artery (PA) pressures can be attributed to increased LV filling pressures. PA systolic pressure is estimated using the peak velocity of the tricuspid regurgitation jet by CW Doppler (Figure 12) and the noninvasive estimate of mean right atrial pressure [52]. PA diastolic pressure is estimated using the end diastolic velocity of the pulmonary regurgitation jet by CW Doppler (Figure 13) and the noninvasive estimate of mean right atrial pressure [52]. Both signals can be enhanced, if needed, using saline contrast injection with care taken to avoid velocity overestimation from blooming signals.

**Conclusions**

Echocardiography plays an essential role in the evaluation of LV diastolic function in cardiac patients. The technique provides important diagnostic and prognostic information [53]. In patients with depressed EF, mitral and pulmonary venous flow can be applied reliably to predict LV filling pressures. In cardiac patients with normal EF, E/e’ ratio is the starting point for the prediction of filling pressures. A ratio <8 (septal, lateral, or average) usually occurs when the filling pressures are normal, whereas a septal ratio >15, a lateral >12, or average >13 are observed when the filling pressures are increased. When E/e’ ratio falls between these 2 values, other measurements should be applied, which include LA volume index, PA pressures, Ar-A duration, and IVRT/Te’ ratio.

**References**


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