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An Approach to Analysis of Left Ventricular Diastolic Function and Loading Conditions in the Echocardiography Laboratory

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About one-third of patients presenting with a clinical syndrome of heart failure (HF) have normal left ventricular (LV) systolic function (EF \geq 45%). This group is described as having diastolic dysfunction with diastolic HF.¹ In the evaluation of patients with suspected cardiogenic dyspnea, echocardiography provides information about both LV function (systolic and diastolic) and LV loading conditions.² Obtaining reliable, reproducible data relative to diastolic ventricular performance can be challenging. This review summarizes the echocardiographic assessment of diastolic function and LV filling pressures, as well as pitfalls in acquisition and interpretation of applicable data.

Diastole is defined clinically as that period of the cardiac cycle beginning with aortic valve closure (AVC), and ending with mitral valve closure (MVC).³ Exactly when ventricular relaxation begins is not clear. At the cellular level, diastole starts with actin–myosin crossbridge unlinking, allowing sarcomere relaxation in an energy-consuming process requiring ATP hydrolysis. Active relaxation does not begin simultaneously throughout the heart; the process of crossbridge unlinking begins in some areas of the myocardium while active contraction

continues in others. When a sufficient number of myocardial cells enter the active relaxation phase, ventricular pressure begins to fall and the aortic valve closes.⁴

There are four clinical phases of diastole (Fig. 1).^{5,6} The first is *isovolumic relaxation*, beginning with AVC and ending with mitral valve opening (MVO). *Rapid filling* begins at MVO with continued active myocardial relaxation causing LV pressure to drop below left atrial (LA) pressure (resulting in diastolic “suction”). The third phase, *diastasis*, is characterized by passive LV filling. During this phase, LV and LA pressures are nearly equal and LV filling mostly occurs by pulmonary vein (PV) flow and fluid inertia. The LA acts as a passive conduit, allowing PV flow to directly enter the LV. The last phase is *atrial systole*, during which atrial contraction contributes about 15% of LV filling in normal patients.^{6–8}

Active relaxation occurs early in diastole, during the isovolumic relaxation and rapid filling phases. Active relaxation is normally complete by mid-diastole. Diastasis and atrial contraction constitute the passive parts of diastole, during which LV passive stiffness is the predominant factor determining compliance. Interventricular interaction (septal impingement into the LV cavity) and the pericardium (limiting chamber enlargement via extra-ventricular restriction) also have important roles in late diastole.⁹

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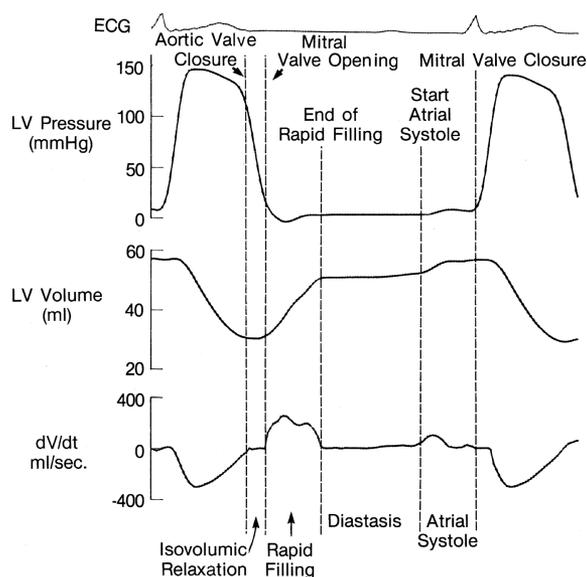


Figure 1. Recording of LV pressure, volume, and the change in volume as a function of time (dv/dt). The four phases of diastole are illustrated. (Reproduced with permission from Little WC, Downs TR. Clinical evaluation of left ventricular diastolic performance. *Prog Cardiovasc Dis* Jan/Feb 1990;17(4):274.)

Diastolic LV dysfunction is the impaired capacity of the LV to fill and maintain its stroke volume without a compensatory increase of LA pressure,¹⁰ and is considered clinically relevant when LV filling becomes impeded, with resultant symptoms of low cardiac output (from loss of Starling forces), elevated pulmonary venous pressure, or both.⁵ Elevated diastolic pressures are transmitted through the PVs to the proximal pulmonary vasculature, causing a hydrostatic increase in mean pulmonary artery pressure. Over time, secondary changes occur in the pulmonary arterioles, with (first) reactive and eventually fixed pulmonary arterial hypertension.^{11,12}

Almost any form of organic heart disease can be associated with LV diastolic dysfunction, with hypertension, diabetes, obesity, coronary artery disease, LV systolic dysfunction, stenotic valvular disease, hypertrophic cardiomyopathy, and infiltrative disorders being most common.¹³ In addition, with increasing age, a pattern of diastolic abnormalities is routinely present: by age 65, changes in filling parameters can be seen, while by age 70, a pattern of frank impaired relaxation is usually observable.¹⁴

Patient Profile

When evaluating a patient for cardiac dyspnea, in addition to searching for significant valvular disease, systolic failure, and active ischemia, the clinician should assess diastolic performance: echo parameters related to active relaxation (early diastole) and passive relaxation (late diastole), and how ventricular loading conditions affect those parameters. Diastolic pressures estimated in the echo laboratory include LA mean pressure (LAP) (estimated by the pulmonary artery occlusion pressure [PAOP] when pulmonary venous disease is absent), and the LV end diastolic pressure (LVEDP).¹⁵ It is the resultant elevation in pulmonary venous pressure, by various means, which results in clinical dyspnea.

Historical factors important in interpreting echo findings include patient age, history of coronary artery disease and/or myocardial infarction, diabetes mellitus, and hypertension. Blood pressure at the time of the study, if available, is also useful in interpreting loading conditions. Pathological Q-wave and left ventricular hypertrophy (LVH) on electrocardiography are also suggestive of LV diastolic abnormality.

M-Mode/Two-dimensional Echocardiography

Several M-mode and two-dimensional (2D) echo findings help the examiner determine the pretest (pre-Doppler) probability of diastolic dysfunction. Therefore, evaluation of LA and LV size and function is important.

LVH, cavity enlargement, and segmental wall motion abnormalities are indicative of disorders associated with impaired relaxation. In the evaluation of LV volume, mass and function, both quantitative and qualitative assessments should be performed.

