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DIASTOLIC FUNCTION AND DYSFUNCTION

THE ECHO-DOPPLER EVALUATION OF LEFT VENTRICULAR DIASTOLIC FUNCTION
A Current Perspective

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The role of left ventricular (LV) diastolic function in health and disease is still incompletely understood and underappreciated by most primary care physicians and many cardiologists. This is not surprising because diastole is a complex phenomenon with many determinants that are difficult to individually study, and has several phases that encompass the relaxation and then filling of the ventricle. [6] [38] [42] [65] **Physical examination, electrocardiogram (ECG), and chest radiographs are unreliable in making the diagnosis of LV diastolic dysfunction in most individuals, and invasive measurements of cardiac pressures, rates of LV relaxation, and LV compliance are costly, clinically impracticable as they carry increased risk, and require special catheters and software analysis programs.** [66]

This situation changed with the development of echocardiography. Because of its noninvasive nature, large numbers of normal individuals and patients were studied and different LV filling patterns were described, first with M-mode echocardiography [35] [36] [43] **and later using pulsed-wave (PW) Doppler technique interrogating mitral inflow.** [45] [46] [53] [73] [110] [112] **Validation of these mitral filling patterns against radionuclide and angiographic techniques soon followed;** [96] [104] **however, enthusiasm for relating LV filling patterns to diastolic function was dampened by reports that the velocity and proportion of early and late diastolic filling and their peak velocities were affected by preload,** [16] [106] **afterload,** [77] **and heart rate.** [4] [77]

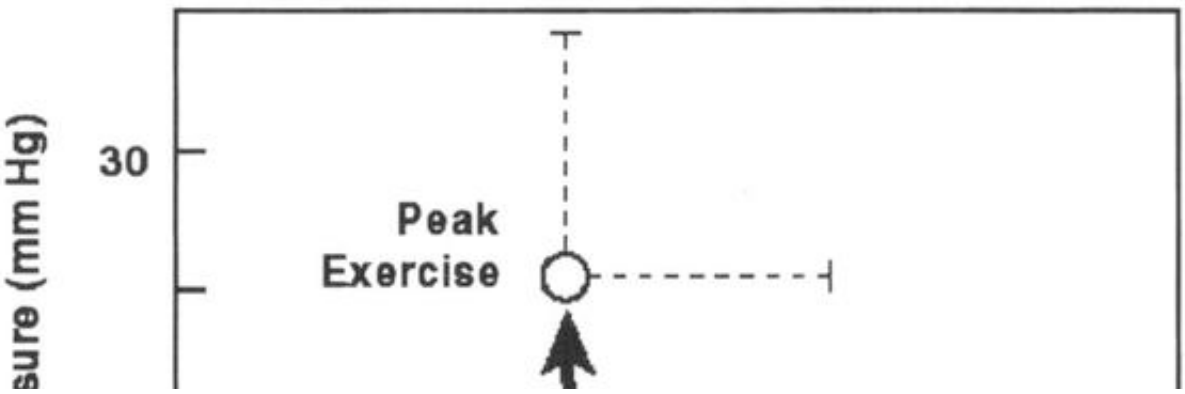
In 1988, hemodynamic pressure measurements were related to individual LV filling patterns, independent of disease state. [9] Three basic abnormal filling patterns were described and were soon found to have clinical significance and prognostic value regardless of cardiac disease type. [7] [56] [84] [90] [117] [124] The field of *diastology* using echo-Doppler evaluation was born [20] and steady progress continued. Today this LV diastolic evaluation includes interrogation of mitral and pulmonary venous flow velocities, the rate of mitral inflow velocity by color Doppler flow propagation, and the evaluation of mitral annular motion by tissue Doppler imaging (TDI). In addition, manipulation of preload and afterload assesses how sensitive abnormal LV filling patterns are to changes in loading conditions. [21] [47] [92] Although all echo-Doppler indices remain imperfect and much remains to be learned, the aggregate sum of this information remains our best and most practical way to assess LV diastolic function, and to objectively follow serial changes after medical intervention or with disease progression.

To begin to use echo-Doppler information for patient evaluation and management requires a basic understanding of cardiac physiology, particularly LV diastolic properties and LV filling patterns, and reproducible high-quality Doppler flow velocity recording. [10] The routine performance of a diastolic function examination on every patient referred for echocardiography is recommended for acquiring experience to eliminate technical and interpretive pitfalls. This article explains a practical way for approaching the echo-Doppler analysis of LV diastolic function, and how the information obtained may be used clinically to aid patient diagnosis and therapy.

LEFT VENTRICULAR DIASTOLIC DYSFUNCTION

Definition

Abnormal **diastolic** function is a disorder of LV filling. As systolic function effects LV relaxation and often LV compliance, all patients with a decrease in LV ejection fraction have **diastolic** abnormalities. Many patients with symptoms of congestive heart failure (CHF) or reduced exercise capacity, however, have a normal LV ejection fraction or *isolated* LV **diastolic** dysfunction as the etiology of their cardiac problem. A definition for *LV **diastolic** dysfunction* includes: 1) an inability to fill the left ventricle, during rest or exercise, to a normal end-diastolic volume without an abnormal increase in LV end-diastolic or mean left atrial (LA) pressure; or 2) a failure to increase LV end-diastolic volume, and therefore cardiac output during exercise (Fig. 1) . In its earliest stages, **diastolic** dysfunction may cause only a mild slowing of LV relaxation without elevated pressures and the patient may be asymptomatic.



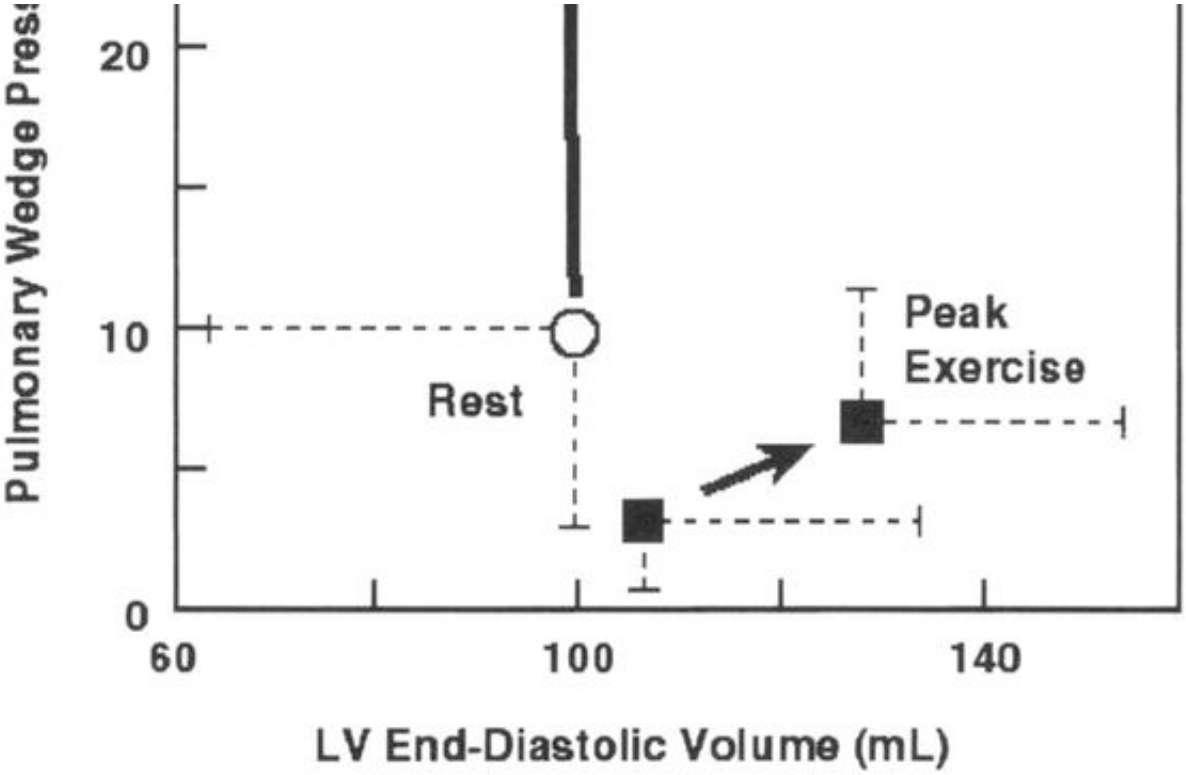


Figure 1. Pulmonary wedge pressure (PWP) versus left ventricular (LV) end-diastolic volume in normal subjects (*square*) and seven patients (*circle*) with congestive heart failure (CHF) but normal LV ejection fraction, and no significant coronary or valvular heart disease. Compared with the normal subjects, patients with **diastolic** CHF were unable to increase their LV end-diastolic volume and also had a marked increase in PWP. This led to marked exercise intolerance with approximately 50% reduction in peak oxygen consumption, primarily because of the reduction in cardiac index. *(From Kitzman DW, Higginbotham MB, Cobb FR, et al: Exercise intolerance in patients with heart failure and preserved left ventricular systolic function: Failure of the Frank-Starling mechanism. J Am Coll Cardiol 17:1065-1072, 1991; with permission.)*

DIASTOLE

A Historical Perspective

One of the first attempts to explain ventricular filling was provided by Galen in 100 BC, who proposed that the heart is filled by dilation of the right ventricle. Centuries later, in 1628, William Harvey recognized the heart was the central pump in a circulatory system containing arteries and veins. This discovery was followed by recognition that most cases of CHF were caused by damage or weakening of the heart muscle and a decrease in LV pumping function. Diastole was largely ignored as simply the interval in which the cardiac chambers passively filled between each pumping cycle.

