LV DIASTOLIC FUNCTION

Normal diastolic function can be characterized as the complete and efficient filling of the LV without the need for an abnormally high LA pressure and without an associated abnormal increase in pressure during filling. The two major determinants of LV filling are ventricular relaxation and chamber compliance. Phases of diastole:

1. **Isovolumetric relaxation:** diastole commences with the closure of the aortic and pulmonary valves. Intraventricular pressure falls but there is very little increase in ventricular volume.
2. **Rapid early filling:** once ventricular pressure falls below atrial pressure, the mitral and tricuspid valves open and ventricular filling begins. Initially, the pressure gradient between the atria and the ventricles is high and ventricular filling is rapid. Under normal circumstances about 70% of ventricular filling occurs during this phase.
3. **Diastasis:** as diastole progresses, ventricular pressure rises and the rate of filling slows.
4. **Atrial systole:** The final 25% of filling during ventricular diastole results from atrial contraction. When the pressure in the ventricles rises above the pressure in the atria the mitral and tricuspid valves close and diastole is complete.

Ventricular relaxation is a complex energy-requiring process. Isovolumetric relaxation and the first part of rapid early filling are active, energy-requiring processes during which the contractile elements are deactivated and the myofibrils return to their original (pre-contraction) length.

The optimal performance of the LV depends on its ability to cycle between two states: (1) compliance in diastole that allows the LV to fill from low LA pressure (represented by dV/dP) and (2) stiffness (rapidly rising pressure) in systole that ejects the stroke volume at high arterial pressures (represented by dP/dt). N.B: diastolic stiffness (represented by dP/dV) is the inverse of compliance.

Causes of impaired LV diastolic function is thought to reflect ‘stiffness’ or impaired relaxation of the LV, and so occurs in conditions where the LV becomes less compliant (↓dV/dP):

- Ageing
- Hypertension
- LVH
- Myocardial ischaemia
- Aortic stenosis
- Infiltrative cardiomyopathies.

The following might reduce diastolic flow from LA to LV

- Pericardial disease: The presence of pericardial calcification and constrictive physiology would restrict the ability of the LV to fully distend and therefore fill properly.
- Atrial fibrillation- reduces diastolic LV filling through loss of the trans-mitral A wave
- Dehydration- reduces diastolic LV filling through simple loss of vascular volume.
- **I**nspiration increases the flow of blood returning to the r**I**ght heart and decreases the flow of blood into the left heart

The following might increase diastolic flow from LA to LV

- MR- causes increased trans-mitral flow and eventually elevated LA pressures, both increasing diastolic filling of the LV.
- Bradycardia- increases diastolic time and hence increases filling.
- **E**xpiration increases the flow of blood to the l**E**ft heart and decreases the flow of blood into the right heart.

Echo assessment of LV diastolic function

Many methods are available to characterize LV diastolic function on echo, but the most widely used are **(1)** Mitral inflow velocity, **(2)** Colour M-mode Mitral inflow velocity, **(3)** Mitral annular velocity by TDI, **(4)** IVRT and **(5)** Pulmonary vein velocity.

1. Mitral Inflow PW Doppler velocities

Mitral inflow velocity is the single most important parameter for the assessment of diastolic function. Mitral inflow is recorded from the apical 4C view with the sample volume between the tips of the mitral leaflets. Once the view is properly aligned, the sample volume of the PW Doppler is positioned at the tips of the mitral leaflets. The measurements obtained are: (1) E and A velocities, (2) E wave deceleration times.