Several methods have been validated to obtain linear and volumetric measurements of the LV. The examiner should be familiar with the advantages and disadvantages of each method. Linear measurements (septal wall thickness, posterior wall thickness, and LV internal dimensions at end diastole and end systole) are obtained from the parasternal views using M-mode, 2D images or 2D targeted M-mode echocardiography. These values are reproducible; however, they can be off axis and not representative in abnormally shaped ventricles.¹⁶ Volumetric methods correct for shape distortion; however, they require optimal

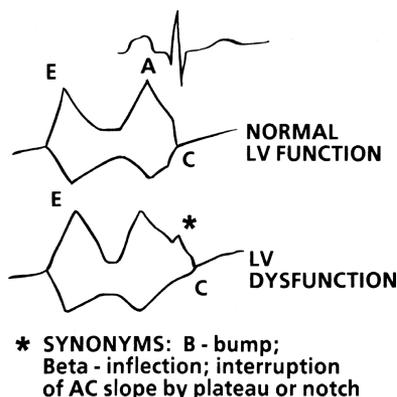
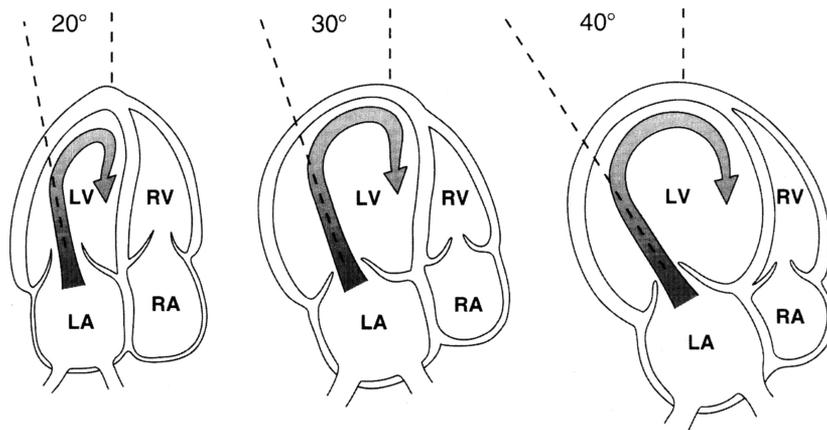


Figure 2. Normal M-mode mitral AC slope and prolonged AC slope. A B-bump is evident. (Reproduced with permission from D'Curz IA, Kleinman D, Aboulatta H, Orander P, Hand, RC. A reappraisal of the mitral B-bump (B-inflection): its relationship to left ventricular dysfunction. *Echocardiography* 1990;7(1):70.)

visualization of endocardial and epicardial borders. In addition, there are a few accumulated data from normal populations. Volumetric measurements are obtained from the mid-papillary short axis view and the apical two-chamber and four-chamber views using mathematical formulas or biplane Simpson's method (see Ref. 16 for calculations).

In the absence of mitral valve (MV) regurgitation or stenosis, left atrial enlargement (LAE) reflects chronic elevation of LV filling pressure and thus suggests diastolic dysfunction.¹⁸ Left atrial diameter (LAD) is measured from the parasternal long axis view using M-mode, often with 2D guidance, and is specific but not very sensitive for LAE. Left atrial volume (LAV), however, is a better measure of LA size. An ellipse formula may be used to calculate LAV:

Figure 3. Mitral valve (MV) inflow as recorded in the 2D apical four-chamber view. Normally MV inflow is ~20° laterally directed, but increases as the LV enlarges. The transducer should be laterally placed with respect to the LV apex, so that MV inflow is directed straight toward the transducer. Color flow Doppler superimposed on the 2D image helps transducer and PW cursor positioning. (Reproduced with permission from Appleton CP, Jensen JL, Hatle LK, Oh JK. Doppler evaluation of left and right ventricular diastolic function: A technical guide for obtaining optimal flow velocity recordings. *J Am Soc Echocardiogr* 1997;10(3):272.)



$$LAV = (\pi/6) (LAD)(Lx)(Sx)$$

where Lx is the apical four-chamber long axis dimension and Sx is the apical four-chamber short axis dimension, both measured at end systole.^{16,19} Simpson's method is another way to calculate LAV, but it is more cumbersome as it requires tracing the LA endocardium.

The American Society of Echocardiography recommends using the area-length method with the following equation:

$$LAV = (8/3\pi) (A_1A_2/D)$$

where A₁ and A₂ are LA areas traced at ventricular end systole (maximum LA size) from the apical four and two-chamber views respectively, and D is the length from the LA posterior wall to the line joining the MV hinge points from either the two- or four-chamber apical views (whichever is shorter).¹⁶ The LAV is often indexed to body surface area to obtain the LAV index (LAVI), which does not change significantly with age and remains at 22 ± 6 ml/m² throughout life in healthy subjects.^{16,17}

A B-bump (Fig. 2) on the MV M-mode tracing demonstrates delayed MVC and suggests an elevated LVEDP, usually ≥ 15 mmHg in patients with LV systolic dysfunction.²⁰

Doppler Echocardiography

Doppler-derived parameters of diastolic function appear to be most accurate in the setting of LV systolic dysfunction (EF < 0.45), with somewhat less accuracy when LV systolic function is normal.^{4,21}

Pulsed-wave (PW) Doppler of mitral inflow is obtained from an apical four-chamber view, with the PW sample box placed at the tips of the MV leaflets. A small sample box (1–2 mm) and wall filter ~200 Hz result in sharper

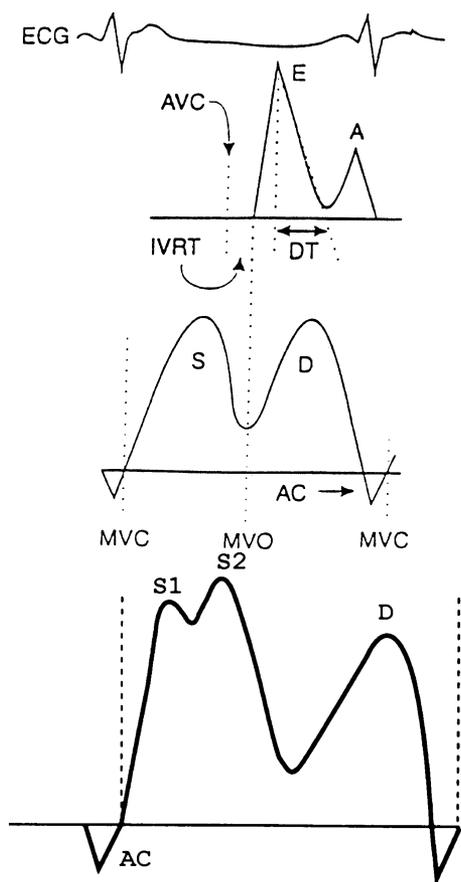


Figure 4. A. Pulse-wave Doppler mitral inflow and pulmonary vein patterns. Isovolumic relaxation time (IVRT) is the time from aortic valve closure (AVC) to mitral valve opening (MVO). Atrial contraction and mitral valve closure (MVC) are illustrated. Deceleration time (DT) is the time for the peak E velocity to decline to the zero baseline. Pulmonary vein systolic (S) and diastolic (D) flows are illustrated. (Reproduced with permission from Ref. 21.) **B.** The pulmonary systolic flow could appear biphasic with an early (S1) and late (S2) waves. (Reproduced with permission from Ref. 22.)

velocity waveforms. The sonographer should position the transducer lateral to the cardiac apex to facilitate mitral inflow directly toward the transducer (Fig. 3). Color Doppler helps guide sample box placement parallel to flow and within the maximum flow profile.