Gradually, clues emerged that LV **diastolic** dysfunction alone could cause symptoms, and that **diastolic** and systolic LV function were interrelated. One discovery was the Frank-Starling mechanism whereby LV end-diastolic volume helps regulate LV stroke volume on a beat-to-beat basis. Another landmark observation was made by Katz, who observed that after mitral valve opening in mammalian hearts LV pressure continues to decrease while volume is increasing, therefore demonstrating that the heart acts as a *suction* pump. [50] It was also recognized that a limited filling capacity was the cardinal feature of constrictive pericarditis that reduced cardiac output and resulted in marked peripheral edema and generalized wasting.

With the advent of cardiac catheterization in the 1960s, the study of cardiovascular biomechanics accelerated.

Although most research continued to focus on LV systolic function, cardiac diseases with thickened and noncompliant ventricles (i.e., restrictive and hypertrophic cardiomyopathies) were reported. [105] Soon, angiographic differences in LV filling patterns between normals and patients with various heart diseases were noted. [42] Methods to quantitate the rate of LV relaxation [122] and LV compliance [27] were described, and it became apparent that patients with the same LV ejection fraction could have markedly different **diastolic** properties and LV filling characteristics. At the same time, the importance of LV systolic function in determining LV restoring forces and rate of LV relaxation was also appreciated. Gradually, systole and diastole came to be viewed more as an intertwined continuum, with each part affecting the other.

In the mid-1980s, echocardiographic studies helped show that 20% to 40% of patients with symptoms of CHF had normal LV ejection fractions and, therefore, presumably *isolated* **diastolic** dysfunction as the etiology for their heart failure. [103] [115] Because of the difficulties in quantitating individual LV **diastolic** properties, the clinical study of LV **diastolic** dysfunction proceeded slowly through the analysis of digitized M-mode, angiographic, or radionuclide LV filling patterns. [35] [36] [43] In 1982, the use of PW Doppler mitral flow velocities to study LV filling was described. [53] Because of its ease of use, noninvasive nature, and ability to study changes in LV filling after interventions and over time, this technique revolutionized the study of LV **diastolic** function. Correlations between LV filling pressures and mitral flow velocity patterns were performed, [9] normal age-related changes in LV filling were established, [33] [55] [73] and three basic abnormal LV filling patterns independent of underlying cardiac disease were recognized as part of the "natural history of LV filling." [7] Shortly thereafter, pulmonary venous flow velocity-derived variables were described that characterized LA filling and also aided the interpretation of LV filling patterns and pressures. [7] [52] [59] [63] Today, Doppler mitral flow velocity-derived variables are recognized as powerful prognostic tools in patients with various cardiac diseases, including CHF [94] and dilated [90] [124] and restrictive [57] cardiomyopathies. At the same time, newer methods such as TDI mitral annular motion (MAM), the rate of color Doppler mitral inflow propagation (Vp), and model-based image processing continue to advance the field of diastology. * As a result, the clinical syndromes caused by LV **diastolic** dysfunction and LV filling disorders are now more readily recognized by healthcare practitioners, and treatment strategies for these patients are being developed. [120]

Epidemiology of Left Ventricular Diastolic Dysfunction

Although isolated LV **diastolic** dysfunction can be seen in all age groups, it is chiefly a disease of the elderly. In a meta-analysis of the problem, the overall incidence was 30% to 35% with a range varying from 13% to 17%. [118] This prevalence is strikingly age-related, with patients younger than 65 years of age having a incidence of approximately 15%, whereas patients older than 70 years of age have an incidence of symptomatic CHF with normal ejection fraction as high as 40% to 50%. [118] [119] This higher incidence reflects the most common cause of isolated **diastolic** dysfunction, hypertensive heart disease of the elderly. This problem is associated with increasing systolic blood pressures with age and the development of LV hypertrophy. It is estimated that approximately 50% of women over the age of 70 have LV hypertrophy on echocardiograms, with only a slightly smaller prevalence in males. Patients greater than or equal to 70 years of age with CHF and normal LV ejection fraction have an increased 1-year mortality associated with worsening Doppler echo-derived **diastolic** function variables. [94]

The prognosis for patients with isolated LV **diastolic** dysfunction is more favorable than for patients with systolic dysfunction; however, when compared with age- and gender-matched normal subjects, the mortality risk is increased fourfold. [119] The disease also causes considerable morbidity with its symptoms of pulmonary congestion and decrease in functional capacity owing to reduced exercise capacity. At the present time, prospective studies looking at the epidemiology of LV **diastolic** dysfunction are underway.

Diastolic Properties of the Left Ventricle

Diastole has traditionally been divided into four phases: isovolumic relaxation, early **diastolic** filling, diastasis in mid-diastole, and atrial contraction (for additional details see the article by Yellin and Meisner, elsewhere in this issue). Part of the difficulty in studying LV **diastolic** function has been that the majordeterminants of LV **diastolic** performance occur during different phases of diastole, often overlap in their timing and are affected not only by each other but also by LV systolic function, heart rate, and the cardiac conduction system. [66]

Although there are numerous independent factors that affect LV **diastolic** properties and the filling of the left ventricle, all factors work through their combined, resultant effects on the transmitral pressure gradient (TMPG), which is the actual physical determinant of LV filling (Fig. 2) . The effects of two key **diastolic** properties, the rate of LV relaxation and LV compliance (which affects LA filling pressure), are especially important in understanding LV filling patterns in health and disease.

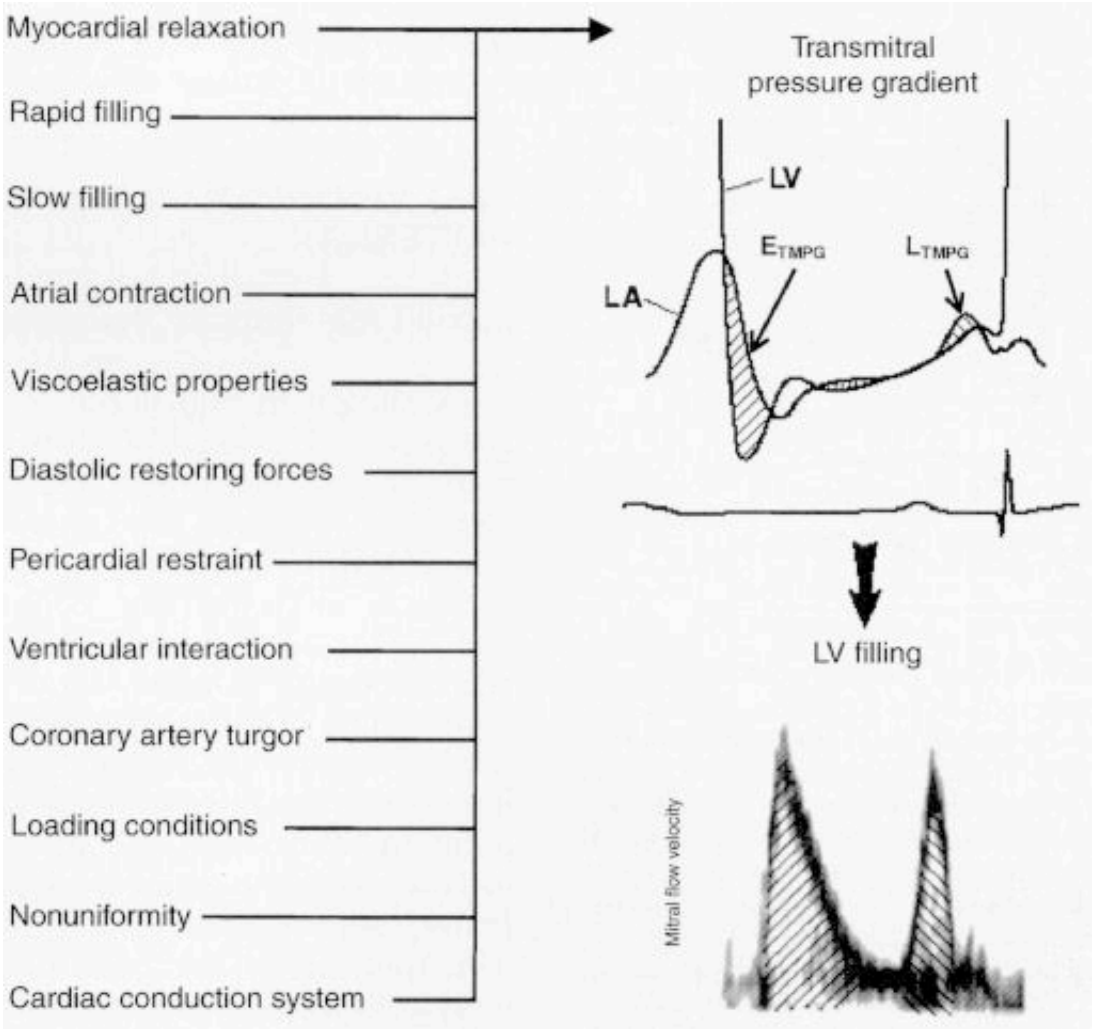


Figure 2. Numerous factors affect LV **diastolic** properties and filling; however, all factors work through their effects on the transmitral pressure gradient (TMPG), which is the actual determinant of LV filling. An early positive TMPG (E_{TMPG}) relates to early **diastolic** LV filling as assessed by pulse-wave Doppler mitral flow velocity. A reverse pressure gradient in mid-diastole decelerates early filling, with late filling (L_{TMPG}) occurring as a result of the increase in the left atrial pressure owing to atrial contraction.

