Diastolic Function Assessment Incorporating New Techniques in Doppler Echocardiography

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Congestive heart failure (CHF) is the leading cause of cardiac morbidity and mortality from cardiovascular disease. Although left ventricular (LV) diastolic dysfunction occurs in all patients with systolic dysfunction and CHF, fully one third of patients have CHF due to isolated diastolic dysfunction. Despite this, the role of diastolic function in heart failure is underappreciated by many primary care physicians and even by cardiologists. Development and validation of several noninvasive Doppler echocardiographic techniques that are relatively load-independent have made echocardiography the clinical standard for the assessment of LV diastolic function. Echocardiography uses portable equipment; is readily accessible and safe; and excludes other causes of CHF, such as valvular heart disease, pericardial disease, and systolic dysfunction. This review summarizes the use of recently developed Doppler techniques for the assessment of LV diastolic function, as well as their application in assessing prognosis and in guiding therapy for various cardiovascular disease states. [Rev Cardiovasc Med. *2003;4(2):81–99*]

Key words: Color Doppler echocardiography • Congestive heart failure • Diastolic dysfunction • Doppler tissue imaging • Echocardiography • M-mode echocardiography • Pulsed-wave Doppler echocardiography

A significant number of patients with congestive heart failure (CHF) have normal left ventricular (LV) systolic function.[1–3] As many as 35%–40% of men and 65%–75% of women with CHF may have preserved left ventricular ejection fraction (LVEF) (≥50%).[3–5] Recent studies suggest that diastolic dysfunction is a major cause of CHF. Diastolic function predicts prognosis of patients with CHF independent of the degree of LV systolic dysfunction[2,6–10] and is therefore important to clinicians. The portability and noninvasive nature of ultrasonography, along with recent advances in its technology, make it a useful tool for assessing diastolic function.

Diastolic function is a complex interplay of numerous components, including LV relaxation, diastolic suction, viscoelastic forces of the myocardium, pericardial restraint, ventricular interaction, and atrial contribution.[11] The two major determinants of LV filling are ventricular relaxation and effective chamber compliance.[12] Myocardial wall relaxation is related to the time constant of intracavitary pressure decay during isovolumic relaxation, whereas myocardial wall compliance and stiffness are related more to the local slope of the pressure/volume curve.

The most common methods for assessing LV diastolic function employ echocardiography, using mitral and pulmonary vein inflow pulsed-wave (PW) Doppler.[13–16] These techniques do not evaluate the primary event of LV relaxation but instead measure the impact of altered LV diastolic properties by assessing diastolic flow velocities, which result from pressure gradient changes at the mitral orifice and systolic and diastolic flow velocities in the pulmonary veins. The diagnostic value of such Doppler-derived indices is somewhat limited by the strong influence of heart rate and ventricular loading conditions.[17,18] More recently, two new techniques—myocardial or mitral annulus motion by PW Doppler tissue imaging (DTI) and color M-mode velocity propagation within the LV cavity—have been used to assess LV diastolic function. DTI analysis has the potential to evaluate the primary event—the myocardial velocity dynamics of ventricular relaxation[19–22]—whereas color M-mode measures the impact of LV relaxation on intraventricular pressure gradients and blood flow propagation within the LV cavity.[23] Unlike mitral inflow and pulmonary vein Doppler, DTI and color M-mode are

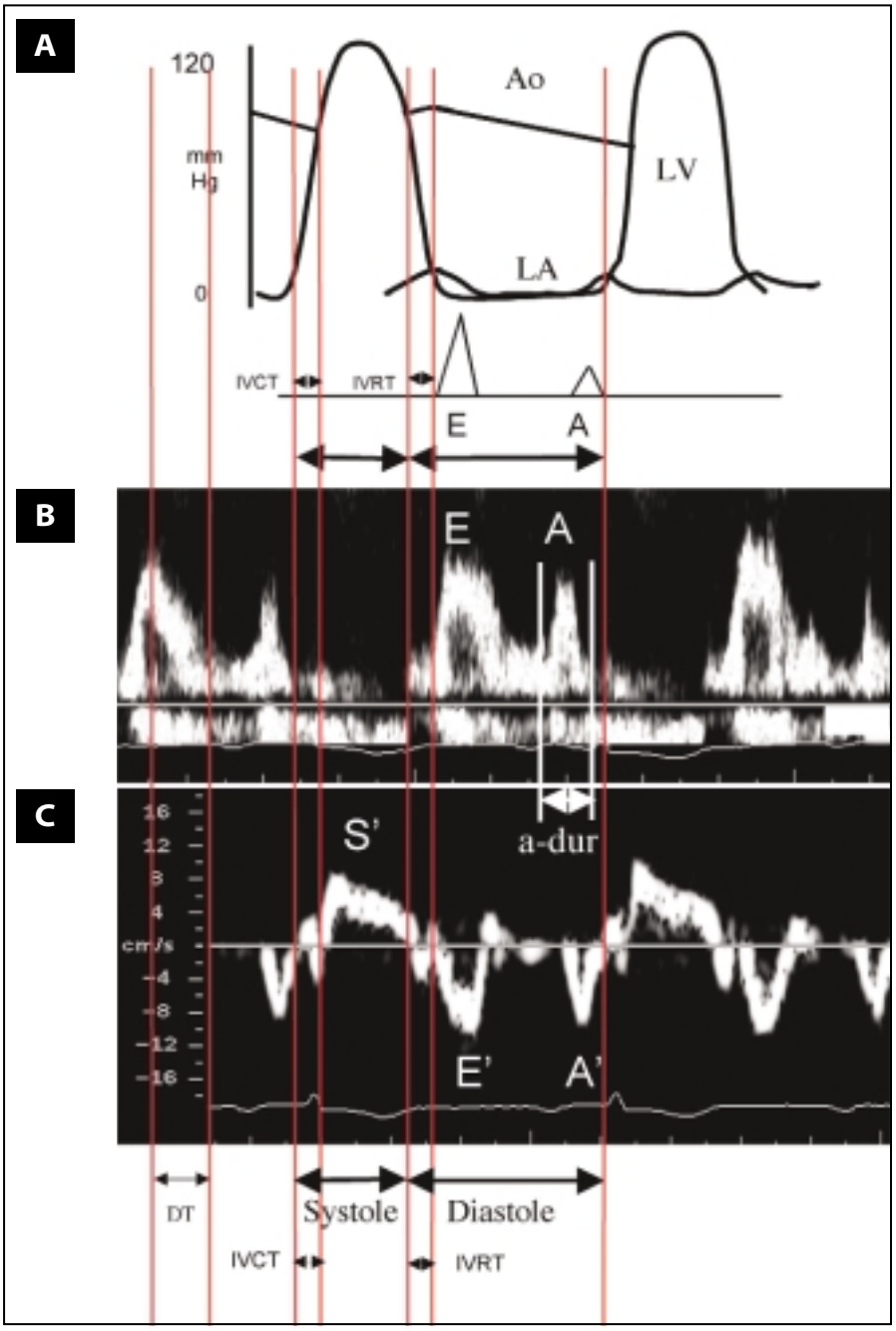

Figure 1. *Schematic drawing showing* **(A)** *normal left atrial and ventricular pressures,* **(B)** *mitral inflow, resulting from atrioventricular gradients, and* **(C)** *myocardial pulsed-wave (PW) Doppler depicting myocardial motion in a healthy subject. Mitral inflow velocities were obtained by placing the PW Doppler sample volume between the tips of the mitral leaflets and Doppler tissue imaging by placing the PW Doppler sample volume at the lateral mitral annulus. Large black horizontal arrows depict duration of ventricular systole and ventricular diastole. In healthy subjects older than 20 years, mitral inflow IVRT ranges from 67 ± 8 to 87 ± 7 ms, deceleration time (DT) from 166 ± 14 to 200 ± 29 ms, mitral inflow E/A ratio from 1.5 ± 0.40 to 0.96± 0.18, E wave from 75 ± 13 to 71 ± 11 cm/s, A wave from 51 ± 11 to 75 ± 12 cm/s, and a-dur from 127 ± 13 to 138 ± 19 ms; the initial numbers in these ranges represent results in younger age groups (21–40 years) and the upper numbers those in older age groups (> 60 years). A-dur, atrial duration mitral inflow (white arrowhead B); Ao, aortic pressure tracing; LV, left ventricular pressure tracing; LA, left atrial pressure tracing; E, mitral inflow early filling wave; A, mitral inflow late filling wave; S', myocardial systolic wave; E', myocardial early relaxation wave; A', late myocardial diastolic wave; deceleration time (DT) (small black arrows); IVCT (small black arrowheads), isovolumetric contraction time; IVRT (small black arrowheads), isovolumetric relaxation time.*

relatively load-independent, as discussed below. This review focuses on these more recently developed techniques for assessing diastolic function.