The mitral Doppler early diastolic velocity profile, or E-wave, reflects rapid filling (Fig. 4A). As LV pressure rises, transmitral velocity decreases progressively. The fall in velocity is represented by the deceleration time (DT), defined as the time interval between the peak of the E-wave and a point in time where the descending limb of the E-wave crosses the baseline. Fol-

lowing the E-wave is a period of diastasis with low transmitral velocities. Atrial systole follows manifesting as an A-wave. Normally, the ratio of E and A peak velocities is greater than 1.^{7,8}

Isovolumic relaxation time (IVRT) is measured from an apical five-chamber view. Either PW or continuous wave (CW) Doppler can be used. With PW Doppler, the sample gate should be placed close between the aortic and MVs and set wide to facilitate recording the AVC click followed by MVO.²² M-mode echocardiography can also be used to measure the IVRT, when both AVC and MVO are obtained. However, Doppler-derived IVRT values are 10–25 millisecond longer than those obtained using M-mode echo, as mitral inflow is slightly delayed after MVO.²²

PV flow Doppler is usually recorded from an apical four-chamber view, using PW Doppler. The sample volume is placed within the PV 1–2 cm from its orifice. Color Doppler helps localize PV flow for optimal positioning of the PW Doppler sample box.²² Normal PV recording has a systolic profile, S-wave, which can be monophasic or biphasic (Fig. 4B). The first S-wave (S1) results from atrial diastole (LA relaxation) and the second S-wave (S2) is thought to result from forward flow from the right ventricle or from mitral annular descent, causing a “suction” effect accelerating flow into the LA.²³ The PV diastolic profile, D-wave, occurs concurrently and varies in a similar pattern and timing to the mitral E-wave. Normally, the S-wave will have the same or slightly higher velocity than the D-wave. Reversed flow occurs within the PV during atrial systole manifesting as the AC wave. Both width and amplitude of the AC component are significant in estimating LV filling pressure.^{23,24}

Based on recordings of mitral and PV flow, diastolic function is semiquantitatively categorized, ranging from normal through four grades of progressive diastolic dysfunction (Fig. 5). *Abnormal relaxation* (grade I) (Fig. 6) occurs with abnormal diastolic function and normal LV filling pressures. Early mitral inflow is reduced (lower E-wave peak) with increased contribution of atrial contraction to LV filling (prominent A-wave peak). As a result, the E–A ratio is less than 1. Also, the IVRT and DT are prolonged. The S–D ratio of the PV flow remains ≥ 1 (Table 1).

When LV filling pressure increases, a mitral inflow pattern develops that resembles normal flow. This is termed *pseudonormalization* (grade II diastolic dysfunction). The S velocity

ANALYSIS OF DIASTOLIC FUNCTION

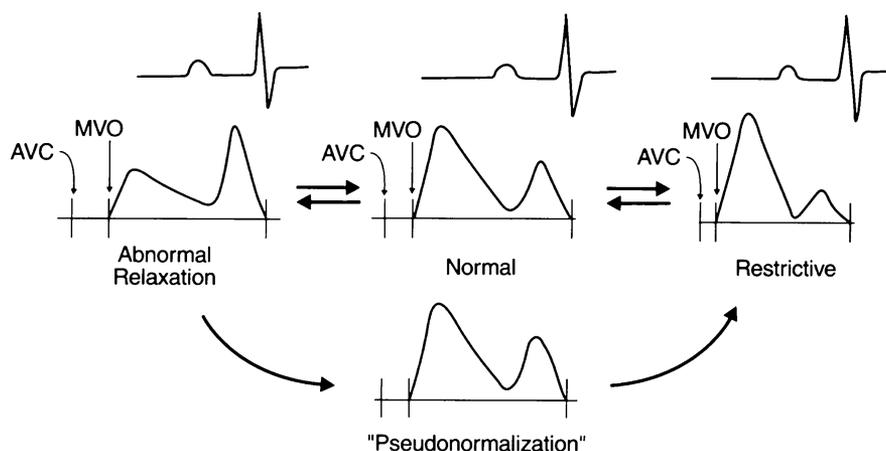


Figure 5. Patterns of mitral inflow by pulse-wave Doppler, recorded at the tips of the mitral valve in the apical four-chamber view. (Reproduced with permission from Ref. 22.)

of PV flow is blunted, and generally the S-D ratio is below 1. Also, the PV AC amplitude and width are increased (Fig. 7). As patients transition from grade I to grade II, elevated filling pressures can be noticed in association with an abnormal relaxation pattern.

As LV filling pressure continues to increase, a pattern of *restrictive filling* (grade III) (Fig. 8) becomes apparent. A large increase in pressure

occurs for a relatively small increase in volume. Therefore, early mitral flow is rapid. There is then a small contribution from atrial contraction; hence, the E-A ratio exceeds 2. The IVRT and DT are shortened. By definition, patients with grade III diastolic dysfunction will transiently manifest a pattern of abnormal relaxation (or pseudonormalization) with the strain phase of the Valsalva maneuver (reversible