LV relaxation describes the rate of LV pressure decline during isovolumic relaxation. It is controlled by cellular events that regulate cytosolic Ca^{++} concentration in myocytes. [81] In contrast to LV systole in which Ca^{++} is passively released from the sarcoplasmic reticulum and interacts with the actin-troponin myosin contractile elements, LV relaxation is energy (adenosine triphosphate [ATP]) dependent and requires this Ca^{++} to be returned to the sarcoplasmic reticulum by Ca^{++} ATPase-dependent pumps against a 10,000:1

concentration gradient. These enzymes and their endogenous regulator phospholamban are affected by the adrenergic nervous system, cytosolic Ca^{++} concentration, and also genetic transformation in which the isoforms of the enzymes may actually change the rate of Ca^{++} uptake in the presence of LV hypertrophy or other cardiac disorders. This energy dependence of Ca^{++} re-uptake is the reason that LV relaxation tends to become abnormal early in cardiac disease states whereas systolic function can remain normal.

Quantitation of LV relaxation is done by describing the rate of LV pressure decline during isovolumic relaxation. [121] As shown in Figure 3 , this is done by fitting an exponential equation to LV pressure decline, usually between max-dP/dt and 5 mm Hg greater than LV end-diastolic pressure, and calculating a time constant of isovolumic relaxation called tau (tau). LV tau is approximately 30 to 40 ms in humans and is considered to be *complete* after three time constants (approximately 90 to 120 ms in normal subjects), which is roughly simultaneous with normal peak early **diastolic** filling. The shorter the tau, the more rapid the LV pressure decline and the faster the LV relaxation. In physical terms, tau is the amount of time required for the pressure to drop by a factor of $1/e = 0.368$, where e is the base of the natural logarithm.

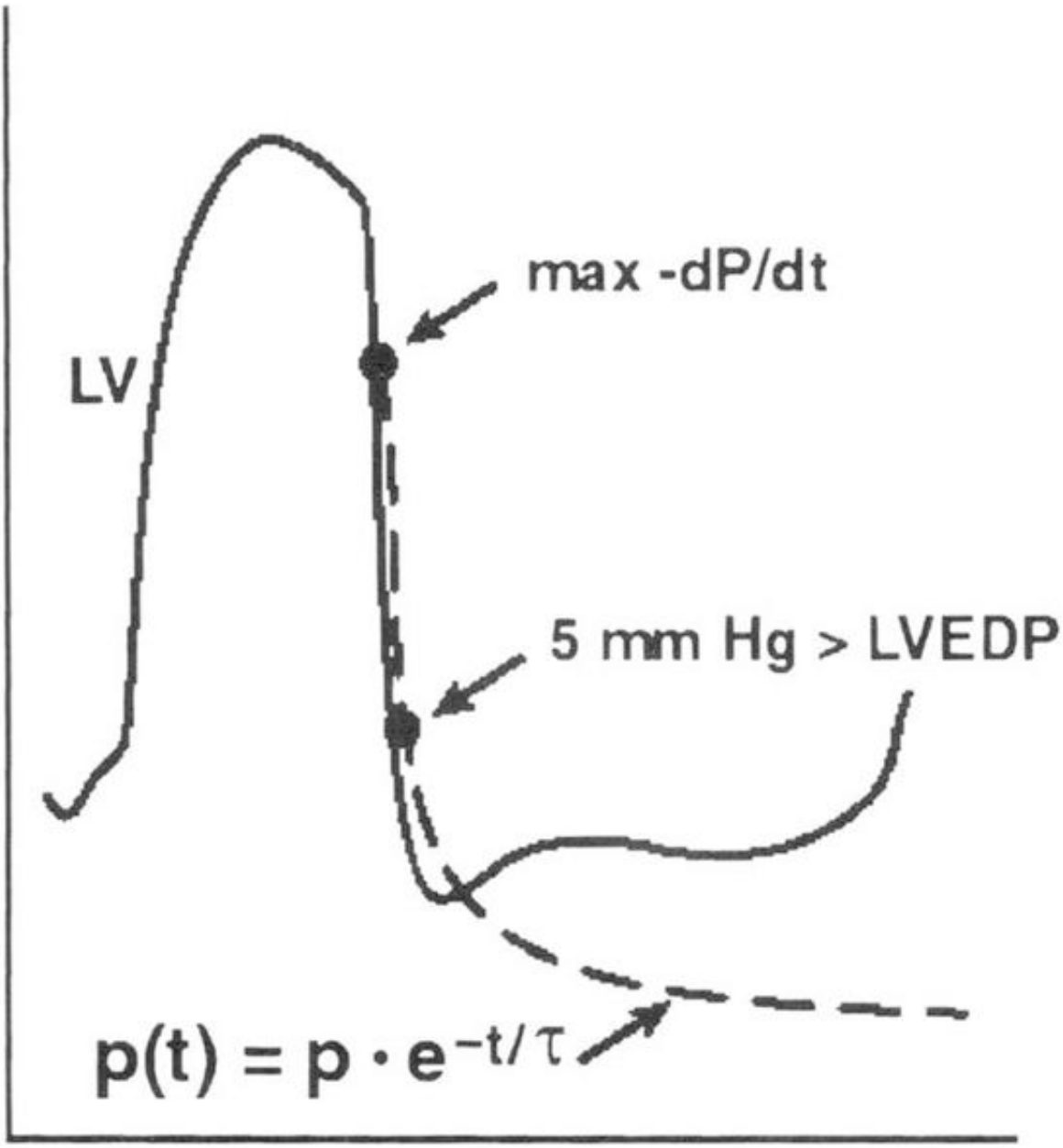


Figure 3. The calculation of the time constant of LV isovolumic relaxation (tau) shown on a pressure versus time plot. Pressure is measured by high-fidelity micromanometer-tipped catheters. The LV pressure from the time of maximum negative dP/dt to 5 mm

above LV end-diastolic pressure (LVEDP) is fitted by the monoexponential equation shown, and the time constant of relaxation (tau) is obtained. e = natural logarithm; P = pressure; t = time. *(Modified from Nishimura RA, Housmans PR, Hatle LK, et al: Assessment of **diastolic** function of the heart: Background and current applications of Doppler echocardiography. Part 1. Physiologic and pathophysiologic features. Mayo Clin Proc 64:71-81, 1989; with permission.)*

Another key LV **diastolic** property is the operating chamber compliance (dV/dP). This affects LA and LV filling pressures, and is composed of *stiffness* (or its reciprocal, compliance) of the myocardium and the LV chamber. [66] Left ventricular chamber *stiffness* is described by a tangent (usually drawn at LV end-diastolic pressure) to the exponential LV **diastolic** pressure-volume (P-V) relation (Fig. 4) . The steeper the slope of the tangent, the *stiffer* (i.e., less compliant) the ventricle. A leftward shift of the P-V curve indicates a less compliant ventricle, whereas a rightward shift indicates greater compliance. With the exception of restrictive cardiomyopathies, most cardiac diseases cause a shift of the P-V curve to the right so that an increasing LV end-diastolic volume can occur without marked increase in filling pressures. Most cardiac diseases also cause the shape of the P-V curve to change.