- **Diastolic dysfunction grade 1**: delayed LV relaxation → higher LV pressure in early diastole → decreased rapid early filling (E-wave) → E/A ratio < 1 and prolonged DT>200ms and IVRT >100ms.
- **Diastolic dysfunction grade 2**: progressive worsening of diastolic dysfunction → increased LA pressure → the early diastolic pressure gradient is restored despite increased diastolic LV pressures → return of the E wave, DT & IVRT to the normal range (pseudo-normalization).
- **Diastolic dysfunction grade 3**: stiff non-compliant LV → most LV filling occurs early in diastole → large trans-mitral E wave and comparatively smaller A wave, and shortened DT<150 and IVRT<50
- **Diastolic dysfunction grade 3**: this most severe form of diastolic dysfunction differs from grade 3 only by the fact that a Valsalva manoeuvre is unable to reverse the pattern to a pseudonormal one

N.B: E and A fusion is common and indicates AV dyssynchrony (in the absence of sinus tachycardia)

2. Colour M-mode recording of mitral inflow propagation velocity (Vp)- is another approach to the assessment of diastolic function. Rather than tracing the mitral inflow velocity at single location (at the MV leaflets tips) by PW, here we trace the mitral inflow propagation velocity throughout the LV form the MV annulus towards the apex (by colour M-mode).

Using routine colour flow imaging for orientation, the M-mode cursor is placed at the centre of the inflow jet. The M-mode display reveals the acceleration of blood in early diastole through the mitral valve toward the apex.

The slope of the red-blue interface represents the propagation velocity (Vp) of mitral inflow and correlates with the rate of myocardial relaxation or elastic recoil of the chamber in early diastole. Thus, impaired relaxation will slow the propagation of blood and thereby reduce the slope of the line. **Remember**: with normal **LV systolic function**, colour M-mode of the **MR jet** produces a near vertical slope, correlating with the rapid rate of rise in ventricular pressure (**dP/dt**) during systole.

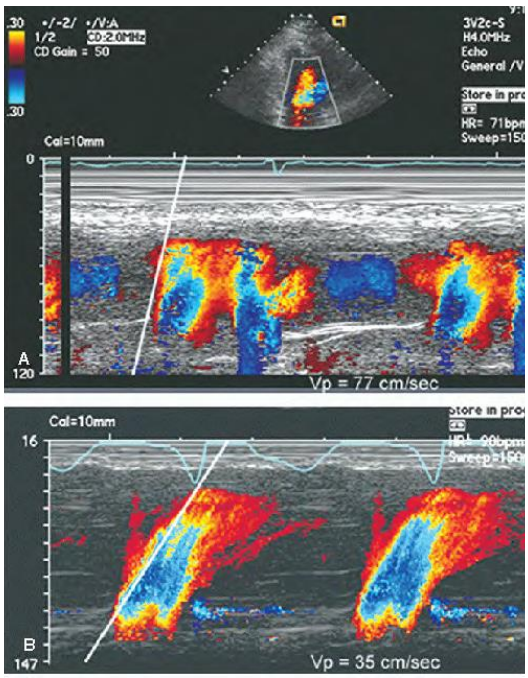


Fig. **A:** Normal flow propagation velocity (Vp = 77 cm/sec) is demonstrated as evidenced by the steep slope of the early diastolic valve-to-apex contour. **B:** The reduced slope and lower velocity (Vp = 35 cm/sec) is consistent with decreased chamber compliance

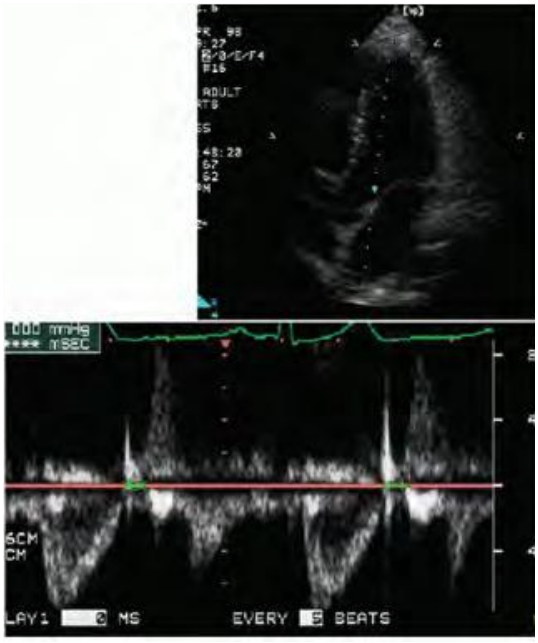
The ratio between E and Vp (the E/Vp ratio) correlates with LVFP. Normal E/Vp < 1. The higher the E/Vp, the higher the LVFP and E/Vp > 2 indicates high likelihood that LVFP is increased. The idea here is to relate a parameter (E) that depends on both LV relaxation and LVFP to another parameter (Vp) that depends mainly on LV relaxation, to cancel out the effect of relaxation and create a parameter (E/Vp) that correlates directly with LVFP, similar to (E/e') ratio

.