Pulsed-Wave Doppler Correlates of LV Gradients and Filling

Seminal work by Appleton and colleagues,[24] using invasive determination of LV pressure and simultaneous Doppler echocardiography, demonstrated the relationship between intraventricular gradients and Doppler velocity shifts during ventricular filling. Figure 1 represents the changes in the LV pressure in early diastole, PW Doppler mitral inflow, and myocardial Doppler pattern in a healthy subject. During the isovolumic relaxation time (IVRT), prior depolarization of the myocardium leads to the onset of active relaxation of the outer myocardial wall and to rapid LV volume change. The increase in LV diastolic volume while ventricular blood mass remains constant leads to a sudden absolute decrease in LV intracavitary pressure.

This continuous process of myocardial wall relaxation and intracavitary pressure drop causes LV pressure to become lower than left atrial (LA) pressure, ending the IVRT and causing mitral valve opening. The LA-LV pressure gradient and a "suction" effect following IVRT allow for early LV filling (E, defined as the early diastolic filling wave on PW mitral inflow Doppler). The rate of decrease of E velocity in early diastole depends on the rate of increase in LV pressure and is measured as the deceleration time (DT). It is the time interval between peak of E to the end of E wave (Figure 1). DT is determined by a combination of forces: LA-LV pressure gradient at the time of mitral valve opening, LA compliance, LV chamber compliance,[25] rate of LV relaxation,[26] viscoelastic forces of the myocardium, pericardial restraint, and LV-right ventricular interaction.[27] Once pressures are equilibrated in mid-diastole, forward flow continues because of inertial forces. Left atrial contraction then leads to another LA-LV pressure gradient that results in late LV filling (A wave, defined as the late diastolic filling wave on PW mitral inflow Doppler). Because LA contraction usually occurs after LV relaxation is completed, the peak A velocity and duration depend on LV chamber compliance[25,28,29] and atrial volume, as well as on atrial contractility.

Mitral inflow Doppler is obtained by placing the PW Doppler sample volume between the mitral leaflet tips. Mitral inflow E/A ratio is age-dependent[30] and has four major patterns (Figure 2).[11,14,15] *Normal mitral inflow* E/A ratio is >1.0 in healthy states until age 60 years.[30] In the early phase of diastolic dysfunction, the duration of LV relaxation is prolonged into mid or late diastole, causing a slower decline in LV pressure. With normal LV and LA compliance, however, LA and LV pressures remain normal. A small E wave, prolonged IVRT and DT, and a reversal of E/A ratio result from high residual atrial preload and normal LA contractility.

This pattern of mitral inflow is called *abnormal relaxation pattern*. There is a close relationship among the degree of LV hypertrophy, the mitral inflow A wave, and the myocardial A wave,[31] suggesting that the atrial contribution plays an important role with increasing LV hypertrophy. As opposed to healthy subjects, in whom LA contraction contributes up to 20% of cardiac output, patients with abnormal relaxation may have LA contraction that contributes up to 35% of cardiac output.[32] In patients with advanced disease, increased myocardial stiffness results in a decrease in chamber compliance during diastolic filling. The resulting increase in LA pressure overrides the effects of impaired LV relaxation,[17,18] causing a *"pseudonormal" mitral inflow* that hides the underlying abnormality of LV relaxation.[33] The preload as well as the LV relaxation dependency of the transmitral flow velocity leads to a poor correlation of mitral inflow with invasive variables of LV diastolic properties.[18,33]

Diastolic function predicts prognosis of patients with CHF, independent of the degree of LV systolic dysfunction.

Strategies that lower LV preload, such as the Valsalva maneuver or administration of nitroglycerin or diuretics, decrease E/A ratio (with a change of more than 0.5) and prolong DT, so that a pseudonormal mitral inflow pattern may become an abnormal relaxation or even a normal inflow pattern.[34] With severe abnormalities of ventricular compliance, advanced diastolic dysfunction develops, characterized by a markedly increased E velocity. DT becomes short from rapid equalization of LA-LV pressure soon after early diastolic filling in a noncompliant ventricle. Because of poor LA function and limited late diastolic LA-LV pressure gradient from an elevated LV diastolic pressure, A wave amplitude becomes small.

Initially, this *restrictive mitral inflow* pattern is reversible upon preload reduction with the Valsalva

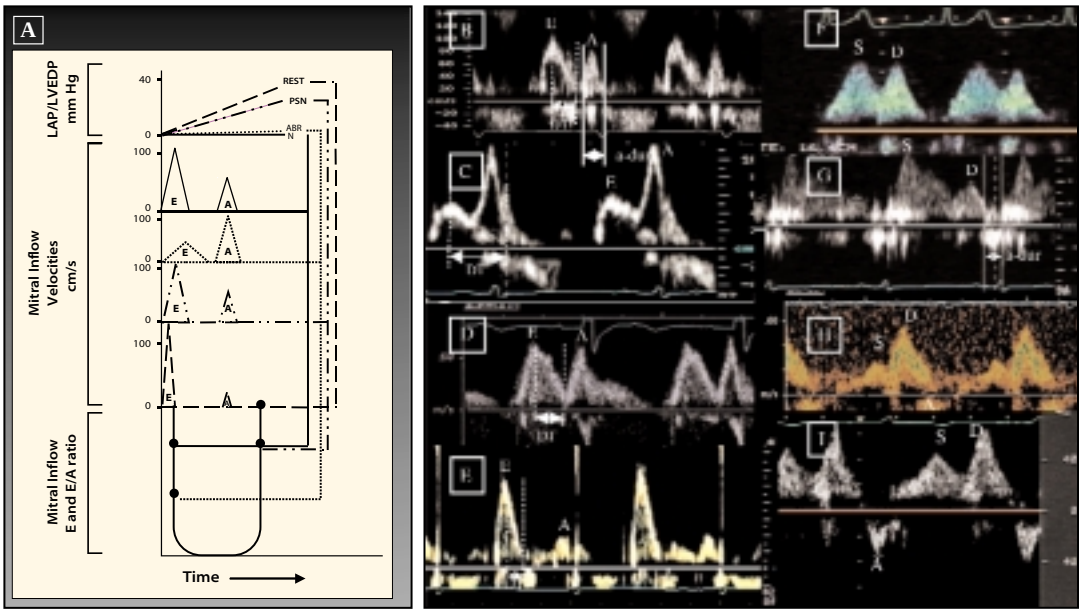

Figure 2. (A) *Diagram of left ventricular diastolic/left atrial pressures, corresponding mitral inflow velocities, and changing E and E/A ratios with increasing diastolic dysfunction, giving a U-shaped pattern. N, normal filling pattern; ABR, abnormal relaxation; PSN, pseudonormal filling pattern; REST, restrictive filling pattern; LVED, left ventricular end-diastolic pressure.* **(B–E)** *Mitral inflow PW Doppler patterns in* **(B)** *a normal subject,* **(C)** *a patient with abnormal LV relaxation and an LVEF of 70%,* **(D)** *a patient with an LVEF of 35% and abnormal LV relaxation and compliance causing pseudonormal mitral inflow, and* **(E)** *a patient with a restrictive filling pattern and an LVEF of 20%.* **(F–I)** *Pulmonary vein PW Doppler patterns in* **(F)** *a normal subject,* **(G)** *a patient with abnormal LV relaxation,* **(H)** *a patient with abnormal LV relaxation and compliance, and* **(I)** *a patient with a restrictive filling pattern. S, pulmonary vein systolic wave; D, pulmonary vein diastolic wave; A, pulmonary vein atrial wave; a-dur, duration of mitral and pulmonary a-waves. Pulmonary vein velocities were obtained by placing the PW Doppler sample volume in the right superior pulmonary vein. Note that in the presence of pseudonormal mitral inflow, pulmonary vein Doppler shows reversal of the S/D ratio and increased atrial reversal velocity and duration. In healthy subjects older than 20 years, pulmonary vein S velocity ranges from 44 ± 10 to 52 ± 11 cm/s, D velocity from 47 ± 11 to 39 ± 11 cm/s, A velocity from 21 ± 8 to 25 ± 9 cm/s, a-dur from 96 ± 33 to 113 ± 30 ms, and S/D ratio from 0.98 ± 0.32 to 1.39 ± 0.47, and mitral inflow a-dur is greater than pulmonary vein a-dur. The initial numbers in the ranges listed above represent values in younger patients (21–40 years) and later numbers in older patients (> 60 years).*

maneuver or nitroglycerin or diuretic administration. Eventually, an irreversible restrictive pattern develops, with no significant change through preload reduction. Thus, mitral inflow E wave and E/A ratio follow a U-shaped pattern with increasing diastolic dysfunction (Figure 2A).

Pulmonary Vein PW Doppler

Used to depict Doppler velocity shifts due to LA filling from the pulmonary veins, pulmonary vein Doppler is obtained by placing a color flow-guided 3- to 4-mm Doppler PW sample volume 1–3 cm deep within the pulmonary vein whose flow is most nearly parallel to the ultrasound beam.[14,15] Pulmonary vein filling patterns corresponding to mitral inflow filling patterns are shown in Figure 2B–2I.