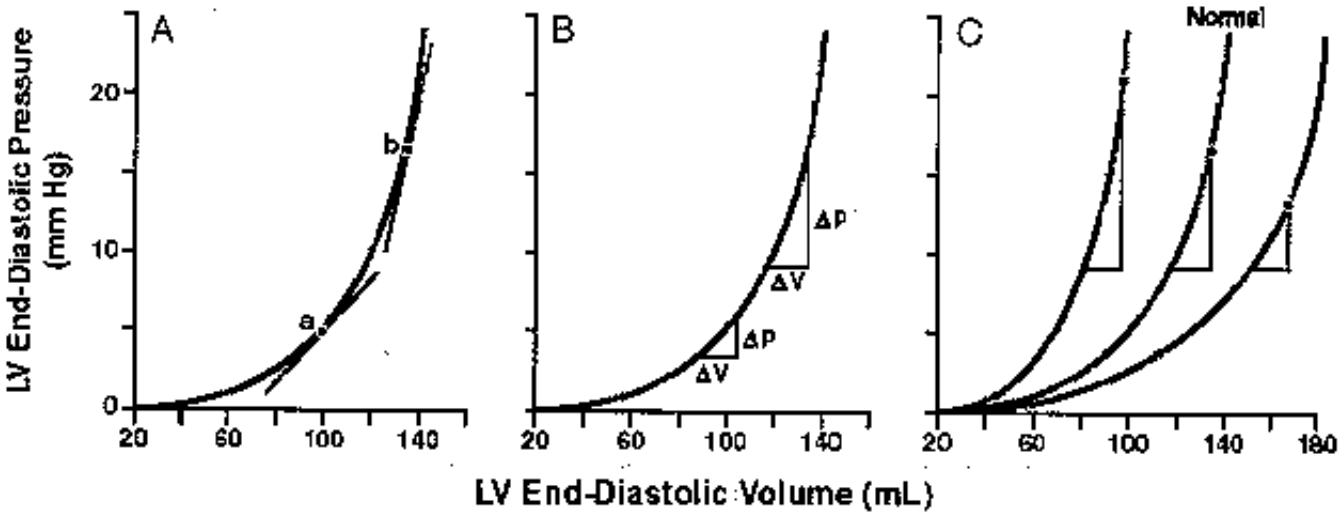


Figure 4. LV pressure-volume (P-V) relations. LV P-V relationships are shown for end-diastole. *A,* Normal physiology. The tangent drawn at LV end-diastolic pressure describes LV operating chamber stiffness (dP/dV). The steeper the tangent (**b** versus **a**), the less compliant or *stiffer* the ventricle. *B,* Increased stiffness (larger change in pressure for the same change in volume) as one moves upward along the curve. Shift of the P-V curve (*C*) leftward indicates a stiffer ventricle, whereas a rightward shift indicates greater compliance.

The TMPG (see Fig. 2) determines the LV filling pattern and is influenced by the speed of LV relaxation and LV compliance. For any given LV pressure, faster LV relaxation results in a larger early TMPG, more filling in early diastole and, consequently, less filling in late diastole. Conversely, when LV relaxation is slowed, the proportion of early **diastolic** filling declines and a greater proportion is seen at atrial contraction. For the same rate of LV relaxation, a decrease in LV compliance and associated increase in LA pressure has the opposite effect, which may, in part, offset a slower rate of LV relaxation. Because the rate of LV relaxation and LA pressures is a continuum, many different TMPGs and LV filling patterns are possible. [9] As a result, the same LV filling pattern may occur with different combinations of these two variables. For example, a younger individual with rapid LV relaxation will have a predominance of early **diastolic** LV filling, but so will an older individual with symptomatic heart disease who has impaired LV relaxation and markedly increased LA pressure. Impaired or slowed LV relaxation is the earliest and commonest **diastolic** abnormality, with a decrease in LV compliance and an increase in filling pressures seen in patients with more advanced and symptomatic cardiac disease.

LEFT VENTRICULAR FILLING PATTERNS

Mitral Flow Velocity Variables

As shown in Figure 5 , LV filling patterns are assessed using PW Doppler mitral flow velocity recordings and variables. Left ventricular isovolumic relaxation time (IVRT) is the time interval from aortic valve closure to mitral valve opening. Longer IVRT values (>100 ms) are associated with impaired LV relaxation and normal filling pressures. This lengthening of the IVRT interval is the earliest change seen with **diastolic** dysfunction, and is sensitive to slowing of the rate of LV relaxation. A short LV IVRT indicates an earlier mitral valve opening and can be seen in young normal individuals or patients with increased mean LA pressure. Peak E-wave velocity reflects the early **diastolic** TMPG and the **diastolic** properties previously discussed. Similarly, peak mitral A-wave velocity reflects the late **diastolic** TMPG. The overall type of filling pattern is generally characterized by the mitral E- to A-wave ratio. The mitral flow velocity at the start of atrial contraction, known as the E at A velocity, is important to note because values >20 cm/s (usually caused by a faster heart rate or first degree AV block) indicate partial fusion of early and late **diastolic** filling, which increases A-wave velocity and duration, [4] making the interpretation of E to A ratio and A-wave variables more difficult (Fig. 6) . Mitral deceleration time reflects LV compliance in early diastole in patients with known heart disease and reduced (<35%) LV ejection fraction [34] and provides prognostic value in patients with various cardiac diseases. [48] [57] [90] [91] [94] [104] The mitral A-wave duration and time velocity integral is affected by multiple factors including heart rate, PR interval, the amount and duration of E-wave filling, LV compliance in late diastole, and LA stroke volume.

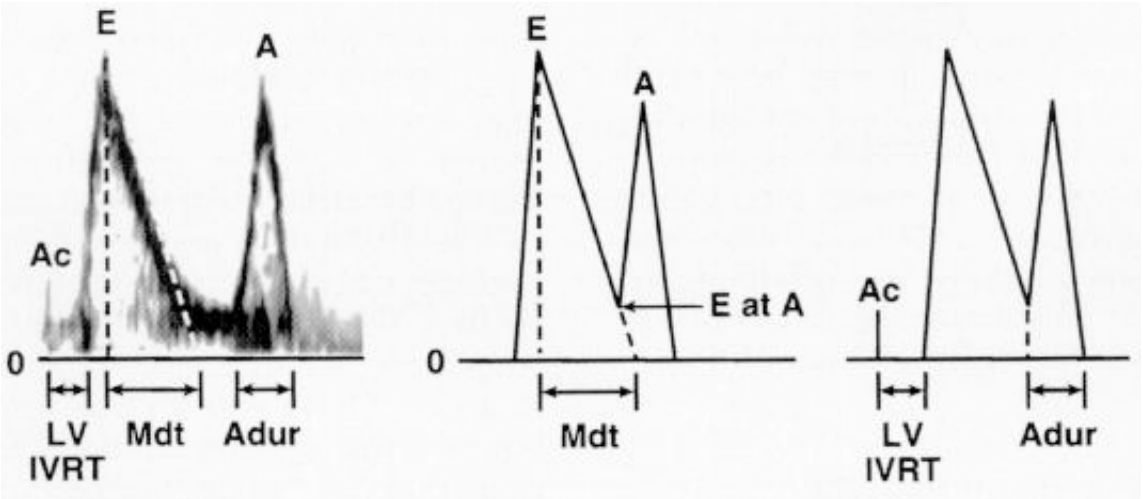
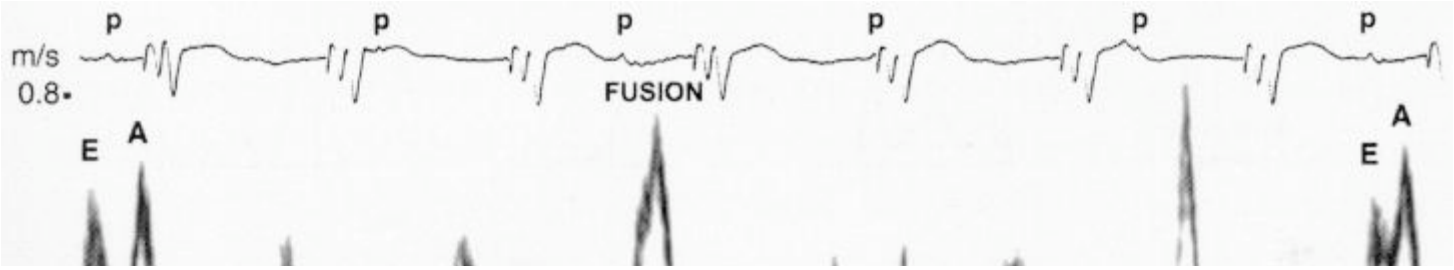


Figure 5. Pulsed-wave Doppler mitral flow velocity pattern illustrating the mitral flow velocity variables measured during a **diastolic** function examination. These include peak E-wave velocity, peak A-wave velocity, and E- at A-wave velocity. Time intervals measured include the LV isovolumic relaxation time (IVRT) (the interval from aortic valve closure to start of mitral flow). The mitral deceleration time (DT) is defined as the interval from peak E-wave velocity to the point on the velocity baseline obtained by linear extrapolation along the velocity deceleration slope. The A-wave duration (A dur) is measured from the E- at A-wave velocity to the end of mitral flow after atrial contraction. When E- at A-wave velocity is increased, a *vertical line* is drawn to this point as shown in the *far right panel.*