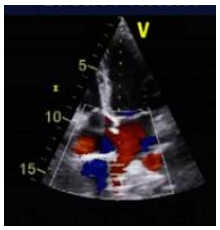
3. Mitral annular velocity by TDI

- TDI of the mitral annulus is undertaken in the apical 4C, placing the sample volume (which should be small, usually 2–3 mm) in the myocardium of the septum and then the lateral wall. The optimal location is 1 cm below the mitral annulus. In each location make a PW tissue Doppler recording using a low gain setting and an aliasing velocity 15–20 cm/s. Set the sweep speed at 50–100 mm/s and take at least three sets of measurements with the patient's breath held at end-expiration
- Although single-site measurements are sometimes used in patients with globally normal or abnormal LV systolic function, it is recommended to use the average (septal and lateral) e' velocity in the presence of regional LV dysfunction (you may consider in addition the anterior and the inferior mitral annular velocities from apical 2C)
- Sampling of the septal annulus is less influenced by the translation movement of the heart as it moves parallel to the ultrasound beam but it may be influenced by the RV interaction
- A decrease in e' is one of the earliest markers of LV diastolic dysfunction and this decrease is present in all stages of diastolic dysfunction
- Because e' velocity remains reduced and mitral E velocity increases with higher filling pressure, the ratio between E and e' (the E/e' ratio) correlates with LVFP or PCWP. The idea here is to relate a parameter (E) that depends on both LV relaxation and LVFP to another parameter (e') that depends mainly on LV relaxation, to cancel out the effect of relaxation and create a parameter (E/e') that correlates with LVFP, similar to (E/Vp) ratio.
- Lateral E/e' ratio > 12 is associated with high LVFP
- Average (septal and lateral) E/e' ratio > 13 should be used to define an undoubtedly LVFP increase
- e′ velocity primarily depends on LV relaxation and, when diastolic function is abnormal, e′ is relatively independent of preload. However, when diastolic function is normal, e′ increases with higher filling pressure. For this reason, the use of the e' has limitations in normal subjects. In patients with diastolic dysfunction, however, e' can be used to mitigate the effect of LV relaxation on the E-wave velocity. The lateral e' may correlate better with filling pressures in the setting of a normal LV EF.
- e' velocity is usually reduced, and hence the E/e' ratio should not be used, in patients with significant annular calcification, surgical rings, mitral stenosis, prosthetic mitral valves and with ischaemia or scar in the respective wall (septum/lateral)
- e' is increased in patients with moderate to severe primary MR (and normal LV relaxation) due to increased flow across the regurgitant valve. In these patients, abnormal LV relaxation might be indicated by reduced –dP/dt (estimated from MR or AR), while the E/e' ratio should not be used. IVRT/TE-e' ratio can be applied
- The E/e' ratio is not accurate as an index of filling pressures in patients with constrictive pericarditis and may not be accurate in severely dilated LV with severely decreased systolic function
- **Other tissue Doppler parameters (TE-e'):** with conventional Doppler one measures the time interval from the beginning of the QRS complex to the onset of the E-wave. With TDI one measures the time interval from the beginning of the QRS complex to the onset of the e´ wave. The former value is then subtracted from the latter. Thus, in essence TE-e´ describes the time interval between E an e´. The longer this interval is, the more severe is diastolic dysfunction. As these measurements are obtained from different modalities and different beats, the investigator must ensure that the lengths of the beats match. TE-e' is particularly useful in subjects with normal cardiac function or those with mitral valve disease and when the E/e´ ratio is 8-15. The average of four annular sites is more accurate than a single-site measurement.
- **IVRT/TE-e' ratio** < 2 has reasonable accuracy in identifying patients with increased LVFP