Unlike ventricular filling, LA filling occurs both in systole and in diastole, so that pulmonary vein Doppler in healthy adults is composed of a systolic (S) and a diastolic (D) wave. The systolic component may be further subdivided into an early component (S_1, from atrial relaxation) and a late component (S_2, due to an increase in pulmonary venous flow following right ventricular systole and an increase in LA area following mitral annular descent). Systolic filling following atrial contraction is also influenced by LA compliance, mean LA pressure,[35] LV pressure,[36] and presence or absence of mitral regurgitation.[37] Diastolic atrial filling (D wave) results from the pulmonary vein–LA pressure gradient created during atrioventricular filling in early LV diastole and is dependent on the same factors that influence early mitral velocity and its DT.

In the presence of normal LA pressure, systolic flow is dominant, and the systolic filling fraction of the LA is usually greater than 60%. There is a small reverse component following S and D waves, reflecting atrial contraction (A wave). This flow occurs due to the lack of valves at the pulmonary vein–atrial junction[16,38] and is insignificant, as normal gradients and compliance drive forward atrioventricular filling during LA contraction.[39] As LA pressure increases, antegrade systolic flow decreases and the diastolic wave becomes more prominent. The DT of the D wave also becomes shorter, by the same mechanism as the mitral inflow E wave DT. With abnormal LV relaxation and compliance, an increase in LV end-diastolic pressure leads to minimal atrioventricular filling upon atrial contraction and a prominent and prolonged pulmonary vein A-wave reversal (a-dur, defined as duration of reverse pulmonary vein a-wave) that becomes greater than the mitral inflow a-dur. Finally, impairment of LA contraction due to mechanical atrial failure leads to a decrease in amplitude and duration of the pulmonary vein A wave.[40] Like mitral inflow and DT, which follow a

U-shaped pattern, pulmonary vein S/D ratio follows an (inverted) U-shaped pattern with increasing LV diastolic dysfunction. Maneuvers that lower LA pressure (Valsalva, nitroglycerin administration, diuretic therapy) may reverse some of these changes in pulmonary vein flow.

A number of studies have shown that, in the setting of isolated diastolic dysfunction and normal LV systolic function, mitral and pulmonary vein flow (excluding the difference between mitral and pulmonary a-dur) are not clearly related to filling pressures. In addition, the accuracy of mitral and pulmonary venous indices in predicting filling pressures is dependent on the presence of sinus rhythm. The new Doppler parameters DTI and color M-mode velocity propagation (Vp), as discussed below, retain their accuracy for assessing filling pressures in atrial fibrillation[41,42] and, in cases of fusion or near fusion, of the early and late mitral inflow velocities.

Normal velocities in the bloodstream may reach 150 cm/s, whereas solid tissues seldom show velocities above 15 cm/s.

Doppler Tissue Imaging

Two main sources contribute to the Doppler shift of the returned ultrasonic signals: red blood cells, which move with the blood flow, and slow-moving solid structures, including the ventricular walls and cardiac valves. Velocities in the bloodstream may reach 150 cm/s, whereas solid tissues seldom show velocities above 15 cm/s.[43–47] Therefore, the frequency spectrum of the ultrasound Doppler signal has two main components: a high-frequency, low-amplitude band corresponding to blood flow, and a low-frequency, high-amplitude band related to heart motion. In conventional Doppler systems, designed to deal with blood flow, Doppler signals from tissue motion are considered "noise" and eliminated by means of a high-pass filter. In DTI, the meaningful information is contained in the low-frequency, high-amplitude signal of myocardial motion. Pulsed DTI evaluates myocardial wall relaxation, while mitral inflow PW Doppler flow assesses global LV filling.[48–55]

PW myocardial Doppler sampling that displays the velocity of a selected myocardial region against time provides high temporal resolution and allows reliable and direct quantitation of myocardial relaxation. Segmental myocardial diastolic function can be assessed by placing the PW sample volume within the myocardium, typically in the basal myocardial segment.[12] For the assessment of global diastolic function, DTI of mitral annular motion is obtained from the apical four-chamber view, and the E′ wave at the lateral corner of the mitral annulus is used, provided no regional wall motion abnormalities are present.[41,56] The evaluation of the septal corner has shown similar results in this assessment. The method of obtaining DTI velocities is detailed in Appendix 1, and its pitfalls are described in Appendix 2. Figure 1C and Figure 3A show PW DTI tracings from the lateral mitral annulus in a healthy subject. Myocardial or mitral annular PW Doppler displays five consecutive waves, whose directions vary according to the phase of the cardiac cycle. During systole, a single positive wave corresponding to LV ejection (S), beginning at the end of QRS complex and ending at the end of the T wave, and during diastole, two negative waves—an early (E′) rapid wave and a late (A′) wave correspon-

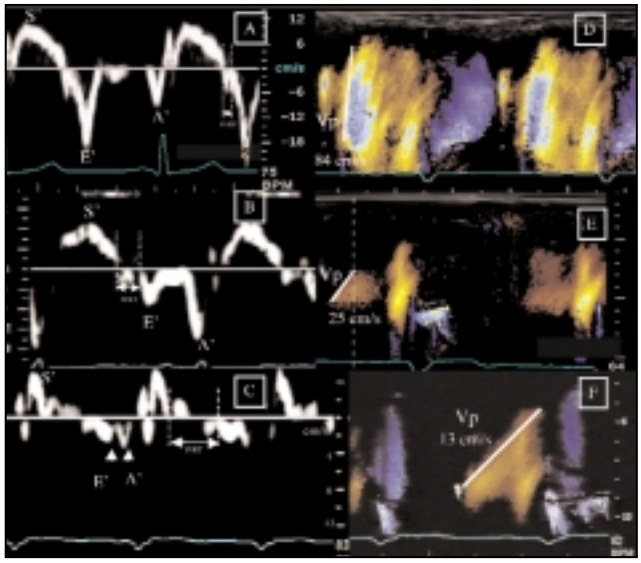

Figure 3. (A-C) *Mitral annular pulsed-wave (PW) Doppler tissue imaging tracings in* **(A)** *a normal subject,* **(B)** *a patient with abnormal left ventricular (LV) relaxation, and* **(C)** *a patient with restrictive cardiomyopathy. Mitral annular PW Doppler displays five consecutive waves, whose directions vary according to the phase of the cardiac cycle. During systole, one single wave corresponding to LV ejection (S′), beginning at the end of QRS complex and ending at the end of the T wave, and during diastole, two negative waves—an early (E′) rapid filling wave and a late (A′) filling wave corresponding to atrial contraction—are sequentially observed. Isovolumetric relaxation time (IVRT, white horizontal arrow) is the interval between the end of the S′ wave and the beginning of the E′ wave. Color M-mode Doppler ultrasound of the LV diastolic flow velocity propagation in* **(D)** *a normal subject,* **(E)** *a patient with abnormal LV relaxation, and* **(F)** *a patient with restrictive cardiomyopathy. S′, myocardial systolic wave; E′, myocardial early relaxation velocity; A′, late myocardial diastolic velocity; Vp, velocity propagation. Note the decreasing E′ and Vp and increasing myocardial IVRT with increasing relaxation and compliance abnormality.*

ding to myocardial relaxation and atrial contraction, respectively—are sequentially observed. The IVRT is the time interval between the end of the S wave (on DTI) or the second heart sound (on phonocardiography) and the onset of the early diastolic E′ wave.[57]

Relation of Transmitral PW Doppler and DTI

There is a direct correspondence between the PW Doppler velocities obtained by mitral inflow and those obtained by mitral annular/myocardial Doppler (DTI), reflecting the major physiologic events that occur during the diastolic phase of the cardiac cycle (Figure 1).

Unlike mitral inflow velocity, peak early myocardial mitral annular diastolic velocity is relatively load-independent and provides more accurate assessment of LV filling pressure.[58] It correlates with the invasively derived time constant of isovolumetric relaxation.[59–61] Unlike biphasic mitral inflow E wave and E/A ratio, DTI E′ wave and E′/A′ ratio show progressive abnormality with increasing diastolic relaxation[62] (Figure 3B and 3C) and, hence, can differentiate a pseudonormal from a normal Doppler mitral inflow pattern.[34,62] Myocardial DTI E′/A′ wave ratio is helpful in the early assessment of diastolic dysfunction in patients with hypertension,[63] transplantation rejection,[64] or restrictive cardiomyopathy.[65] Although recent observations suggest load dependency of the DTI E′ wave, particularly in healthy human subjects with normal LV relaxation,[66] preload was found to have a minimal effect on DTI E′ wave in the presence of abnormal LV relaxation in experimental animal models.[61]

Temporal events as assessed by DTI also permit assessment of LV relaxation. In a recent study of healthy volunteers and patients with or without left ventricular hypertrophy (LVH) and normal systolic function,[31] myocardial IVRT and myocardial a-dur differed significantly among the three groups, when mitral inflow a-dur and IVRT were comparable. Myocardial DTI E′ wave ($r = -0.43$), IVRT ($r = 0.52$), and a-dur ($r = 0.59$) correlated with LV wall thickness. Only mitral inflow A wave velocity correlated with LV hypertrophy ($r = 0.43$). This close relationship among the degree of LV hypertrophy, the mitral inflow A wave, and the myocardial A wave suggests that atrial contribution plays an increasingly important role with increasing LV hypertrophy. Late mitral annular velocity also correlates with LV end-diastolic pressure. In an animal study, the late diastolic velocity at both corners of the mitral annulus had significant positive correlation with LA dP/dt (p = pressure, t = time) ($r = 0.67$) and LA relaxation ($r = 0.73$) but an inverse correlation with LV end-diastolic pressure ($r = -0.53$).[61] Unlike conventionally measured IVRT, IVRT as measured by myocardial DTI becomes progressively prolonged with increasing LV hypertrophy and helps differentiate pseudonormal from normal mitral inflow pattern (Figure 3).