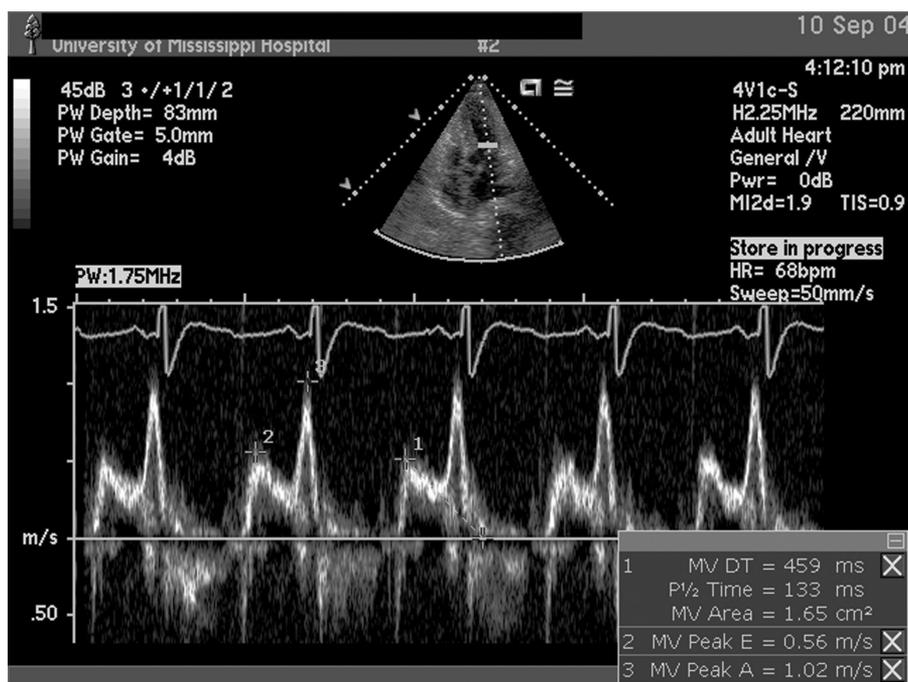


Figure 6. Abnormal relaxation pattern in a 54-year-old male with history of hypertension and left ventricular hypertrophy. DT is prolonged; E/A is < 1.

	Normal	Abnormal relaxation	Restrictive
IVRT	55–90 ms	>110 ms	<60 ms
DT	160–240 ms	>240 ms	<150 ms
E-wave	0.8–1.5 m/s	↓	↔↑
A-wave	0.4–0.7 m/s	↑	↓
E/A	>1	<1	>2

restrictive filling) as LV preload transiently decreases. Finally, with grade IV diastolic dysfunction no change in mitral inflow pattern occurs with Valsalva (*irreversible restrictive filling*).^{25,26}

Mitral E- and A-waves, and PV S and D-waves, reflect diastolic function, and in patients with depressed LV systolic function, MV inflow correlates well with LV filling pressure. In these patients the PAOP is predictably greater than 20 mm Hg, when E/A exceeds 2 and DT is less than 150 ms (Table 2).^{27,28} PV Doppler helps identify a pseudonormal pattern in hearts with both normal and depressed LV systolic function. When the PR interval on EKG is normal, if the AC velocity is greater than 25 cm/s or

its duration is 30 ms longer than the A-wave, the LVEDP is likely higher than 20 mm Hg (Fig. 7).^{24,26}

When measuring A-wave duration, one should keep in mind that a sharper A-wave can be obtained by moving the sample volume a few millimeters closer to the mitral annulus. However, relocating the sample volume all the way to the level of the annulus should be avoided because the mitral A-wave duration at this site can be shorter than that measured more toward the leaflet tips.²⁹

Occasionally, low velocity flow (L-wave) will be noticed during diastasis (Fig. 9). It is often found in normal patients with a relatively slow heart rate. The L-wave can also be noted in patients with LVH and normal systolic function if abnormal relaxation and elevated LV filling pressures are present.²²

As mentioned above, hemodynamic maneuvers performed during echo imaging can help evaluate LV loading conditions. Transient reduction of preload is accomplished with Valsalva or sublingual nitroglycerin administration. The Valsalva maneuver is performed by having the patient blow into a manometer to maintain 40 mm Hg or more. Practically, in the echo laboratory, the Valsalva

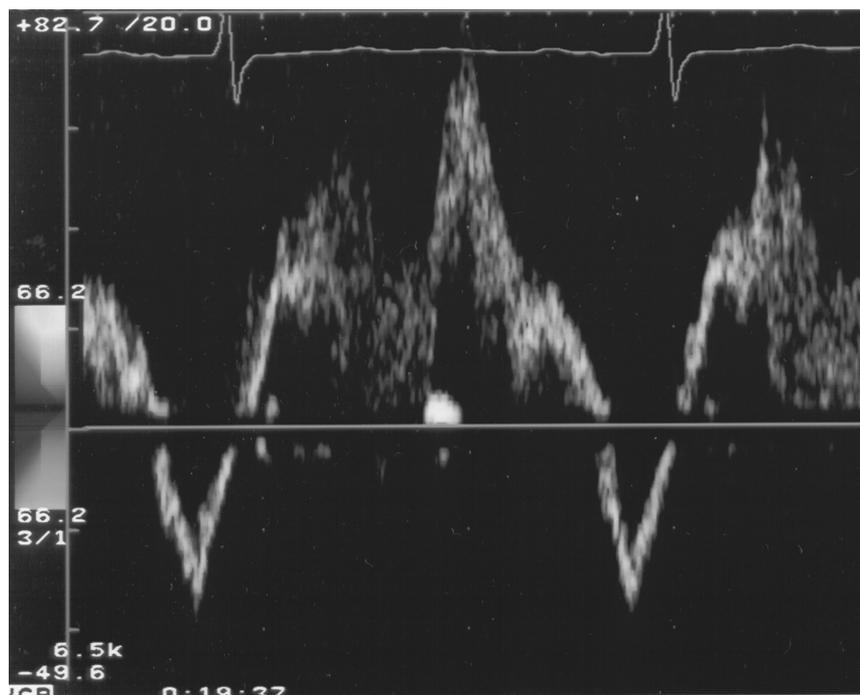


Figure 7. Pulmonary vein Doppler pattern in a patient with pseudonormalization. While the patient has normal mitral flow pattern, prominent AC-wave and S/D < 1 indicate elevated left ventricular filling pressure.

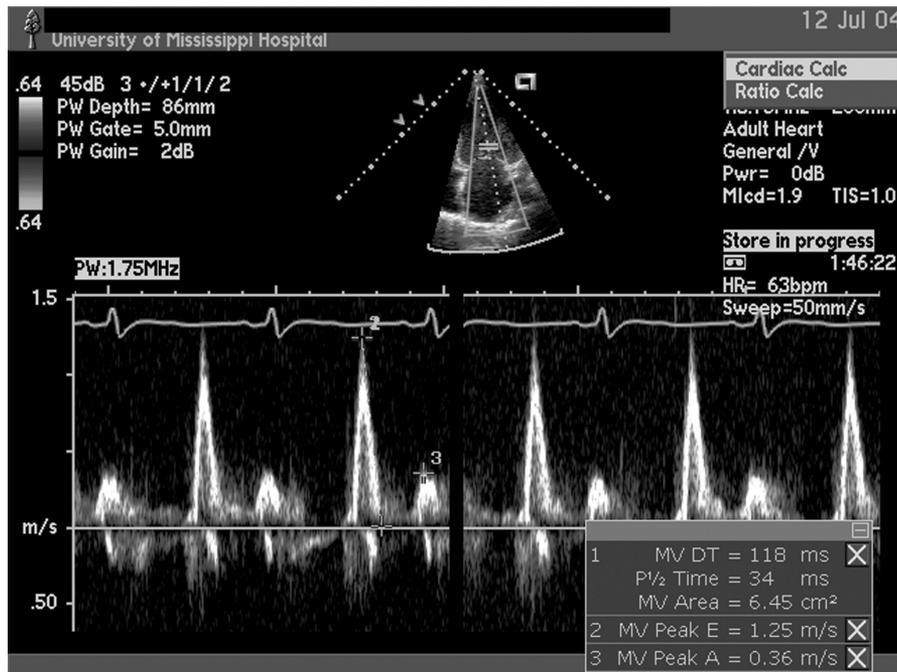


Figure 8. Restrictive pattern in a patient with hypertension and dilated cardiomyopathy.