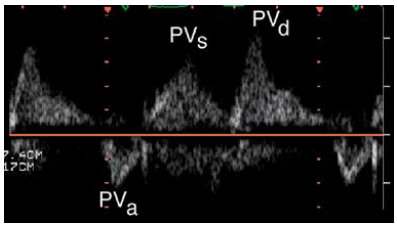
4. IVRT (between aortic outflow and mitral inflow)



- IVRT is the time period between AV closure and MV opening, during which LV pressure falls but there is no change in LV volume and all left-sided valves are closed.
- IVRT is normally 50–100 ms. and is lengthened (>100) in Mild LVDD (delayed relaxation), pseudo-normalized (50-100) in moderate LVDD, and shortened (<50) in severe LVDD (restrictive filling). IVRT < 40ms has a high negative predictive value for PHT. The IVRT does vary with heart rate and age.
- The IVRT can be measured by placing a PW Doppler midway between the MV and AV in the apical 5-chamber view, so that trans-mitral and transaortic flows are picked up; the time duration between them is the IVRT. Generally, a fast sweep speed is used and measurements are performed at end-expiration. At least three measurements of IVRT should be obtained and averaged.
- IVRT can be measured using PW TDI in the A4CH view. It is recommended that the sample volume be placed at the basal lateral RV myocardium. The measurement is taken at end-expiration from the offset of S' to onset of E'; however, IVRT is best measured with conventional PW Doppler as myocardial movement does not necessarily correlate with valve opening and closure.



5. Pulmonary vein velocity. Analysis of the pulmonary vein velocities (i.e. LA filling velocity) can provide insight into the diastolic properties of the LV that complement the information derived from the mitral inflow velocity. Locate the right upper pulmonary vein flow (red flow near the IAS), place the sample volume of PW Doppler 2-5 mm inside the vein to record the forwards flow waves (S, systolic wave and D, diastolic wave) and backward flow wave ("a" or "ar", reversed or negative flow wave occurring just before QRS in sinus rhythm, correlating with the contraction of the LA).



The S wave represents the filling of the LA in diastole while the MV is closed and the velocity of the S wave is related to the gradient between pulmonary veins and LA, therefore, the higher the pressure in the LA, the smaller the S wave (i.e. the samller the systolic LA filling fraction). The opposite is also true as there is practically a linear relationship between PVs and LA pressure gradient-difference and the S wave velocity. The better the LV diastolic function the higher the S wave. In patients with significant MR, the S wave is decreased, while sometimes reversed.

Both the A wave of the mitral inflow and the "ar" wave of the pulmonary vein velocity curve corellate with the atrial contraction. In LVDD, the pressure is high in the LV and, therefore, the atrium preferntially ejects blood backwards into the pulmonary vein rather than forward into the LV, resulting in increased duration of the pulmonary vein "ar" wave in comparison to the duration of the mitral A wave. **The "a_{dur}–A_{dur}" parameter works well even in patinets with preserved LV systolic function**, unlike the other parameters of the pulmonary vein velcity parameters and the mitral inflow parameters, which works well in patients with reduced LVEF, but are not relaiable in patients with preserved LV systolic function.

6. LA dilations, LVH and symptoms

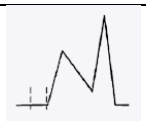
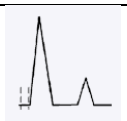
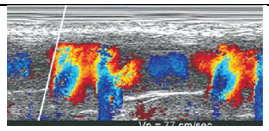
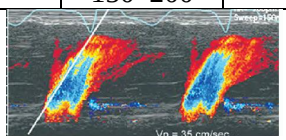
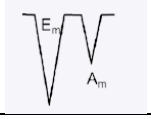
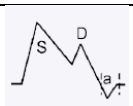
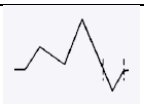
In patients with LV diastolic dysfunction, concentric or eccentric hypertrophy can be found (LV mass index > 115 g/m^2 in ♂ or > 90 g/m^2 in ♀)

Increased LA volume (LA volume index > 34 ml/m^2) reflects the cumulative effects of the increased LV filling pressures over time (**chronicity** of the disease). The atrial volume cannot increase significantly with an abrupt increase in its pressure but rather with a chronic increase due to significant diastolic dysfunction.