Color M-Mode Vp

Color M-mode echocardiography permits spatial (approximately 1 mm) and temporal (2.5–10 ms) visualization of flow propagation inside the whole LV cavity, from the mitral annulus to the LV apex.[23,67] The information displayed on color M-mode is comparable to that provided by multiple simultaneous PW Doppler tracings placed serially at different levels from the mitral orifice to the LV apex. Single-gated PW Doppler echocardiography can offer the same temporal resolution but fails to provide simultaneous information in different locations. Two-dimensional color Doppler ultrasound can provide the same spatial resolution but provides poor temporal resolution (approximately 20 frames/s).

On color M-mode echocardiography, the extent of flow propagation can be analyzed during both early and late filling.[42] A first wave propagates from the LA to the LV apex, reflecting early diastolic relaxation; a second wave corresponds to LA contraction.

With normal LV diastolic filling, rapid LV relaxation generates a dynamic pressure gradient, initially at the mitral orifice.[17] This early diastolic intraventricular pressure gradient between LV base and apex, representing the driving force for base-to-apical flow during early filling (according to the Bernoulli equation), was first described by Ling and colleagues.[68] The intraventricular minimal pressure does not increase significantly, and the pressure gradient is still maintained in the middle of the LV during diastole.[69] Thus, peak LV filling can be rapidly propagated sequentially from the mitral orifice toward the LV apex. In contrast, filling related to LA contraction does not pass the mid portion of the ventricle[23] (Figure 3D). In older normal subjects, early and late filling progress toward the apex at an equal rate.

In the case of diastolic dysfunction, the transmitral pressure gradient, diminished by the impaired relaxation process, results in decreased transmitral flow velocity.[17] The early diastolic intraventricular gradient is lost because of rapidly increased LV minimal pressure,[26,33] causing slower propagation of early filling flow. In a state of pseudonormalized mitral flow, an elevated transmitral pressure gradient causes increased early transmitral velocity.

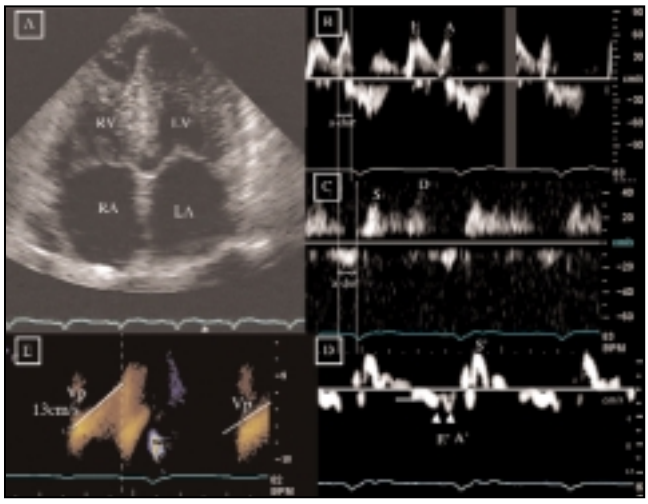

Figure 4. *Apical 4-chamber view in a 64-year-old male patient with cardiac amyloidosis.* **(A)** *Marked diffuse increase in myocardial thickness and biatrial enlargement.* **(B)** *Mitral inflow PW Doppler image showing pseudonormal mitral inflow, E/A ratio, and deceleration time (190 ms).* **(C)** *Pulmonary vein PW Doppler echocardiogram showing prolonged A-wave duration (horizontal arrow, a-dur 135 ms) but low (20 cm/s) pulmonary vein atrial reversal velocity compared to mitral A-wave duration (horizontal arrow, a-dur 95 ms).* **(D)** *Mitral annular PW Doppler showing markedly prolonged isovolumetric relaxation time (IVRT, horizontal line) and markedly decreased myocardial diastolic velocities (E′ and A′, white arrowheads).* **(E)** *Color M-mode image showing decreased early diastolic velocity propagation (Vp 13 cm/s). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. Other abbreviations as in previous figure legends.*

In the setting of severely reduced LV distensibility, LV pressure increases immediately after initial LV filling.[70] Thus, the large atrioventricular difference decays rapidly, and the driving force of the LV filling is quickly dampened near the mitral orifice.[24,69] Consequently, the filling flow propagation is rapidly attenuated in spite of increased early transmitral velocity. In this situation, when peak early to late mitral inflow velocity ratio remains normal, the color M-mode pattern is similar to the pattern observed in young healthy subjects, but the progression toward the apex is delayed and can take up an entire cardiac cycle. When the mitral inflow velocity ratio is abnormal (E < A), early filling does not always reach the apical region of the LV, which is instead attained by the flow related to LA contraction (Figure 3E). In patients with dilated and restrictive cardiomyopathy, when both peak early and late transmural velocities are low, flow is not recorded beyond the mid portion of the LV (Figure 3F).

The method of assessment of color M-mode Doppler echocardiography is detailed in Appendix 3, and common pitfalls are described in Appendix 4. Normal LV relaxation causes rapid Vp during early diastole. Young healthy adults have a color M-mode Vp >50 cm/s[23,71,72] (Figure 3D). A color M-mode early Vp of <50 cm/s reliably detects patients with all grades of diastolic dysfunction.[73] Delayed LV relaxation, such as that which occurs with advanced age,[23] LV hypertrophy, or restrictive heart disease, causes a slowing of velocity propagation and a slow Vp (Figure 3E and 3F). Figures 3 and 4 illustrate progressive abnormality in Vp on color M-mode echocardiography with increasing diastolic dysfunction. The patient in Figure 4 had a relatively normal mitral inflow and pulmonary vein velocity pattern but marked abnormality on both myocardial PW Doppler and color M-mode velocity propagation. This patient had severe diastolic dysfunction and CHF due to cardiac amyloidosis. Although both mitral annular PW Doppler and color M-mode velocity propagation are relatively load-independent compared with mitral inflow and pulmonary vein inflow,[74] it should be emphasized that Vp is most accurate in the presence of LV systolic dysfunction.[75–77] In patients with isolated diastolic dysfunction, this velocity can be applied provided LV volumes are normal or increased.

Strain Rate Imaging

Myocardial longitudinal motion velocities increase from zero at the apex to a maximum at the base of the ventricle during systole and diastole. Strain rate imaging is a

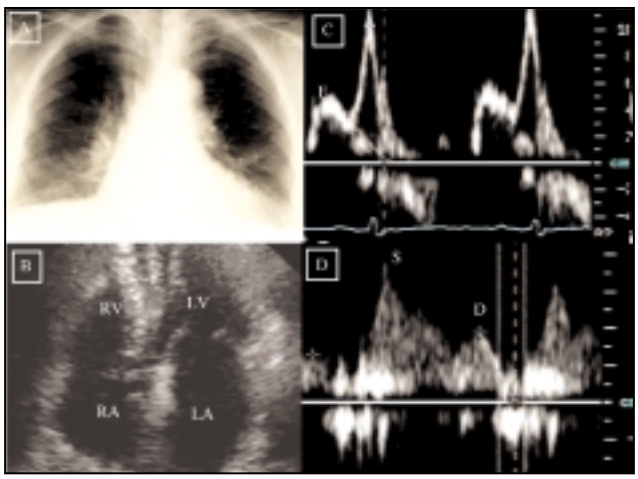

Figure 5. (A) *Chest X-ray film,* **(B)** *two-dimensional and* **(C, D)** *Doppler echocardiograms of a 76-year-old female patient with diabetes mellitus and hypertension who presented with advanced heart failure (New York Heart Association class III) from diastolic dysfunction. The left ventricular ejection fraction was 70%. Note the marked biatrial enlargement (in the superoinferior plane). Mitral inflow shows an E/A <1* **(C)***; pulmonary vein Doppler shows predominantly systolic forward flow* **(D)***. The pulmonary vein A-wave is 30 ms longer than the mitral inflow A wave (ms). Abbreviations as in previous figure legends.*

color DTI-derived method that depicts intramyocardial velocities as a velocity gradient from apex to base. Its high frame rate allows interrogation of segmental systolic data as well as complex patterns of ventricular deformation during diastole. The velocities caused by translation of the whole heart are subtracted. The phases of early filling and late filling during atrial systole can be seen to consist of stretch waves in the myocardium, propagating from the base to the apex. Both peak segmental myocardial strain rate and propagation velocity of strain rate in early diastolic filling are reduced in patients with hypertension.[78] Strain rate imaging is superior to myocardial velocity measurement for assessment of myocardial ischemia during coronary angioplasty.[79] Diastolic strain rate peak measurements may not be as reliable as systolic measurements, because of noise and the short duration of diastolic events.