maneuver is performed by having the patient forcefully exhale against a closed glottis for 10 second after a deep inspiration. If this maneuver is difficult for a patient to perform effectively, the echocardiographer places his hand on the patient's abdomen while the patient strains will raise intrathoracic pressure and approximate Valsalva hemodynamics.³⁰ With Valsalva, a pseudonormal pattern will revert to abnormal relaxation, whereas a normal mitral filling pattern generally will result in lower flow, but an unchanged E–A ratio.^{27,31} Increasing preload by augmenting systemic venous return with passive leg raising will change a pseudonormal pattern to a restrictive one.

Tissue Doppler Echocardiography

Tissue Doppler imaging (TDI) helps measure myocardial motion. Evaluation of diastolic mitral annulus motion with this technique can quantify LV relaxation. From an apical view, the PW sample box is placed in the mitral annulus. The sample box should be 3–7 mm. Circumferential mitral annulus velocities may differ within the annulus, especially if regional wall motion abnormalities exist. In clinical practice, septal and lateral measurements are generally sufficient. However, the mean velocity of the

septal, lateral, anterior, and posterior segments should be used in the presence of regional wall motion abnormalities, although there is no consensus on how best to obtain tissue Doppler measurements.

The normal TDI pattern (Fig. 10) is composed of a positive systolic velocity wave as the annulus moves towards the LV apex. A negative diastolic wave (E') occurs during early LV filling, and a late negative diastolic wave (A') occurs during atrial contraction. In normal individuals E' is greater than 8 cm/s.

The diastolic E'-wave is reduced (<8 cm/s) with impaired relaxation, and is fairly independent of preload in patients with

TABLE II

Formulas for Estimation of LV Filling Pressure

Depressed EF:
$17 (5 \times E/A) - (0.11 \times IVRT)$
Normal or depressed EF:
–Sinus rhythm:
$1.9 + 1.24 (E/E')$
$4.66 + 5.27 (E/V_p)$
–Sinus tachycardia:
$1.55 + 1.47 (E/E')$
–Atrial fibrillation:
$6.49 + 0.82 (E/E')$

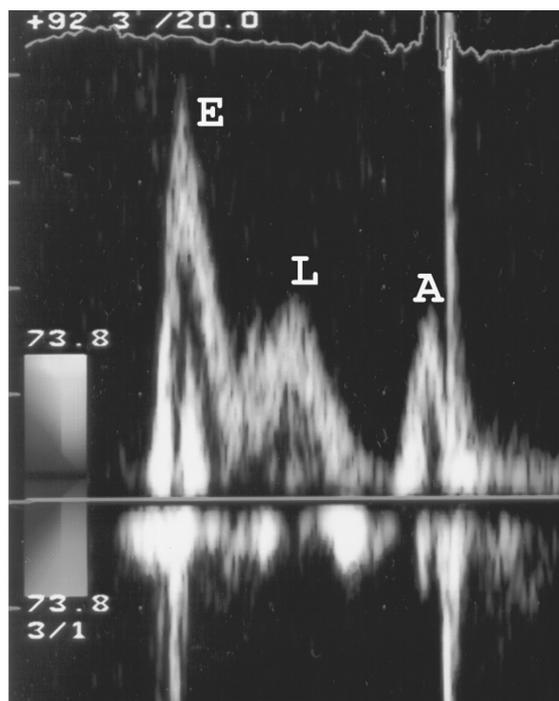


Figure 9. Mitral inflow pattern in a patient with long-standing hypertension and moderate mitral regurgitation. A prominent low velocity L-wave is noted during diastasis. (Reproduced with permission from Ref. 22.)

depressed systolic function. However, it appears to change somewhat proportionately to changes in preload in patients with normal systolic function. In addition, E' varies inversely with afterload.^{15,32,33}

The ratio of the mitral E to E' is relatively insensitive to changes in preload and is therefore useful in differentiating normal from pseudo-normal mitral inflow patterns. This ratio appears to be reliable for estimation of LV filling pressures in patients with both normal and depressed systolic function, including those with hypertrophic cardiomyopathy, atrial fibrillation, and sinus tachycardia (Table 2).³⁴⁻³⁷ An $E/E' < 8$ is seen with normal filling pressure; an $E/E' > 15$ is present when filling pressure is elevated (PAOP > 15 mmHg). When E/E' lies between 8 and 15, other echocardiographic measures should be employed to better predict filling pressures.^{15,26,28}

With impaired myocardial relaxation, the onset of E' is delayed relative to the E -wave. The time interval between E and E' onsets appears to predict filling pressures independent of loading conditions. As E and E' cannot be measured simultaneously, the times from the electrocar-

diogram QRS onset to both E and E' are used to calculate the E' delay relative to E ($TE' - E$). An $IVRT/(TE' - E)$ ratio < 2 predicts a PAOP above 15 mmHg.^{26,38}

Finally, TDI is also helpful in differentiating between restrictive and constrictive physiology. In restrictive cardiomyopathy, E' is < 8 cm/sec while constrictive pericarditis typically is associated with an $E' \geq 8$ cm/sec.^{39,40}

Color M-Mode Flow Propagation

Color M-mode allows for temporal and spatial assessment of diastolic flow propagation from the LA into the LV. This parameter is determined by LV relaxation rate and diastolic suction, but appears to be somewhat dependent upon loading conditions.^{41,42}

Flow propagation velocity (V_p) is obtained from an apical four-chamber view. With color Doppler activated, the M-mode cursor is placed within the mitral inflow to include the LV and part of the LA. The color scale should be set to 55–60 cm/s and sweep speed 100–200 mm/s to obtain an aliased edge of uniform color. The slope at the edge of early diastolic flow from the MV tip to the LV apex represents the V_p (Fig. 11). One should be careful not to include IVRT intracavitary flow. Also, color M-mode flow propagation is limited in small hyperdynamic ventricles.