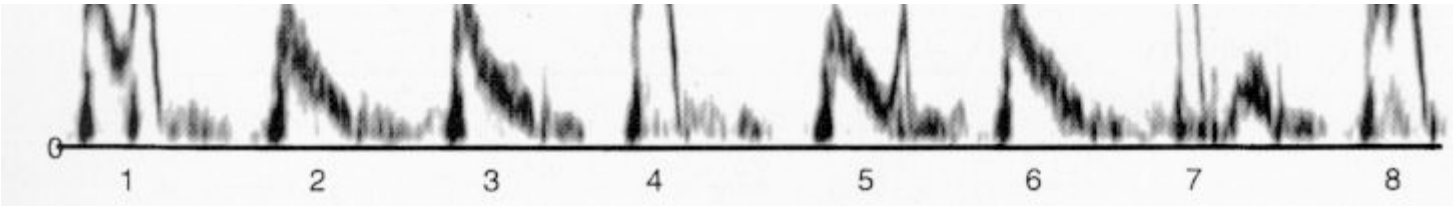


Figure 6. Example of a patient with complete heart block and VVI pacing. Note the effect that atrial contraction occurring at different times in the cardiac cycle has on mitral flow velocity and E- to A-wave ratio. As can be seen by comparing beats 1, 5, and 8, the E- at A-wave velocity has an obvious effect on the mitral E/A ratio. Also note the near complete fusion of E- and A-waves on beats 4 and 8, and that only an A-wave is seen on beat 7.

Normal Changes with Aging

Elastic recoil and rapid LV relaxation in adolescents and young adults result in a predominance of early **diastolic** filling (E-wave) with much less filling (10% to 15%) caused by atrial contraction. With normal aging, LV systolic function changes little but LV relaxation slows in most individuals. This appears to be caused by an increase in systolic blood pressure and LV mass. The result is reduced LV filling in early diastole and increased filling at atrial contraction. [33] [55] [73] In most individuals, the peak E- and A-wave velocities become approximately equal during the seventh decade of life, with atrial filling contributing up to 35% to 40% of LV **diastolic** stroke volume. In individuals with lower blood pressures and no increase in LV mass, these age-related changes in filling are retarded and normal E-wave predominance can occasionally be seen into the eighth decade of life.

Abnormal Mitral Filling Patterns

In patients with cardiac diseases, three abnormal LV filling patterns are recognized [7] [9] as shown in Figure 7 . The least abnormal and most common is termed *impaired relaxation,* resulting from reduced filling in early diastole, a reduced mitral E- to A-wave ratio, increased A-wave amplitude and filling caused by atrial contraction, and often an S4 gallop. [70] With disease progression, LV compliance becomes reduced and LA pressure increases, which counteracts the impaired LV relaxation. The increased early TMPG results in an LV filling pattern that appears normal but is actually *pseudonormal*. This term indicates that despite the normal mitral E- to A-wave ratio, abnormalities of LV relaxation and LV compliance are present. [9] Finally, in patients with advanced disease and a severe decrease in LV compliance, high pressures cause LV filling to become *restrictive,* with blood rapidly entering a slowly relaxing ventricle in early diastole only to be abruptly decelerated, generating an S3 gallop. [69] With a marked increase in early LV **diastolic** pressure the left atrium is dilated and hypocontractile with little additional filling at atrial contraction.

	Impaired Relaxation	Pseudonormal	Restrictive
Symptoms	None at rest	Exertional dyspnea	Dyspnea with minimal exertion
Functional status	Mild exercise limitation	Moderate impairment	Marked impairment
Left atrium	Normal size ± hypercontractile	Enlarged ± hypocontractile	Enlarged, failing

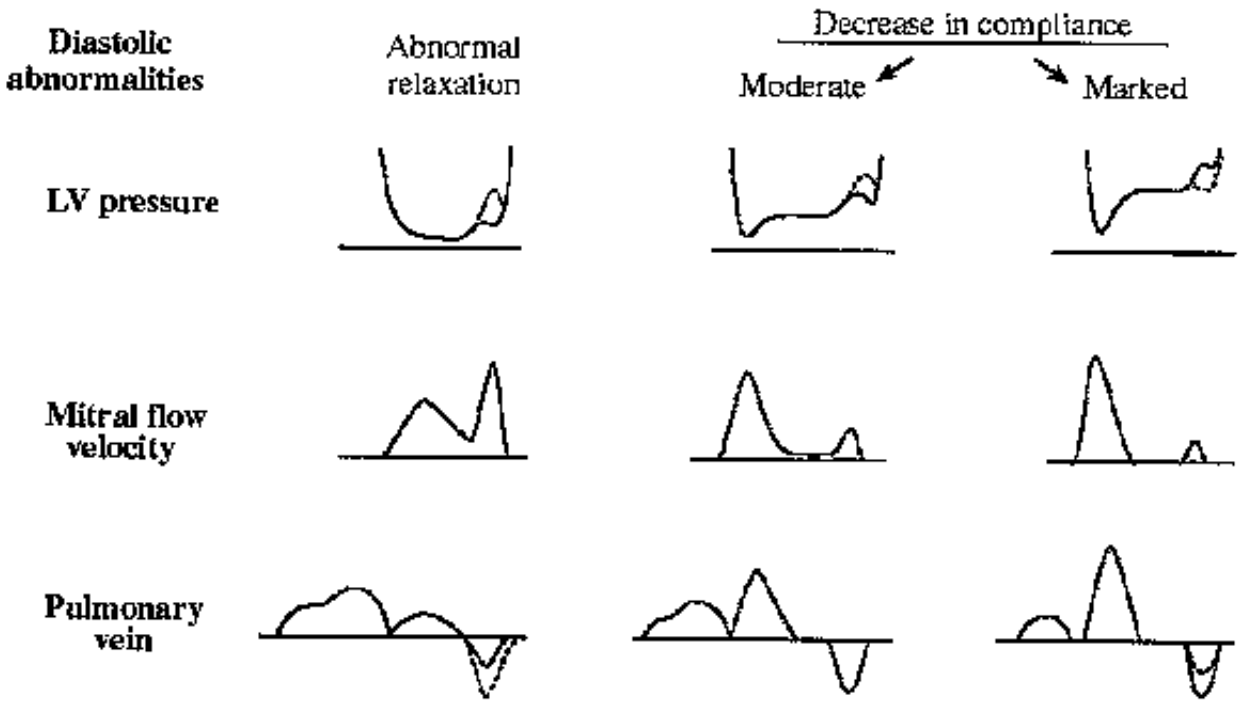
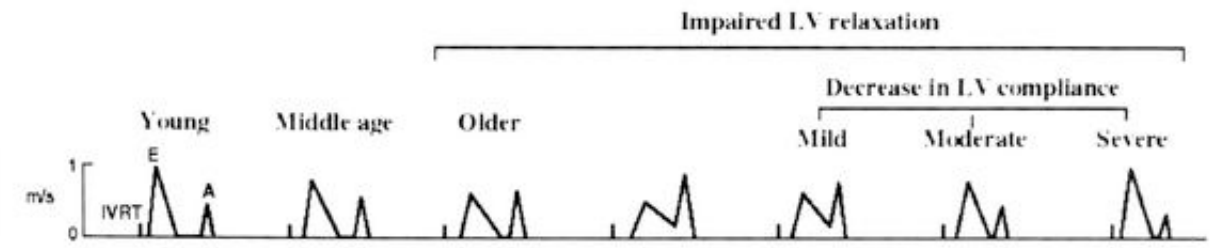


Figure 7. In patients with cardiac diseases, three abnormal LV filling patterns are recognized and named *(top)* as shown. The typical symptoms, functional status, left atrial size, and **diastolic** abnormalities are listed. The *dashed lines* in patients with an impaired relaxation filling pattern indicate that some patients may or may not have elevated pressures. The *dashed lines* and the hemodynamics in patients with a restrictive filling pattern indicate failure of the left atrium and a decrease in peak pulmonary A-wave reversal velocity, although its width still exceeds mitral flow velocity.

The Natural History of Left Ventricular Filling

The changes throughout normal life and changes with cardiac disease states can be combined into a *natural history of LV filling* (Fig. 8) . Although originally theoretical when proposed in 1992, [7] a clinical [58] and a subsequent experimental study [85] indicated that gradual progression in cardiac diseases does result in the sequential filling changes outlined. This *natural history* pattern explains how young normal individuals and patients with a restrictive filling pattern can have an early filling sound (S3 gallop). [69] In both instances, early **diastolic** TMPG and filling are increased. In the young this is caused by vigorous LV relaxation and *elastic recoil* whereas those with severe disease have high filling pressures, which through a short lived but accentuated TMPG increase peak E-wave velocity as blood enters a more slowly relaxing and stiffer ventricle. Figure 8 also shows that several abnormal LV filling patterns have E- to A-wave velocity ratios that are similar to those seen in normal individuals. This can occur because different combinations of LV relaxation and LA pressure may result in the same early **diastolic** TMPG and therefore a similar mitral flow velocity pattern. For this reason, additional data are often helpful in distinguishing normal and abnormal mitral filling patterns, especially of the pseudonormal type.