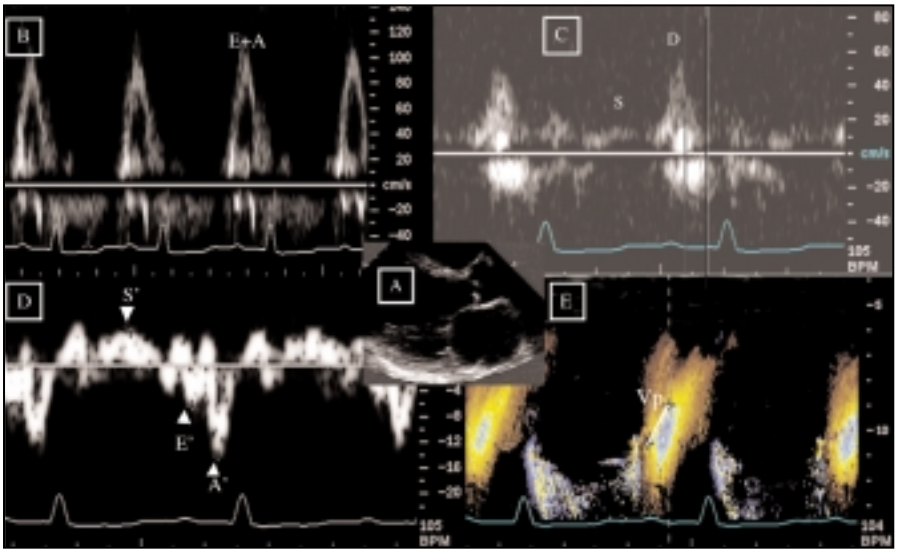

Figure 6. (A) *Two-dimensional/Doppler echocardiogram of a 52-year-old male with dilated cardiomyopathy, LVEF 35%, who presented with left heart failure and a loud S3 gallop. Note the fusion of mitral inflow E and A waves from tachycardia (105 bpm) that does not allow assessment of E/A ratio, E wave DT, or atrial duration* **(B)**. *In this setting, pulmonary vein tracing* **(C)** *is helpful and shows an S/D ratio of 0.27 (S wave 13 cm/s, D wave 56 cm/s), consistent with a noncompliant left atrium and elevated LA pressure. DTI tracing* **(D)** *shows a small E' wave (6 cm/s) and a tall A' wave (14 cm/s), and color M-mode* **(E)** *shows a Vp of 23 cm/s, which suggests slow propagation of early diastolic velocity from mitral inflow to LV apex. Abbreviations as in previous figure legends.*

Other Assessments

Evaluation of LA size is crucial for any assessment of diastolic function. LA enlargement is the earliest manifestation of abnormal LV diastolic function. Its role in assessing severity and chronic nature of diastolic dysfunction is similar to that of HbA1C in diabetes mellitus. In this context, it may be important to compare LA size with body height as well as to measure both the anteroposterior (parasternal long axis view) and superoinferior (apical four-chamber view) LA dimensions, since LA enlargement may occur only in the superoinferior plane and can be missed if only the conventional anteroposterior dimension is measured (Figure 5).

Clinical Utility of Assessment of Diastolic Function by Doppler Echocardiography

Guide to Therapy

Table 1 outlines overall management strategies for patients with various stages of diastolic dysfunction. Doppler echocardiography can guide treatment by allowing assessment of LA pressure, as discussed below (Figure 6). Treatment of the underlying disorder (eg, cardiac ischemia, hypertension, or underlying infiltrative disorder) remains the cornerstone of therapy.

Typically, LV systolic and diastolic function abnormalities are concordant.

Typically, LV systolic and diastolic function abnormalities are concordant. Thus, mild impairment in systolic function is accompanied by an impaired mitral inflow relaxation pattern, an S/D ratio >1.0, reversal of the mitral annular E'/A' ratio, and decreased Vp, along with prominent late diastolic filling on color M-mode echocardiography. Moderate reduction in LV systolic function is associated with a pseudonormal mitral inflow filling pattern, prominent pulmonary vein atrial reversal, and reduced mitral annular E' and Vp, whereas severe reduction in LV systolic function is associated with a restrictive mitral filling pattern, a marked decrease in both E' and A' velocities, and a very small Vp (Figures 2B–I and 3). Discordance such that presence of a restrictive filling pattern is associated with only mild reduction in LV systolic function is suggestive of volume overload or a marked decrease in LV compliance. Patients with such findings respond well to diuretics and treatment of the underlying disorder, usually coronary artery disease. Conversely, in patients with a signif-

Table 1
Echo Doppler Assessment as Guide to Therapy

Treatment	Purpose
1st Stage: Abnormal relaxation and symptomatic patient (exercise intolerance) or unexplained pulmonary hypertension (see Figure 5)	
β-Blockers[127]	Heart rate control particularly during exercise
Nondihydropyridine calcium channel blockers	Heart rate control particularly during exercise
ACE inhibitors[128–130]	Regression of LVH, afterload reduction
Cardioversion	Achieve sinus rhythm, eg, in atrial fibrillation
Note: Elevation in PAP may only be manifest on exercise echocardiogram and not on baseline echocardiogram.	
2nd Stage: Pseudonormal mitral inflow and abnormal relaxation DTI	
Above + diuretics/nitrates	Achieve preload and afterload reduction
3rd Stage: Restrictive mitral inflow, tall pulmonary D wave with rapid DT	
Diuretics	Preload reduction
ACE inhibitors	Preload and afterload reduction, survival benefit
Nitrates	Preload reduction
β-Blockers	LV remodeling, survival benefit
Digoxin	Symptomatic improvement

Treatment of underlying disorder, eg, ischemia and hypertension in each stage. Cautious use of diuretics if filling pressures not elevated in each stage. It is assumed that non-cardiac causes of shortness of breath and pulmonary causes of elevated PAP have been excluded.
ACE, angiotensin-converting enzyme; LVH, left ventricular hypertrophy; PAP, pulmonary artery pressure; DTI, Doppler tissue imaging; D, pulmonary vein diastolic velocity; DT, deceleration time, LV, left ventricle.

icant reduction in LV systolic function, presence of an impaired relaxation pattern indicates healthy atrial filling pressures. These patients require conservative use of diuretics.

Assessment of Pulmonary Capillary Wedge Pressure/LA Pressure

Load dependency of mitral inflow variables has been used to measure pulmonary capillary wedge pressure (PCWP) and LA pressure. In healthy subjects, mitral inflow E wave is dependent on LA pressure, LV relaxation, LV suction, and LV and LA compliance. In patients with disease states such as LV dysfunction, mitral inflow E wave and DT are primarily dependent on driving pressure between the left atrium and the left ventricle, because relaxation is moderately to markedly abnormal and there is little contribution from suction. In these patients, there is a direct correlation between E wave and LA pressure and an inverse correlation between DT and LA pressure. The response of the mitral flow velocity curve to changes in load may be used to distinguish between a normal and a pseudonormal flow pattern.[80,81] In a normal pattern, the E and A velocities both decrease when the preload is lowered with a drug such as nitroglycerin or during the strain phase of the Valsalva maneuver. Conversely, when there is a lowering of the preload in the presence of a pseudonormal pattern, a low E but a high A velocity emerges as an abnormal relaxation pattern.