Normal V_p is greater than 40 cm/s. A reduced V_p implies impaired relaxation and helps distinguish pseudo-normal from normal mitral inflow patterns.^{41,42} The ratio E/V_p correlates reliably with PAOP and is independent of preload. The PAOP is greater than 15 mm Hg when $E/V_p > 2$. This ratio remains accurate in the presence of atrial fibrillation.^{26,28,41,42}

Physiological Influences

An abnormal relaxation pattern may be seen in patients with normal diastolic function and volume depletion.⁴³ This pattern may also be found in individuals with a prolonged PR interval, after a premature contraction, or in the presence of a left bundle branch block (LBBB). Pressure overload of the right ventricle (RV) (due to pulmonary embolism or pulmonary hypertension) and also RV infarction may cause an abnormal LV relaxation pattern due to resultant reduced LV preload and decline in rapid filling.⁴⁴

In young individuals, atrial contraction contributes little to diastolic filling; thus, a

ANALYSIS OF DIASTOLIC FUNCTION

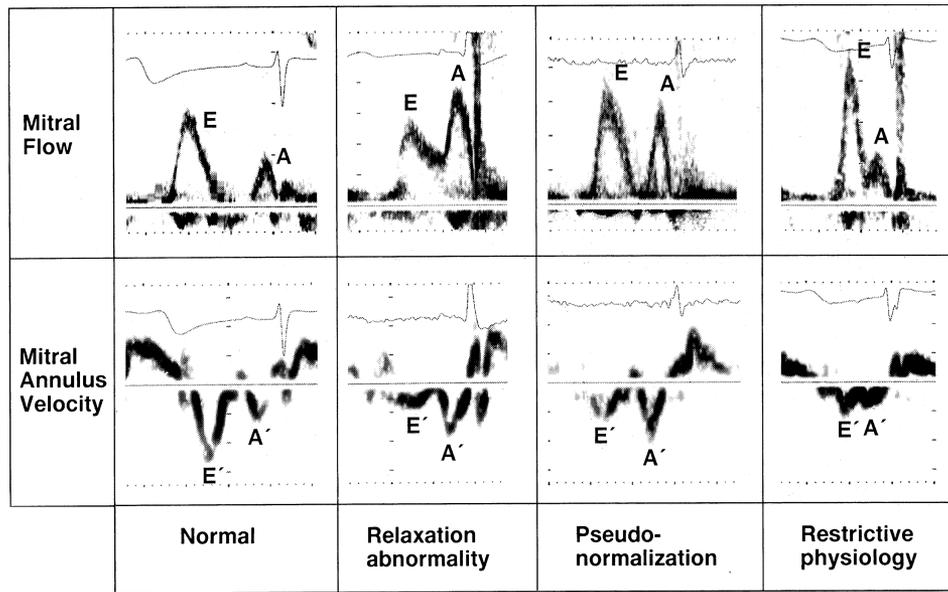


Figure 10. Mitral annulus velocity profiles and associated inflow patterns. (Reproduced with permission from Sohn DW, Chai IH, Lea DJ, et al. Assessment of mitral annulus velocity by Doppler tissue imaging in the evaluation of left ventricular diastolic function. *J Am Coll Cardiol* 1997;30:474.)

pattern similar to restrictive filling can be seen. Mitral regurgitation (causing increased LA pressure) and aortic regurgitation (causing increased LV diastolic pressure) are also associated with a restrictive filling pattern.⁴⁵ Severe obesity, chronic obstructive lung disease, and

simple labored respirations may result in a restrictive LV filling pattern due to elevated right ventricular pressures with ventricular interdependence (bulging of the IVS into the LV cavity, reducing septal contribution to compliance).²²

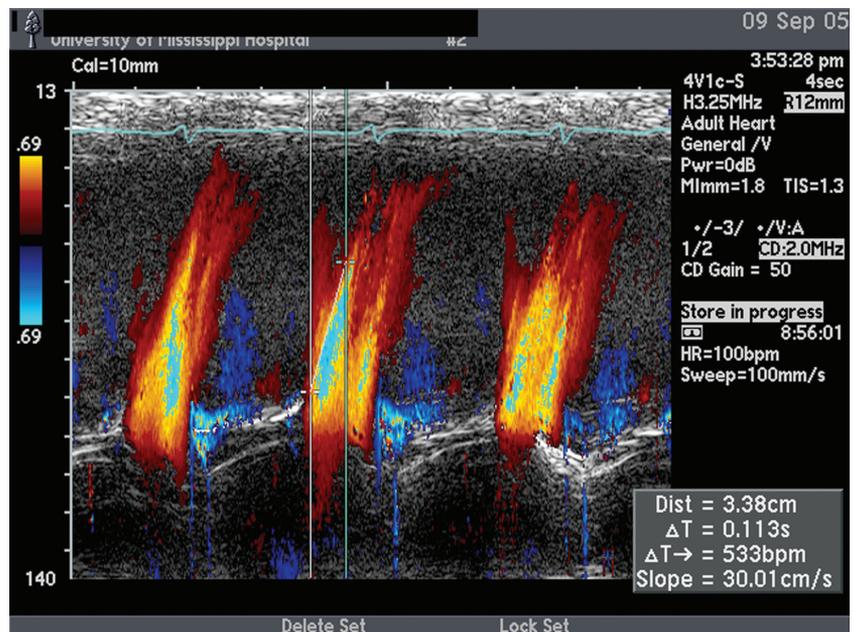
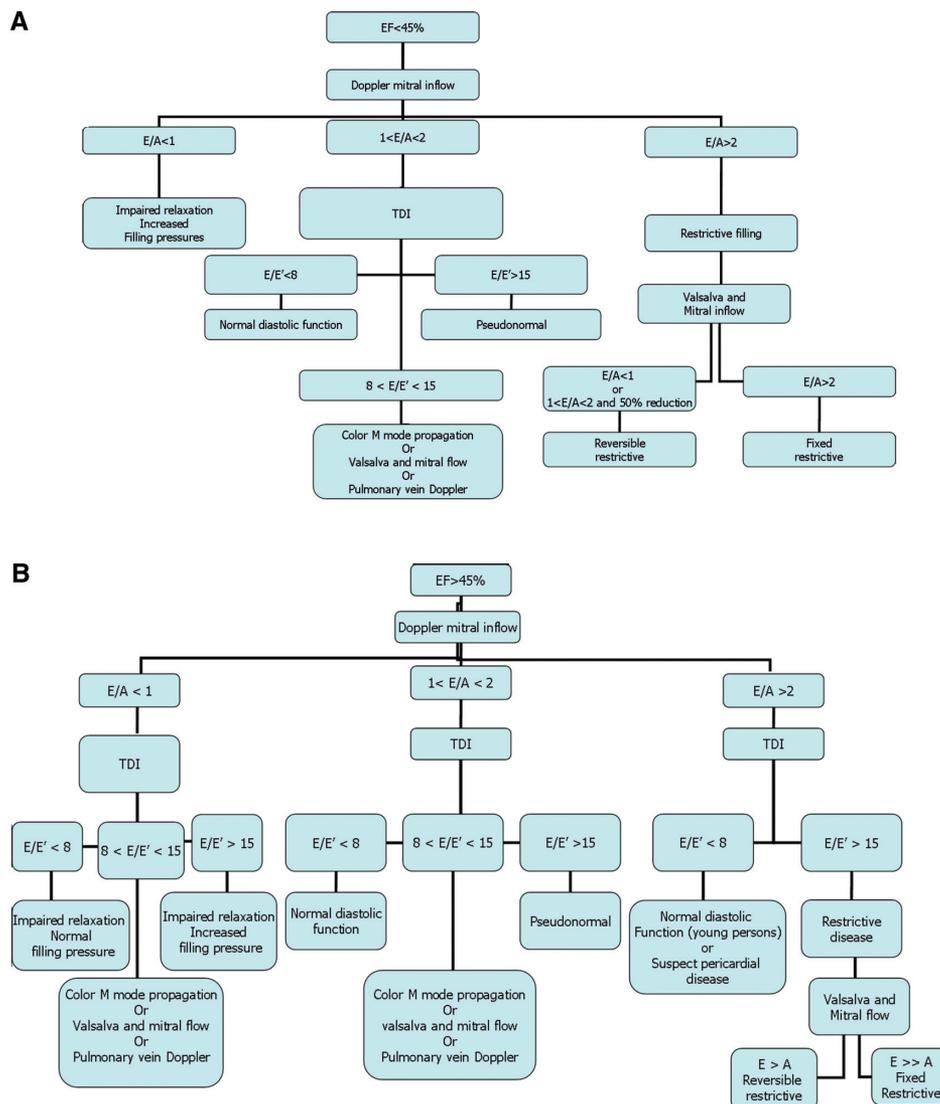