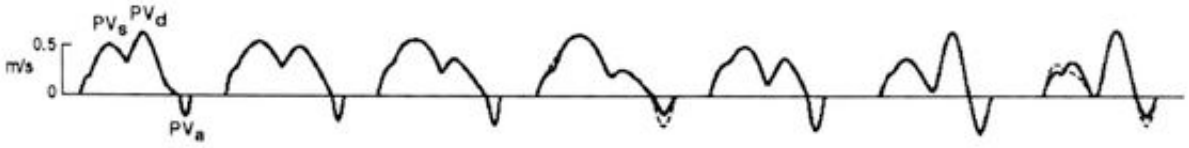


Figure 8. This figure shows the natural history of evolving LV filling patterns as assessed by pulsed-wave Doppler mitral and pulmonary venous flow velocity recordings. See text for full description. A = peak mitral flow velocity at atrial contraction; E = peak mitral flow velocity in early diastole; IVRT = LV isovolumic relaxation time; PVa = reverse pulmonary venous flow at atrial contraction; PVd = pulmonary venous flow velocity in diastole; PVS = pulmonary venous flow velocity in systole. *(Modified from Appleton CP, Hatle LK: The natural history of left venticular filling abnormalities: Assessment by two-dimensional and Doppler echocardiography. Echocardiography 9:437-457, 1992; with permission.)*

PULMONARY VENOUS FLOW VELOCITY VARIABLES

Within a short time after mitral flow velocity patterns were correlated with hemodynamics, it became apparent that pulmonary venous flow velocity obtained using transthoracic PW Doppler technique could be helpful in assessing LV filling patterns. [9] [59] As with mitral flow velocity, pulmonary venous flow velocity changes with normal aging and disease states (see Fig. 8) . With experience, high-quality PW Doppler transthoracic recordings can be obtained in approximately 85% to 90% of patients. [49] The hemodynamic determinants of pulmonary venous flow velocity recently have been studied in vivo [3] [101] (for pulmonary venous flow from a modeling perspective see the article by Kovacs et al, elsewhere in this issue) and variables quantitated (Fig. 9) . These include peak flow velocity in early systole (PVs1), late systole (PVs2), and early diastole (PVd), and peak reverse flow velocity at atrial contraction (PVa) and its duration (PVa dur). PVs1 is seen distinctly on transthoracic recordings only about 30% of the time, [49] but in nearly all transesophageal recordings [12]

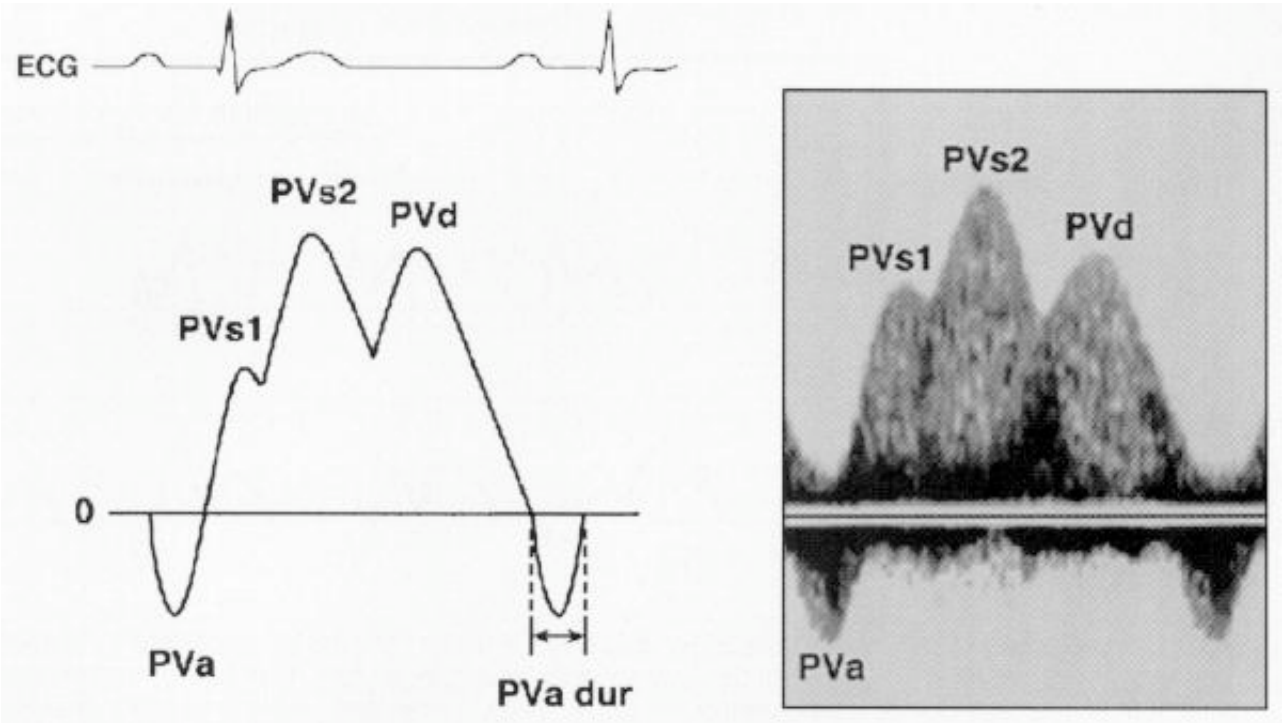


Figure 9. Pulmonary venous variables obtained with the pulse wave Doppler technique include peak flow velocity and early systole (PVs1), late systole (PVs2), and early diastole (PVd), peak reverse flow velocity (PVa), and its duration (PVa dur) at atrial contraction.

The hemodynamic determinants of pulmonary venous flow velocity are shown in Figure 10 . PVs1 occurs as a result of LA relaxation and pressure decrease. PVs2, which peaks later in systole, reflects the interaction of RV stroke volume and LA pressure and compliance. Pulmonary venous **diastolic** flow velocity (PVd) initially follows early **diastolic** mitral flow velocity, but in mid-diastole LV filling slows, whereas PVd flow continues with ongoing LA enlargement. Pulmonary venous flow reversal owing to atrial contraction (PVa) is determined by LA contractility and the compliance of the pulmonary venous bed, left atrium, and left ventricle. Pulmonary venous flow velocity patterns can be matched to their corresponding mitral Doppler patterns (see Fig. 8) . Pulmonary venous systolic to **diastolic** flow velocity ratios help determine the type of LV filling pattern; in middle-aged patients with cardiac disease, a reduced systolic fraction of antegrade flow (<40%) is related to increased mean LA pressure. [63] [97] The relation between pulmonary venous A-wave and mitral A-wave duration is of special importance [2] [6] [89] [97] [125] and is discussed later in the text.

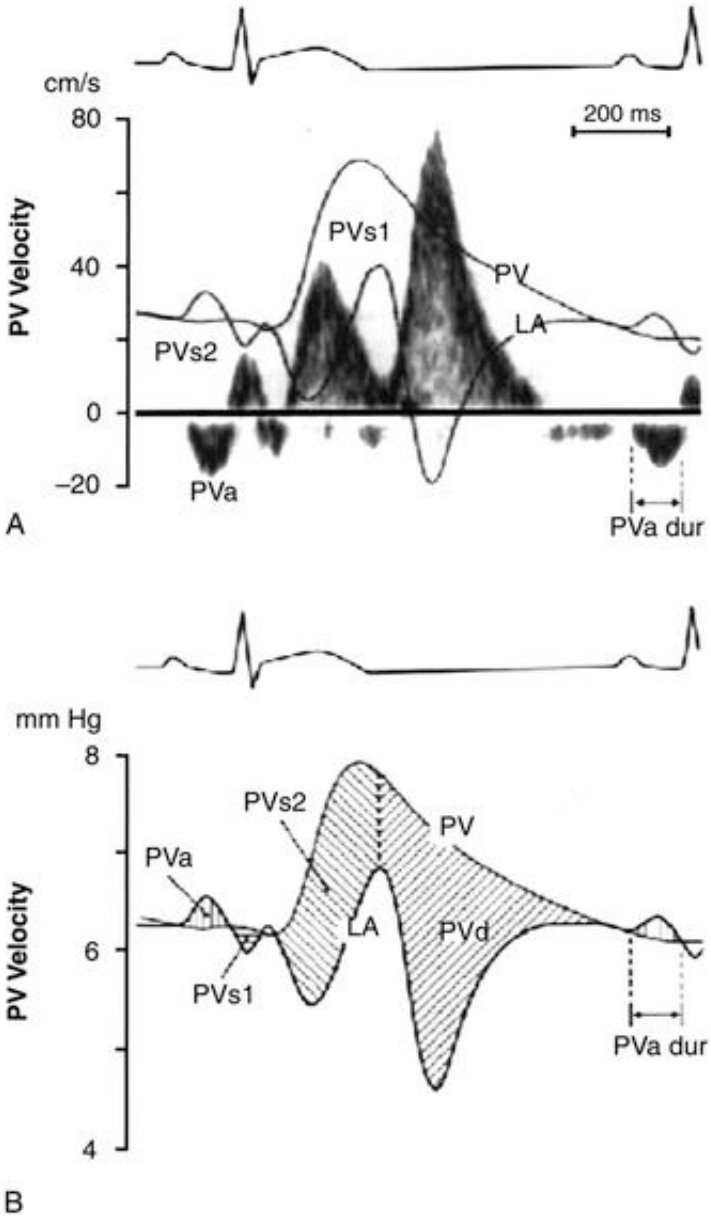


Figure 10. *A,* Simultaneous recording of pulmonary venous flow velocity together with pulmonary venous (PV) and left atrial (LA) pressures. *B,* PV and LA pressures showing the different hemodynamic pressure gradients (*hatched areas*), which determine the four individual pulmonary venous flow velocity components. These components are described in the text. *(From Appleton CP: Hemodynamic determinants of Doppler pulmonary venous flow velocity components: New insights from studies in lightly sedated normal dogs. J Am Coll Cardiol 30:1562-1574, 1997; with permission.)*