The LV end-diastolic pressure can be estimated from the S/D ratio in pulmonary vein flow[82] and the difference between mitral and pulmonary inflow a-dur. In a normal subject, the pulmonary venous a-dur is equal to or less than the mitral a-dur. In the presence of abnormal compliance of the LV and higher end-diastolic pressures, there is a cutoff of the duration of mitral flow velocity at atrial contraction as LV pressure rapidly exceeds LA pressure. Blood flows back into the pulmonary vein as atrial contraction continues, even after cessation of transmitral flow. A pulmonary vein a-dur greater than the mitral a-dur is highly sensitive and specific for increased LV end-diastolic pressure (>15 mm Hg).[83,84] This relation is present with both LV systolic dysfunction and normal LV systolic function. It should be noted that a-dur difference between pulmonary vein and mitral inflow reflects the LV end-diastolic pressure but not necessarily the mean pressure. This parameter may thus be abnormal when other parameters, such as E/E′ or E/Vp (as discussed below), are still normal. Recently, DT of the pulmonary-vein diastolic wave has been used for the assessment of LA pressure and has been found to be superior to all mitral inflow and other pulmonary vein parameters.[85]

Tissue Doppler and color M-mode echocardiography that measure LV relaxation may be combined with mitral inflow PW Doppler parameters that measure both relaxation and filling pressure to more accurately estimate LV filling pressure. A high ratio of mitral inflow E wave to DTI E′ wave predicts an elevated PCWP or LV end-diastolic pressure.[86,87] One study found that an E/E′ ratio of 15 is highly specific for elevated LA pressure, whereas a ratio of 8 is very specific for normal to low filling pressures.[86] Similarly, a high ratio of mitral inflow E wave to Vp predicts elevated PCWP.[87] In patients with restrictive filling and preserved LV systolic function, how-

Table 2
Doppler Echocardiographic Parameters for Increased Pulmonary Capillary/Left Atrial Wedge Pressure in Adults

Mitral inflow E wave DT < 160 ms[131]
Mitral inflow E/A > 2.0[83,132]
Pulmonary vein S < pulmonary vein D[82]
Pulmonary vein a-dur 30 ms > mitral inflow a-dur[39]
Mitral inflow E/A decrease of > 0.5 with Valsalva maneuver[133]
E/E′ > 15[86]
E/Vp > 2.0[124]
Pulmonary vein D wave DT < 160 ms[85]

E, mitral inflow early filling wave; DT, deceleration time; E/A, mitral inflow early to late diastolic velocity ratio; S, systolic wave; D, diastolic wave; a-dur, atrial wave velocity duration; E/E′, ratio of mitral inflow early filling wave to myocardial early diastolic velocity; E/Vp, ratio of mitral inflow early filling wave to early propagation velocity by color M-mode.

ever, a high Vp may result, providing an erroneously low estimate of PCWP.[77] These ratios are also useful in healthy subjects.[88] The combined use of Vp as a surrogate for "tau" (time constant of isovolumic relaxation—an index of LV relaxation) and IVRT provides high sensitivity and specificity for detecting elevated PCWP > 15 mm Hg.[89] Table 2 summarizes echo Doppler features suggestive of elevated LV end-diastolic/left atrial pressure or PCWP.

Prognosis in Disease

Heart failure. LV diastolic function has prognostic value in patients with cardiomyopathy.[90] In both symptomatic and asymptomatic patients with advanced LV systolic dysfunction (LVEF <25%), presence of a short mitral inflow DT (<130 ms) identifies a subgroup with an extremely poor prognosis.[91,92] A DT of less than 130 ms may be associated with an annual mortality of 30% and a 2-year mortality of up to 50%.[93] However, a reversible restrictive pattern carries a favorable prognosis with optimal medical management.[94,95] It has been shown that, in patients with recent-onset idiopathic dilated cardiomyopathy, mitral inflow DT ≥ 160 ms predicts recovery of LV systolic function and improved functional status, as well as fewer cardiac events[96]; it was superior to mitral inflow parameters, LV systolic function, chamber dimensions, and LV sphericity in determining short-term prognosis. In addition, LV hypertrophy was associated with nonrestrictive filling and better prognosis in patients with idiopathic dilated cardiomyopathy.[97]

Transplant rejection. Diastolic myocardial velocities measured by DTI are highly sensitive for detecting rejection in heart transplant patients.[98] Peak-to-peak mitral annular velocity >135 mm/s had 93% sensitivity, 71% specificity, and 98% negative predictive value for detecting rejection by endomyocardial biopsy. In addition, improvement in rejection grade after treatment was associated with improvement in DTI velocities.[64] More recently, myocardial velocities, along with intramyocardial electrocardiograms, were used as a noninvasive rejection surveillance strategy and were compared with routine endomyocardial biopsy, after heart transplantation, for detection of rejection.[99] The noninvasive strategy reliably detected rejection and allowed efficient, safe monitoring during the first post-transplant year, without unnecessary and distressing routine biopsies.

Post–Acute Myocardial Infarction Events. Early estimation of Doppler-derived mitral DT provides a simple and accurate means of predicting late LV dilation, after reperfused acute myocardial infarction (AMI) treated with primary coronary angioplasty.[100] A restrictive filling pattern (mitral E wave DT ≤140 ms) after AMI has been identified as an independent variable, related to the development of in-hospital CHF and cardiac death during follow-up.[101]

The ratio of mitral inflow E wave velocity to color M-mode velocity (Vp) determines functional class as well as prognosis after AMI. In patients with AMI, an E/Vp ratio of ≥1.5 was associated with a significantly higher Killip class and a 30-day mortality of 42%.[102] In this study, an E/Vp ratio of ≥1.5 was superior to systolic measurements in determining short-term survival. Mitral inflow DT <140 ms was the most powerful predictor of cardiac death. Pseudonormal filling, as determined by Vp <45 cm/s and DT <140 ms, is also associated with LV dilation and increased cardiac mortality in patients after AMI.[103] We have found the ratio of mitral inflow (E) to mitral annular (E′) wave to indicate reperfusion in patients with AMI treated with primary percutaneous coronary angioplasty.[104] The ratio of mitral inflow E with DTI E′ of infarcted, as well as noninfarcted, annulus was significantly

higher in patients with thrombolysis in myocardial infarction (TIMI) grade 0–II flow, on angiography within 24 hours of AMI, than in patients with TIMI grade III flow.

Functional Capacity in Congestive Heart Failure

In patients with CHF, abnormalities of diastolic function are the most important determinant of exercise intolerance. A restrictive transmitral flow pattern on Doppler echocardiography identifies patients with diminished cardiopulmonary exercise performance.[90,93,105]

ß-Blockers have become standard therapy for patients with CHF. The effect of β-blockers on diastolic filling may account for subsequent myocardial systolic recovery in patients who receive these agents.[106]

Pacemaker Optimization

Preserved LA contraction contributes significantly to cardiac output in patients with diastolic dysfunction. Dual-chamber pacing has been used for optimization of atrial output in, patients with conduction abnormalities and severe LV systolic dysfunction.[107] Doppler echocardiography is used to optimize atrioventricular intervals and pacing by displaying improvement of cardiac output and LV diastolic function. The noninvasive measurement of timings of the cardiac cycle by PW DTI is also helpful for determining the optimal atrioventricular delay in individual patients. Optimal atrial contribution to LV filling and systolic perform advanced systolic dysfunction, when atrioventricular delay is programmed so that IVCT (isovolumic contraction time, or the mean interval between the end of the A wave and the beginning of the S wave) is 77 ms, similar to the interval measured in the healthy control group by PW DTI.[108]

Biventricular pacing has evolved as a new treatment option for patients with dilated cardiomyopathy and conduction disturbances, by allowing improved electromechanical activation of the LV and acute hemodynamic[109] and clinical[110] improvement. The "electrical" approach aims to normalize the disturbed contraction pattern, thereby improving hemodynamic function by simultaneous stimulation at different ventricular sites. Echocardiography provides hemodynamic data by Doppler techniques; these may be combined with two-dimensional data on LV geometry, volumes, EF, and contractility before and during pacing.[111,112]

Assessment of LV Diastolic Function in Clinical Practice

A comprehensive assessment of diastolic function requires attention to technical detail, expertise, and appropriate ultrasound imaging equipment and software. Adequate evaluation, as discussed above, adds 10–15 minutes to an average examination. Most currently available ultrasound systems permit assessment of diastolic function using the techniques listed above. Some systems have incorporated DTI measurements in the calculation package. The systems vary with respect to frame rate, sweep speed, Doppler ultrasound beam penetration, and pulse repetition frequency (PRF). In general, high frame rate, sweep speed, and PRF are important for the assessment of diastolic function.

Considering the large number of echocardiograms performed each year, routine assessment of diastolic function with the various methods described is not justified in all patients. In routine clinical practice, the different techniques discussed earlier should be applied selectively. Table 3 is a general scheme for assessment of diastolic function in patients referred for echocardiography. It should be emphasized that, in early stages of diastolic dysfunction, clinical history and assessment of LV and LA chamber dimensions, wall thickness, and mitral inflow pattern are usually sufficient to observe relaxation abnormality. The use of other parameters, such as pulmonary vein flow, DTI, and color M-mode, becomes helpful in the presence of a normal-looking mitral inflow pattern in patients who are symptomatic and/or have LV and LA chamber enlargement, depressed LV systolic function, elevated pulmonary artery systolic or diastolic pressure or when restrictive myocardial disease is suspected. One must evaluate the Doppler data in relation to the patient's clinical presentation, LVEF, wall motion, LV wall thickness, LV size, right atrial pressure (assessed via inferior vena cava size and respiratory excursion), and pulmonary artery pressure (PAP).