Figure 11. Color M-mode Doppler in a patient with normal mitral flow pattern. The propagation velocity is decreased which suggests pseudonormalization.



Figures 12: Algorithms for assessment of diastolic function in patients with (A) depressed and (B) normal LV systolic function. (Modified from Nagueh SF, Zoghbi WA. Clinical assessment of diastolic filling by Doppler echocardiography. ACC Curr J Rev 2001 Jul/Aug:49.)

Tachycardia causes augmentation of the A-wave, with shortening of the IVRT, but no change in DT. However, as heart rate increases the E- and A-waves will merge, making mitral inflow immeasurable.⁴⁶ Although no A-wave is present in atrial fibrillation, DT and IVRT can be used to analyze diastolic function.

Summary

Doppler echocardiography offers several parameters for the assessment of diastolic function and loading conditions. The clinician should be familiar with these diagnostic meth-

ods and their limitations, and interpret measurements within the clinical context including patient's history and M-mode and 2D findings. A proposed algorithm for analysis of diastole in patients with depressed and normal systolic LV function is provided (Fig 12A and B).

Pearls of Diastolic Function Analysis

- Always assess diastolic function in light of the patient's medical history and M-mode/2D echo findings.

- Dyspneic patients without history of cardiovascular disease and by echocardiography have normal LV size, thickness and systolic function, and also normal LA size are unlikely to have diastolic dysfunction.
- A patient with “normal” transmitral flow pattern, but LA enlargement in the absence of significant MV disease, likely has elevated filling pressures with the mitral pattern representing pseudonormalization.
- Patients with depressed LV systolic function and a “normal” transmitral flow pattern and E/E' between 8 and 15 likely have elevated filling pressures.
- Patients with E/A < 1 without hypovolemia typically have abnormal active relaxation.
- Younger individuals with LVH can have very active relaxation leading to very rapid early filling manifested by diminished DT and IVRT with E/A > 2; this should be distinguished from restrictive filling.

References

1. Gaasch WH, Zile MR: Left ventricular diastolic dysfunction and diastolic heart failure. *Annu Rev Med* 2004;55:373–394.
2. Wood MJ, Picard MH: Utility of echocardiography in the evaluation of individuals with cardiomyopathy. *Heart* 2004;90:707–712.
3. Guyton AC: *Textbook of Medical Physiology, 5th Ed.* Philadelphia, PA, W.B. Saunders Co., 1976 pp. 164–166.
4. Ommen SR, Nishimura RA: A clinical approach to the assessment of left ventricular diastolic function by Doppler echocardiography: Update 2003. *Heart* 2003;89:18–23.
5. Thomas JD: Doppler echocardiography and left ventricular diastolic function. In Gaasch WH, LeWinter MM (eds): *Left Ventricular Diastolic Dysfunction and Heart Failure*. Philadelphia, PA, Lea & Febiger, 1994, p. 192.
6. Little WC, Downes TR: Clinical evaluation of left ventricular diastolic performance. *Prog Cardiovasc Dis* 1990;32:273–290.
7. Ishida Y, Meisner JS, Tsujioka K, et al: Left ventricular filling dynamics: Influence of left ventricular relaxation and left atrial pressure. *Circulation* 1986;74:187–196.
8. Nishimura RA, Tajik AJ: Evaluation of the diastolic filling of left ventricle in health and disease: Doppler echocardiography is the clinician's Rosetta stone. *J Am Coll Cardiol* 1997;30:8–18.
9. Zile MR, Burtsaert DL: New concepts in diastolic dysfunction and diastolic heart failure: Part II. *Circulation* 2002;105:1503–1508.
10. Gaasch WH, Downes TR: Clinical evaluation of left ventricle: Importance to the clinician. *Adv Int Med* 1990;35:311–340.
11. Enriquez-Sarano M, Rossi A, Pouslen S, et al: Determinants of pulmonary hypertension in left ventricular dysfunction. *J Am Coll Cardiol* 1997;29:153–159.
12. Carbone R, Bossone E, Bottino G, et al: Secondary pulmonary hypertension: Diagnosis and management. *Eur Rev Med Pharmacol Sci* 2005;9:331–342.
13. Colucci WS, Braunwald E: Pathophysiology of heart failure. In Zipes DP, Libby P, Bonow RO, Braunwald E (eds): *Brunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 7th Ed. Philadelphia, PA, Elsevier Saunders, 2005 pp. 509–538.
14. Pearson AC, Gudipati CV, Labovitz AJ: Effects of aging on left ventricular structure and function. *Am Heart J* 1991;121:871–875.
15. Ommen SR, Nishimura RA, Appeltton CP, et al: Clinical utility of Doppler echocardiography and tissue Doppler in the estimation of left ventricular filling pressure. *Circulation* 2000;102:1788–1794.
16. Lang RM, Bierig M, Devereux RB, et al: Recommendations for chamber quantification: A report from the American Society of Echocardiography's guidelines and standards committee and the chamber quantification writing group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiography* 2005;18:1440–1463.
17. Munagala VK, Jacobsen SJ, Mahoney DW, et al: Association of newer diastolic function parameters in healthy subjects: A population-based study. *J Am Soc Echocardiogr* 2003;16:1049–1056.
18. Appeltton CP, Galloway JM, Gonzalez MS, et al: Estimation of left ventricular filling pressure using two-dimensional and Doppler echocardiography in adult patients with cardiac disease: Additional value of analyzing left atrial size, left atrial ejection and the difference in duration of pulmonary venous and mitral flow velocity at atrial contraction. *J Am Coll Cardiol* 1993;22:1972–1982.
19. Tirrito SJ, Augustine DR, Kerut EK: How to measure left atrial volume. *Echocardiography* 2004;21:569–571.
20. Araujo AQ: Elucidating the B-bump on the mitral valve M-mode echogram in patients with severe left ventricular dysfunction. *Int J Cardiol* 2004;95(1):7–12.
21. Gibson DG, Francis DP: Clinical Assessment of left ventricular diastolic function. *Heart* 2003;89:231–238.
22. Kerut EK: Diastolic function. In Kerut EK, McIlwain EF, Plotnick GD (eds): *Handbook of Echo Doppler Interpretation, 2nd Ed.* Elmsford, Blackwell Futura, 2004 pp. 64–80.
23. Klein AL, Tajik AJ: Doppler assessment of pulmonary venous flow in healthy subjects and in patients with heart disease. *J Am Soc Echocardiogr* 1991;4:379–392.
24. Rossvoll O, Hatle Lk: Pulmonary venous flow velocities recorded by transthoracic Doppler ultrasound: Relation to left ventricular diastolic pressures. *J Am Coll Cardiol* 1993;21:1687–1696.
25. Ohno M, Cheng CP, Little WC: Mechanism of altered patterns of left ventricular filling during the development of congestive heart failure. *Circulation* 1994;89:2241–2250.
26. Quinones MA: Assessment of diastolic function. *Prog Cardiovasc Dis* 2005;47:340–355.
27. Hurrell DG, Nishimura RA, Ilstrup DM, et al: Utility of preload alteration in assessment of left ventricular filling pressure by Doppler echocardiography: A simultaneous catheterization and Doppler echocardiography study. *J Am Coll Cardiol* 1997;30:459–467.
28. Pozzoli M, Traversi E, Roelandt J: Non-invasive estimation of left ventricular filling pressure by Doppler echocardiography. *Eur J Echocardiography* 2002;3:75–79.
29. Appeltton CP, Jensen JL, Hatle LK, et al: Doppler evaluation of left and right ventricular diastolic function:

- A technical guide for obtaining optimal flow velocity recordings. *J Am Soc Echocardiogr* 1997;10:271–292.
30. Reagan BW, Helmcke F, Kerut EK: Commonly used respiratory and pharmacological interventions in the echocardiography laboratory. *Echocardiography* 2005;22:455–460.
 31. Pozzoli M, Traversi E, Cioffi G, et al: Loading manipulation improves the prognostic value of Doppler evaluation of mitral flow in patients with chronic heart failure. *Circulation* 1997;95:1222–1230.
 32. Vasan RS, Levy D: Defining diastolic heart failure: A call for standardized diagnostic criteria. *Circulation* 2000;101:2118–2121.
 33. Nagueh SF, Sun H, Kopelen HA, et al: Hemodynamic determinants of the mitral valve annulus diastolic velocities by tissue Doppler. *J Am Coll Cardiol* 2001;37:278–285.
 34. Nagueh S, Lakkis N, Middleton K, et al: Doppler estimation of left ventricular filling pressure in patients with hypertrophic cardiomyopathy. *Circulation* 1999;99:254–261.
 35. Nagueh S, Mikati I, Kopelen H, et al: Doppler estimation of left ventricular filling pressure in sinus tachycardia. *Circulation* 1998;98:1644–1650.
 36. Rivas-Gotz C, Manolios M, Thohan V, et al: Impact of left ventricular ejection fraction on estimation of left ventricular filling pressures using tissue Doppler and flow propagation velocity. *Am J Cardiol* 2003;91:780–784.
 37. Matsumura Y, Elliott PM, Virdee MS, et al: Left ventricular diastolic function assessed using Doppler tissue imaging in patients with hypertrophic cardiomyopathy: Relation to symptoms and exercise capacity. *Heart* 2002;87:247–251.
 38. Rivas-Gotz C, Houry DS, Manolios M, et al: Time interval between onset of mitral inflow and onset of early diastolic velocity by tissue Doppler: A novel index of left ventricular relaxation. *J Am Coll Cardiol* 2003;42:1463–1470.
 39. Ha JW, Ommen SR, Tajik AJ, et al: Differentiation of constrictive pericarditis from restrictive cardiomyopathy using mitral annular velocity by tissue Doppler echocardiography. *Am J Cardiol* 2004;94:316–319.
 40. Sengupta PP, Mohan JC, Mehta V: Accuracy and pitfalls of early diastolic motion of the mitral annulus for diagnosing constrictive pericarditis by tissue Doppler imaging. *Am J Cardiol* 2004;93:886–890.
 41. Takatsuji H, Mikami T, Uraswa K, et al: A new approach for evaluation of left ventricular diastolic function: Spatial and temporal analysis of left ventricular filling flow propagation by color M-mode Doppler echocardiography. *J Am Coll Cardiol* 1996;27:365–371.
 42. Garcia MJ, Smedira NG, Grennberg NL, et al: Color M-mode Doppler flow propagation velocity is a preload insensitive index of left ventricular relaxation: Animal and human validation. *J Am Coll Cardiol* 2000;35:201–208.
 43. Thomas JD, Choong CYP, Flachskampf FA, et al: Analysis of the early transmitral Doppler velocity curve: Effects of primary physiologic changes and compensatory preload adjustment. *J Am Coll Cardiol* 1990;16:644–655.
 44. Feigenbaum H: Echocardiographic evaluation of cardiac chambers. In Feigenbaum H (ed): *Echocardiography, 5th Ed.* Philadelphia, PA, Lea & Febiger, 1994 pp. 134–180.
 45. Zoghbi WA, Enriquez-Sarano M, Foster E, et al: Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography: American society of echocardiography report. *J Am Soc Echocardiogr* 2003;16:777–802.
 46. Harrison MR, Clifton GD, Pennell AT, et al: Effect of heart rate on left ventricular diastolic transmitral flow velocity patterns assessed by Doppler echocardiography in normal subjects. *Am J Cardiol* 1991;67:622–627.