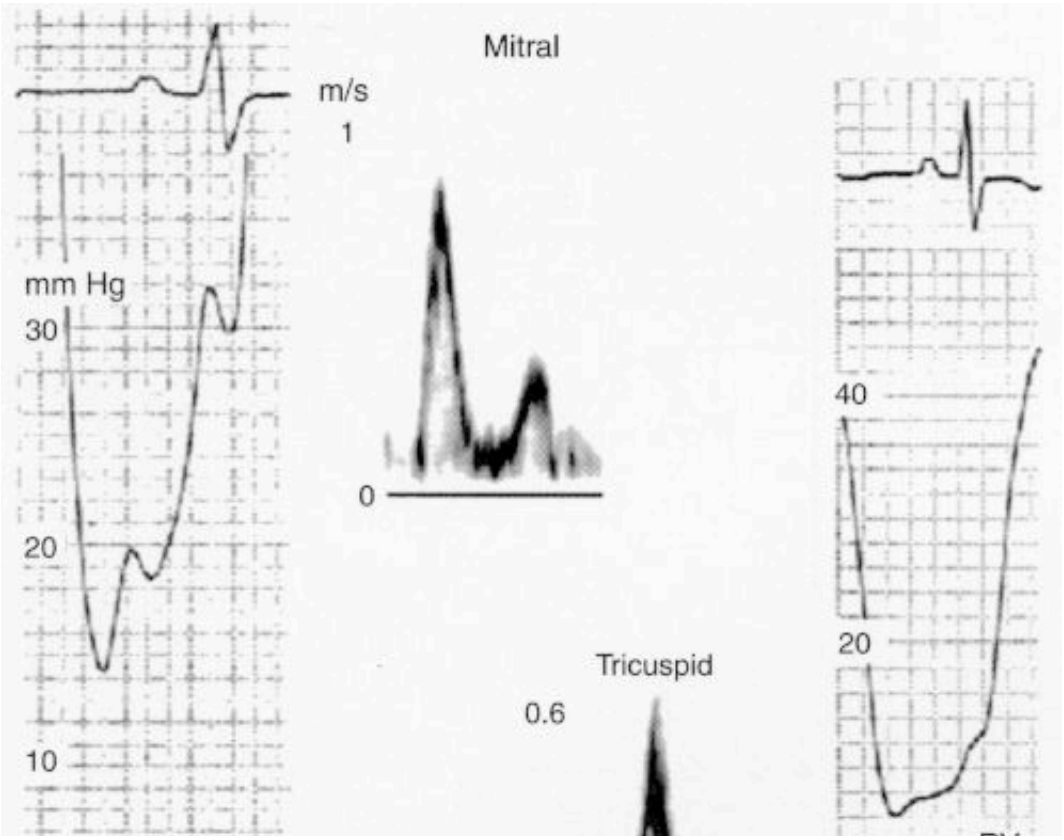
OTHER ANCILLARY DATA THAT HELP IN THE INTERPRETATION OF LEFT VENTRICULAR FILLING PATTERNS

M-mode and Two-dimensional Echocardiography

There is considerable information about LV **diastolic** function and filling pressures available from M-mode and two-dimensional (2D) cardiac ultrasound recordings. Left ventricular hypertrophy slows LV relaxation independent of other cardiac abnormalities and results in an impaired relaxation filling pattern. In the absence of mitral regurgitation or arrhythmias, LA enlargement and hypocontractility (compared with the right atrium) usually indicate elevated filling pressures and are typically associated with pseudonormal and restrictive mitral flow velocity patterns. [6] [14] Conversely, normal LA size and ejection fraction suggest that mean LA pressure is normal. From the apical four-chamber view, a visual disparity in size and speed of contraction and relaxation between the two ventricles and two atria is readily apparent. Left atrial minimum volume is related to pulmonary wedge pressure with a correlation coefficient equal to that of most other Doppler variables. [6]

Tricuspid Flow Velocity

Tricuspid and mitral E to A flow velocity ratios are normally similar, and different filling patterns indicate that one or both ventricles are abnormal. Because most cardiac diseases affect the left atrium and left ventricle, the more abnormal filling pattern is usually on the left side as shown in Figure 11 . In an individual with a left-heart dilated cardiomyopathy, the mitral flow pattern is pseudonormal whereas the tricuspid filling pattern *lags behind* the mitral pattern, showing a pattern of impaired relaxation.



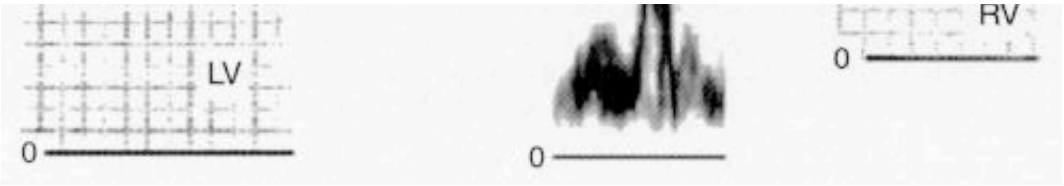
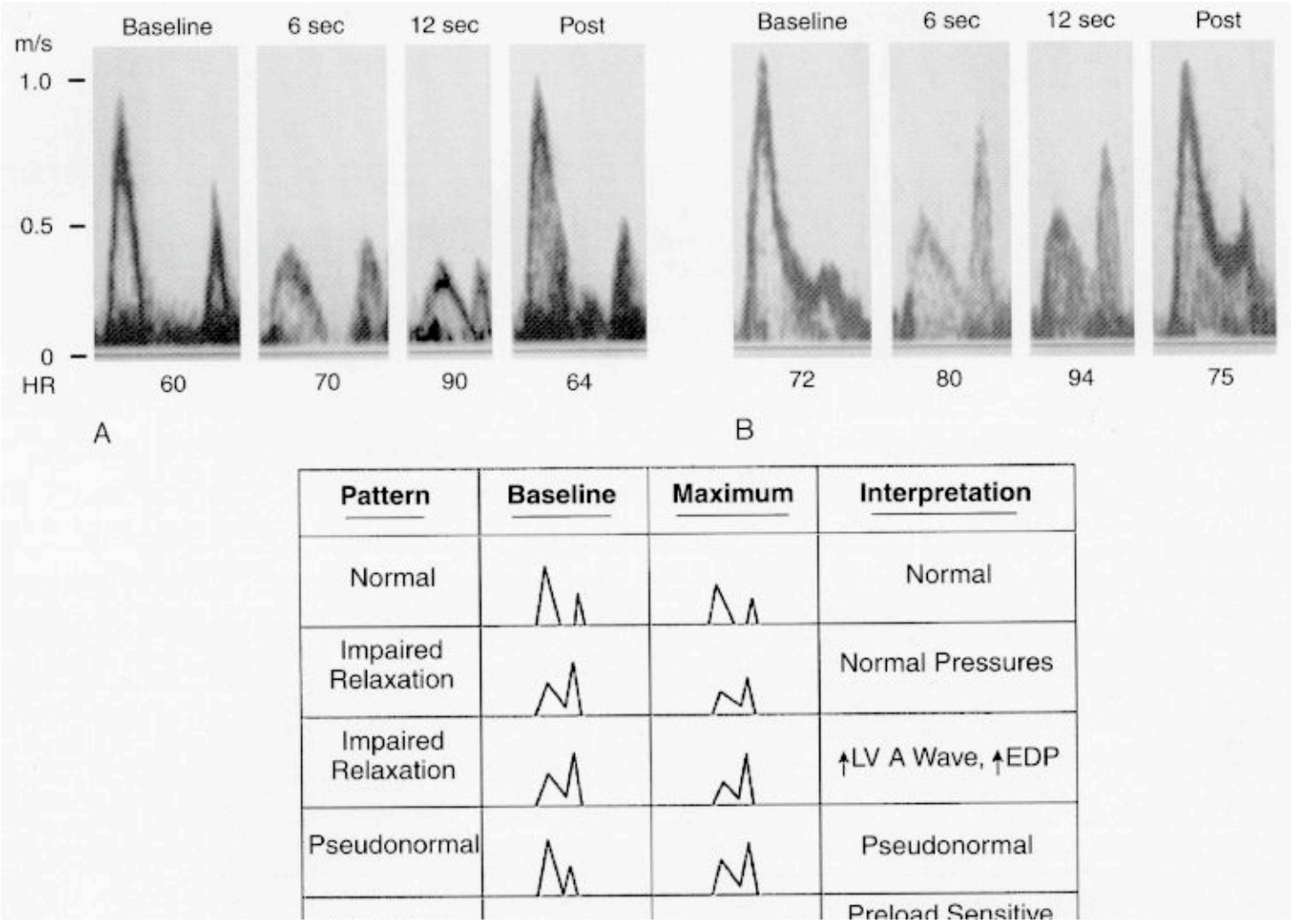