In my practice, I perform a detailed assessment of diastolic function in the following broad groups of patients: a) those with unexplained elevated PAP and an otherwise normal echocardiogram, b) patients in whom mitral inflow pattern is discordant with the degree of LV systolic dysfunction, provided there is no significant mitral or aortic valve disease, c) in symptomatic patients with an otherwise normal echocardiogram, d) when there is a need to assess left ventricular end-diastolic pressure (LVEDP) or PCWP, and e) when restrictive myocardial disease is suspected or needs to be differentiated from constrictive pericarditis. An exercise echocardiogram is helpful to elicit abnormalities such as elevated PAP during exercise in patients with symptoms of exertional dyspnea, an abnormal mitral inflow relaxation pattern, normal resting

Table 3
Assessment of Diastolic Function in Clinical Practice

1. Normal echocardiogram/asymptomatic patient

Mitral inflow E, A, and E/A

2. Normal echocardiogram/symptomatic patient and/or elevated PAP

- Mitral inflow E/A, DT, a-dur
- Pulmonary vein S, D, a-dur, D wave DT
- DTI if mitral inflow pattern looks normal (pseudonormal)
- Exercise echocardiography to assess valve regurgitation and PAP if normal at baseline

3. Abnormal echocardiogram/asymptomatic patient

LVH, biatrial enlargement, normal PAP

- Mitral inflow E/A, DT; pulmonary vein inflow if mitral inflow pattern other than abnormal relaxation; DTI if mitral inflow pattern looks normal

4. Abnormal echocardiogram/symptomatic patient

Normal LV systolic function, LVH, biatrial enlargement, normal or elevated PAP, no significant valvular disease

- Mitral inflow E/A, DT, a-dur; pulmonary vein S, D, a-dur, D wave DT; assess LVEDP from mitral and pulmonary vein a-dur difference; DTI if mitral inflow pattern looks normal (pseudonormal)

Normal LV systolic function, LVH, marked biatrial enlargement

- Mitral inflow E/A, DT, a-dur; pulmonary vein S, D, a-dur, D wave DT; saline contrast to enhance TR envelope + exercise echo to assess PAP with exercise. DTI and color M-mode for LA pressure/assessment of restrictive cardiomyopathy

Mildly decreased LV systolic function, markedly symptomatic patient

- Mitral inflow E/A, DT, a-dur; pulmonary vein S, D, a-dur, D wave DT if mitral inflow pattern other than abnormal relaxation; DTI and color M-mode to assess LA pressure if mitral inflow pattern looks normal or restrictive

Markedly decreased LV systolic function, tricuspid regurgitation envelope not available

- Mitral inflow E/A, DT, a-dur; pulmonary vein S, D, a-dur, D wave DT; DTI, and color-M mode to assess LA pressure

Symptomatic patients include those with shortness of breath on exertion, orthopnea, or pedal edema. For patients with abnormal echocardiogram and normal-looking mitral inflow as well as for those with restrictive mitral inflow, the Valsalva maneuver should be tried to examine the influence of preload reduction on mitral inflow E/A ratio.
Color M-mode may be used in situations in which nondiagnostic data are obtained from mitral inflow and mitral annulus interrogation.
E/A, mitral inflow early to late diastolic velocity ratio; DT, deceleration time; a-dur, A wave duration; LV, left ventricular; LVEDP, left ventricular end-diastolic pressure; LVH, left ventricular hypertrophy; PAP, pulmonary artery pressure; DTI, Doppler tissue imaging.

PAP, and an otherwise normal echocardiogram. This applies particularly to elderly patients, in whom an abnormal relaxation pattern is a regular finding. Use of saline/blood bubble contrast studies frequently helps elicit increased PAP in patients with a weak tricuspid regurgitation envelope. In patients with CHF and restrictive filling pattern, assessment of filling with Valsalva maneuver and/or nitroglycerin administration helps differentiate reversible from irreversible restrictive patterns. Besides measurement of E/E' ratio and E/Vp ratio as described earlier, measurement of systolic and diastolic blood pressure is important for estimation of filling pressures. This helps in the assessment of LA pressure provided there is no ventricular outflow tract (LVOT)/aortic gradient and an interpretable mitral regurgitation envelope for obtaining LV-LA gradient is available (LA pressure = systolic blood pressure [SBP]-LV-LA gradient converted to mm Hg via Bernoulli equation). LVEDP can also be assessed from aortic regurgitation envelope (LVEDP = diastolic blood pressure [DBP]–aortic-LV end-diastolic gradient converted to mm Hg via Bernoulli equation). Similarly, pulmonic insufficiency provides information on diastolic PA pressure (pulmonary artery–right ventricular gradient converted to mm Hg via Bernoulli equation + right atrial pressure [assessed by IVC size and respiratory excursion]). Assessment of blood pressure also provides insight; mitral and aortic regurgitation severity varies with blood pressure.

It is important to exclude pulmonary and non-cardiac, non-pulmonary causes of dyspnea before it is ascribed to cardiac causes. Similarly, before attributing increased PAP to diastolic dysfunction, pulmonary etiology must be excluded.

Occasionally, patients have mitral inflow and pulmonary vein patterns that do not fit any of the major patterns discussed earlier. In this situation, review of clinical data along with other routine echocardiographic data may be helpful. Finally, in patients who undergo invasive assessment of LV end-diastolic pres-

sure and right heart pressures, the invasive measures should be correlated with their Doppler echocardiographic measures to get a baseline against which the effect of interventions may be evaluated noninvasively.

Limitations

It is not uncommon to find disparities between various echocardiographic parameters of diastolic function. In general, temporal Doppler measurements are more susceptible to measurement errors than velocity measurements, which are more susceptible to acquisition errors (eg, incorrect placement of sample volume; excessive angle of incidence between blood flow and Doppler beam; and respiratory variation, particularly in those with labored respiration).

These pitfalls are obvious on evaluation of two-dimensional Doppler images. Measurement errors include misidentification of superimposed wall motion signals, particularly the pulmonary A wave atrial tissue velocity artifact; incorrect cursor placement for assessing temporal events such as DT; and failure to extrapolate to baseline. In some cases, there is genuine disparity. In this situation, clinical signs and symptoms and evidence from other modalities, such as chest x-ray and electrocardiography, should be used to arrive at a diagnosis, which unfortunately may still be driven by underlying biases.

Mitral E and A waves are difficult to evaluate in patients with significant eccentric aortic insufficiency directed toward mitral inflow. Apical two- and three-chamber views for mitral inflow or pulmonary venous flow pattern may be useful in this setting. In atrial tachyarrhythmias of recent onset, with an uncontrolled and highly variable ventricular response, echocardiographic parameters do not provide a reliable assessment of diastolic function. However, mitral inflow,[113] as well as TDI of mitral annulus,[114] can reliably assess filling pressures and diastolic function in patients with chronic atrial fibrillation who show less cyclic variation, provided several measurements are averaged. Finally, since age has a significant influence on mitral inflow, pulmonary vein, and DTI E′ and A′ and Vp, the patient's age must be considered before declaring diastolic function abnormalities from PW Doppler data. Absence of regional wall motion abnormality needs to be ascertained in the corresponding wall before the DTI E′ wave from mitral annulus is measured.

DTI and color M-mode echocardiographic assessment of diastolic function are helpful in the presence of either atrial fibrillation and controlled ventricular response or significant mitral regurgitation, both of which influence pulmonary vein inflow pattern. Significant mitral regurgitation increases mitral inflow E wave velocity and decreases pulmonary vein S wave velocity. Atrial fibrillation blunts the S1 component of pulmonary vein flow and makes the atrial component of pulmonary vein flow unavailable for assessment of velocity and duration. When tachycardia causes E/A fusion, both in mitral inflow and in annular PW Doppler imaging, flow Vp by color M-mode echocardiography may be used to assess LV relaxation. This is because early diastolic filling is less influenced by heart rate than is mid or late diastolic filling.[67] When assessment of LV filling pressure is in question in the presence of sinus tachycardia and complete merging of E and A velocities, the ratio of mitral inflow E to DTI E′ can be used to estimate PCWP with reasonable accuracy.[115]

Summary

Doppler and M-mode echocardiography are noninvasive modalities that can be used to assess LV diastolic function, predict remodeling and

Main Points

- Many congestive heart failure patients have normal left ventricular (LV) systolic function but may have significant diastolic dysfunction.
- The two major determinants of LV filling are ventricular relaxation and effective chamber compliance.
- Ultrasonography, especially with newer Doppler techniques, is a very useful tool for assessing diastolic function.
- In patients with abnormal relaxation, left atrial (LA) contraction may contribute up to 35% of cardiac output.
- Doppler tissue imaging can help differentiate pseudonormal from normal mitral inflow pattern.
- Color M-mode Doppler ultrasound provides information comparable to that given by pulsed-wave Doppler tracings at different levels from the mitral orifice to the LV apex.
- Combining echocardiographic techniques that measure LV relaxation with mitral inflow parameters that measure both relaxation and filling pressure may yield more accurate LV and LA filling pressure estimates.

prognosis in patients with CHF and those post AMI, assess transplant rejection, estimate filling pressures, and guide therapy. Unlike conventional Doppler, DTI and color M-mode velocity propagation have emerged as relatively load-independent parameters for the assessment of LV diastolic dysfunction. These easy techniques can and should be selectively incorporated into the assessment of diastolic function in an echocardiography laboratory. ■

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Appendix 1. Doppler Tissue Imaging—Methods

Myocardial DTI
For DTI of basal myocardial segments to evaluate diastolic function, the entire LV myocardial wall thickness is included in the Doppler sample volume to detect intramyocardial velocity and gradient variations.[19–22,116]

Mitral Annular DTI
The DTI PW Doppler sample volume is placed at the lateral corner of the mitral annulus and, subsequently, at the medial (or septal) corner in the apical four-chamber view. The lateral aspect of the mitral annulus is selected because, in contrast to the case with the parasternal window, the velocities are not influenced by anteroposterior translation. To prevent the sample volume from falling outside the mitral annulus during cardiac cycles, the sample volume is set to 5 mm × 8 mm. Since movement of the heart associated with respiration may still change the position of the PW Doppler sample volume in relation to the mitral annulus, a live two-dimensional view should be obtained from time to time to confirm correct sample volume placement. Recording these velocities during held breathing can eliminate respiratory movements.