Hints:
Assessment of LV systolic function is important as normal systolic function may affect the reliability of the parameters of the LV diastolic function.
Assessment of TR velocity is important as most of patients with significant LVDD have some degree of pulmonary hypertension.
In patients with AF, Doppler assessment of LV diastolic function is limited by the variability in cycle length, the absence of organized atrial activity, and the frequent occurrence of LA enlargement regardless of filling pressures. In general, when LVEF is depressed in patients with AF, mitral DT (≤160 msec) has reasonable accuracy for the prediction of increased LV diastolic pressures and adverse clinical outcomes. Other Doppler measurements that can be applied in AF include:

- Peak acceleration rate of mitral E velocity (≥1,900 cm/sec^2)
- IVRT (≤65 msec)
- DT of pulmonary venous diastolic velocity (≤220 msec)
- E/mitral Vp (E/Vp; ≥1.4)
- E/e′ ratio (≥11). It is critical to average several cardiac cycles and to use matched RR intervals for both E and e′ velocities. This often poses important limitations to the routine application of these measurements in clinical practice

LV diastolic parameters

	Normal	**Mild**	**Moderate**	**Severe**
1. LV Inflow Doppler				
• E/A ratio	1–2 (possibly > 2 in young & athlete)	↓ < 1 *(i.e. reversed) (normal in old > 60)*	Normalize 1–2	↑ > 2 *(normal in young & athlete)*
• DT (ms)	150–200	↑ > 200	Normalize 150–200	↓ < 150
2. LV inflow colour M-mode Slope of the early diastolic valve-to-apex contour (correlates with propagation velocity of LV inflow, Vp)	 Steep	 Reduced		
3. Mitral annular tissue Doppler				
• e'/a'	1-2	< 1	< 1	<<1
4. IVRT (ms)	50–100	↑ > 100	Normalize 50–100	↓ < 50
5. Pulmonary venous Doppler				
• PV_S /PV_D	$PV_S > PV_D$ (possibly $PV_S \leq PV_D$ in young & athlete)	$PV_S > PV_D$	$PV_S < PV_D$ *(i.e. reversal)* (normal in young & athlete)	$PV_S << PV_D$ *(i.e. prominent reversal)*
• PV_a (m/s)	< 0.35	< 0.35	≥ 0.35	≥ 0.35
• a_{dur}–A_{dur} (ms)	< 20	< 20	≥ 20	≥ 20
	a_{dur}–A_{dur} ≥ 30 is consistent with increased LVFP and LVDD in HCM			
6. LA dilations, LVH and symptoms	---		+++	+++

Parameters of Increased LVFP

Parameter	Normal	↑ LVFP
E/e' (septum)	< 8	> 15 (CCF)
E/e' (lateral)	< 10	> 10 (>12)
E/e' (average)		> 13
E/Vp	< 1	> 2
IVRT/TE-e´ ratio	> 2	< 2

Factors influencing velocities o Mitral flow

Factors influencing velocities of mitral inflow	E	A	E/A
Age	↓	↑	↓
Tachycardia/atrio ventricular block first degree		↑	↓
Preload ↓ ◆ Hypovolaemia ◆ Diuretics, venodilators ◆ Valsalva manoeuvre	↓	N/↑	↓
Preload ↑ ◆ Hypervolaemia ◆ Left atrial pressure ↑ ◆ Mitral regurgitation	↑	↓	↑
Left ventricular systolic dysfunction	↑	↓	↑
Left atrial dysfunction ◆ Atrial fibrillation/flutter (cardioversion) ◆ Sinus rhythm		absent ↓	