Settings
Filters are set to exclude high-frequency signals, and the Nyquist limit is adjusted to a velocity range of 15–30 cm/s to eliminate the signals produced by transmitral flow. Gains are minimal (often to 0% power) to allow for a clear tissue signal with minimal background noise. The resulting velocities are recorded for 5–10 cardiac cycles. A recording sweep speed of 100–200 mm/s is recommended for measurements of flow duration, whereas peak velocities can be measured at either 50 mm/s or 200 mm/s.

Appendix 2. Doppler Tissue Imaging—Pitfalls

General Pitfalls of Doppler Imaging
All the theoretical considerations relative to origin of the Doppler shift, amplitude of the reflected echoes, scattering, effect of the incidence angle, and so on for Doppler imaging also hold for DTI.[117–119]

Complex Myocardial Deformation
The wall motion pattern of the LV myocardium is complex and heterogeneous, including the transverse systolic wall thickening, the longitudinal and torsion motion of the left ventricle, and the respiratory motion of the whole heart. In general, motion, in the transverse and longitudinal plane only, is suitable for DTI interrogation. The apical four-chamber view allows assessment of myocardial motion in the longitudinal plane.

Sample Volume
When performing a pulsed DTI analysis of myocardial wall motion, the Doppler sample volume should be adjusted to the individual myocardial wall thickness in order to calculate the real intramyocardial mean DTI velocities.[55,56,120–122] A large sample volume and excessive Doppler gain result in spectral broadening of the velocity envelope that makes measurement of the variables of flow velocity and flow duration more difficult. The sample volume moves in relation to the myocardial wall dynamics in such a way that the selected region of interest for the ventricular myocardium under analysis is not always the same. These factors are also responsible for the presence of frequent motion artifacts superimposed on the pulsed Doppler images and spectrum, signals that should not be confused with abnormal myocardial wall motion.

Frame Rate
Low frame rate is an important technical limitation, especially for temporal resolution. The first generation of DTI equipment had a frame rate of 30–50 frames/s, a characteristic that has been changed to a more advanced level of 50–100 frames/s in the new generation of DTI software.

Physiologic Variability
Peak DTI E' velocity values in healthy subjects range from 10.2 ± 3.0 cm/s to 14.8 ± 3.9 cm/s, with a maximum intersegmental variation of 31%.[121–123] In the normal population, the regional E'/A' ratio of PW DTI velocities ranges from 1.9 ± 0.9

to 3.0 ± 1.4, with a maximum variation of 42%.[121–123] Myocardial IVRT in healthy volunteers ranges from 35.3 ± 15.0 ms to 76.3 ± 25.0 ms, with a mean value of 52.9 ± 15.0 ms.

Beat-to-Beat Variability
Because of the physiologic beat-to-beat variability of the PW DTI data, the observer should systematically average all quantitative values. An alternative is to introduce into the DTI software an indicator of the mean values that can be modified on the screen in an interval of five to 10 cardiac cycles.

Regional Dysfunction
Use of DTI for assessment of LV diastolic function and estimation of filling pressure is usually related to the assumption that the regional diastolic properties of the myocardium reflect global diastolic function. Analysis of lateral annular motion is in part affected by underlying regional function; thus, ischemia or infarction of the basal lateral wall can significantly lower E′. Fortunately, the base of the lateral wall is seldom involved in ischemic heart disease.

Miscellaneous Factors
Annular velocities may vary with the site of sampling at the annulus. An inadequate acoustic window, valvular disease, tachycardia, arrhythmias, or suboptimal machine settings may further confound evaluation.

Appendix 3. Color M-Mode Velocity Propagation—Methods

2D/Color Doppler Imaging
Color Doppler imaging is first used to obtain the orientation of LV inflow in the apical four-chamber view. Normal mitral inflow is directed toward the mid to distal portion of the posterolateral wall of the left ventricle, approximately 20° lateral to the LV apex.[123] With LV dilation, mitral inflow is directed progressively more laterally and posteriorly.[124] Due to these varying intraventricular flow patterns, placement of M-mode cursor for the assessment of flow propagation should be guided by color Doppler ultrasonography.

Machine Settings
To maximize frame rate, the color sector is kept as narrow as possible while still including the mitral annulus and the LV apex. Zoom function is used to enlarge the image, and sweep speed is maximized. The velocity scale is set so that aliasing velocity is 0.5–0.7 m/s. A color M-mode Doppler cursor is then aligned through the center of the mitral ring to the apex, ensuring a minimum angle of incidence (typically < 20°) of ultrasound beam alignment to flow direction, to minimize errors in measurement of peak velocity. The color scale of the velocity filter may be reduced (with a high-pass filter of 12 cm/s) to emphasize low-velocity flow, particularly in patients with wall motion abnormalities and poor LV function. The transducer angulation is adjusted to ensure that a homogenous color flow is seen within the entire LV cavity as much as possible. Movement of the heart associated with respiration may change the position of the M-mode sample volume in relation to the LV cavity. Recording these velocities during held breathing or only at end-expiratory phase can eliminate these effects.

Measurement
Investigators have proposed different methods of measuring velocity of propagation. These include measurement of 1) the leading edge of the propagation wave[23] (the segment beginning with the onset of flow in the LV inlet and ending as far as possible into the LV chamber); 2) the temporal difference between the point of maximal velocity at the mitral level and at the apex[67]; 3) the slope of the first aliasing velocity from the mitral tips to a position 4 cm distal to them[125]; and 4) the slope of a line connecting two points, the point of maximal velocity around the mitral orifice and the point at which this velocity decreases to 70% of its initial value.[126] A modified approach involves baseline shift until a distinct color border (blue within red) is obtained and then measurement of the slope of its most linear component past the valve leaflets. Propagation velocity values are expressed in cm/s and recorded at sweep speeds of 100–200 mm/s.

Appendix 4. Color M-Mode Velocity Propagation—Pitfalls

Alignment Along a Linear Wave Front
Velocity of flow propagation cannot be measured when a linear wave front for early filling is not available in patients with poor echogenicity. The alignment between the flow and the ultrasound beam is crucial. In patients with a significantly dilated left ventricle, in which the mitral inflow progresses along the postero-

lateral wall, parallel alignment of M-mode cursor to blood flow may be difficult and result in falsely low propagation speed. The highest flow velocities should be followed without major loss from the mitral tip to ≥2.5 cm. Images are technically inadequate when there is a lack of continuity in the blood column or apical blood flow is not present in the color M-mode picture.

Limited Lateral Resolution
The ultrasound beam interrogates only a limited part of the ventricle in a single dimension, and there is limited lateral resolution.

Measurement
When using the aliasing boundary method, it may be difficult to display a clear aliasing boundary when the peak early filling velocity is decreased to <25 cm/s. In this case, baseline shift to alias at 75% of peak E-wave velocity should be used.

Beat-to-Beat Variability
There may be significant beat-to-beat variability. In general, the highest velocity of flow propagation should be selected.

Interobserver and Intraobserver Variability
Of all the diastolic parameters discussed in this review, color M-mode Vp shows maximum variability because of its dependence on color flow patterns and aliasing velocity rather than discrete PW Doppler signals. At times, blurred wave front signals or lack of a distinct aliasing boundary make it difficult to determine the margin.

Influence of LV Size
In small ventricles, this index may not accurately reflect LV relaxation properties and may overestimate ventricular relaxation. In addition, this parameter may be normal or may be quicker, at least theoretically, in patients with a pseudonormal or restrictive pattern than in those with isolated relaxation abnormality, if atrial function is intact and LV size is preserved.

Other
Evaluation is difficult in the setting of tachycardia, arrhythmias, eccentric aortic insufficiency, or suboptimal machine settings.

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