Figure 11. Hemodynamic tracings of the left ventricle (LV) and right ventricle (RV) together with their pulsed-wave Doppler mitral and tricuspid flow velocities are shown in a patient with dilated cardiomyopathy. The mitral flow velocity pattern is pseudonormal as indicated by the elevated filling pressures. The tricuspid filling pattern shows impaired LV relaxation and is associated with normal right ventricular filling pressures. In most disease states that affect LV systolic function, the tricuspid filling pattern *lags* behind the mitral as shown in this illustration, creating a disparity between the two inflow velocity ratios.

Changing Cardiac Loading Conditions

Simple maneuvers in the echocardiographic laboratory demonstrate that mitral flow velocity patterns are a dynamic continuum. [21] [47] [92] During the strain phase of a Valsalva maneuver preload declines, and in normals peak mitral E-wave velocity declines by at least 20% with a smaller decrease in peak A velocity (Fig. 12) . In patients with pseudonormal mitral flow patterns, the Valsalva strain lowers LA pressure and unmasks the underlying impaired LV relaxation (see Fig. 12) . [21] In patients with restrictive filling patterns, preload-sensitive individuals will revert to a pseudonormal or even occasionally an impaired relaxation pattern. In individuals who perform an adequate Valsalva maneuver and remain restrictive with a short mitral deceleration time, LV stiffness is markedly increased and the prognosis is poor. Similarly, in patients with reduced systolic function, increasing preload by leg raising may result in a more abnormal mitral flow velocity pattern, and these patients have higher cardiovascular morbidity. [92]



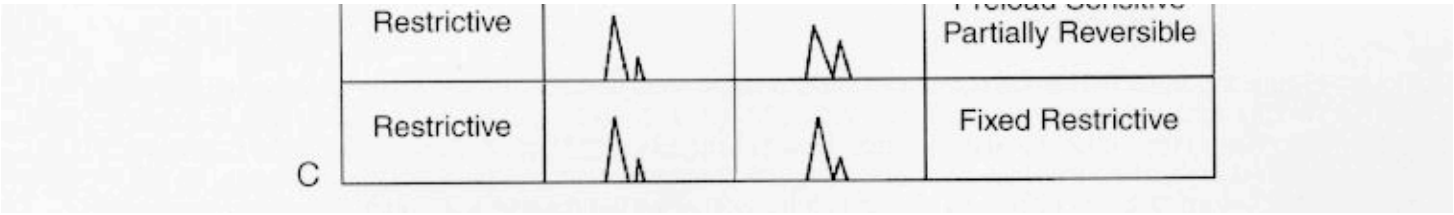


Figure 12. The interpretation of LV filling patterns can be helped by performing a Valsalva maneuver (strain against a closed glottis). The Valsalva maneuver is used to observe changes in the mitral flow velocity pattern with preload reduction. The normal response, which is at least a 20% decrease in E-wave velocity with a smaller decrease in A-wave velocity, is shown in *A*. When a Valsalva maneuver is performed in a patient with pseudonormal LV filling (*B*), the preload reduction unmasks the impaired LV relaxation at 6 and 12 seconds. The different responses to a Valsalva maneuver after approximately 10 seconds of strain are shown in *C*.

Relation of Mitral to Pulmonary Venous A-wave Duration

When the durations are accurately recorded, this relation is an important age-independent indication of LV A-wave pressure increase and LV end-diastolic pressure. [6] [89] [97] [125] Simply stated, when the left atrium contracts, the net volume and duration of flow under normal circumstances should be greater, flowing forward into the left ventricle, rather than backward into the pulmonary veins. If the pulmonary venous A-wave is increased in either velocity (>35 cm/s) or duration (>30 ms longer than mitral A-wave duration), LV A-wave pressure is increased and end-diastolic pressure is elevated. An example of an abnormal relation is shown in Figure 13 . This time interval relation also helps separate patients with impaired relaxation that have normal filling pressures from those with an elevated LV A-wave and LV end-diastolic pressure, the first hemodynamic abnormality seen with **diastolic** dysfunction.

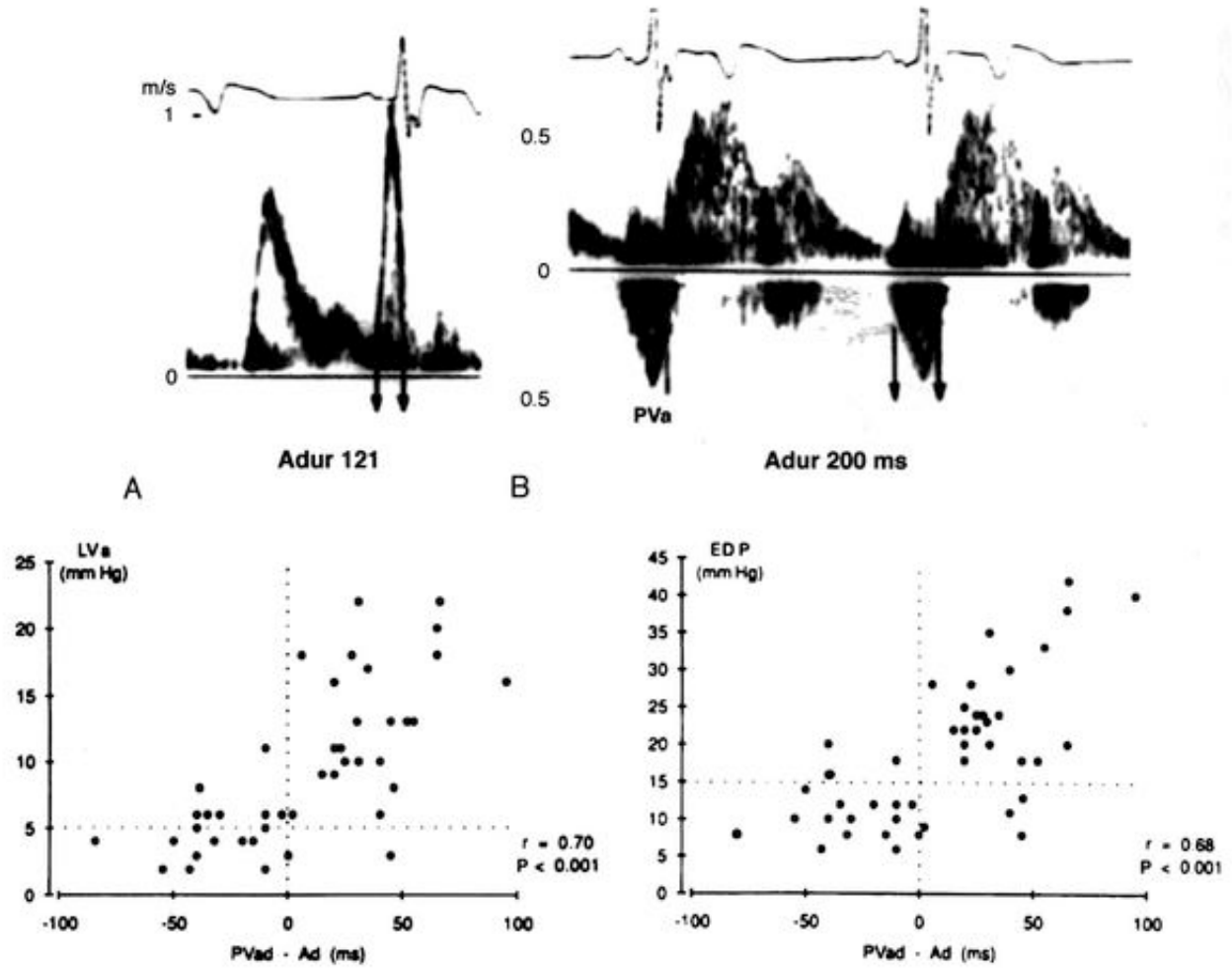
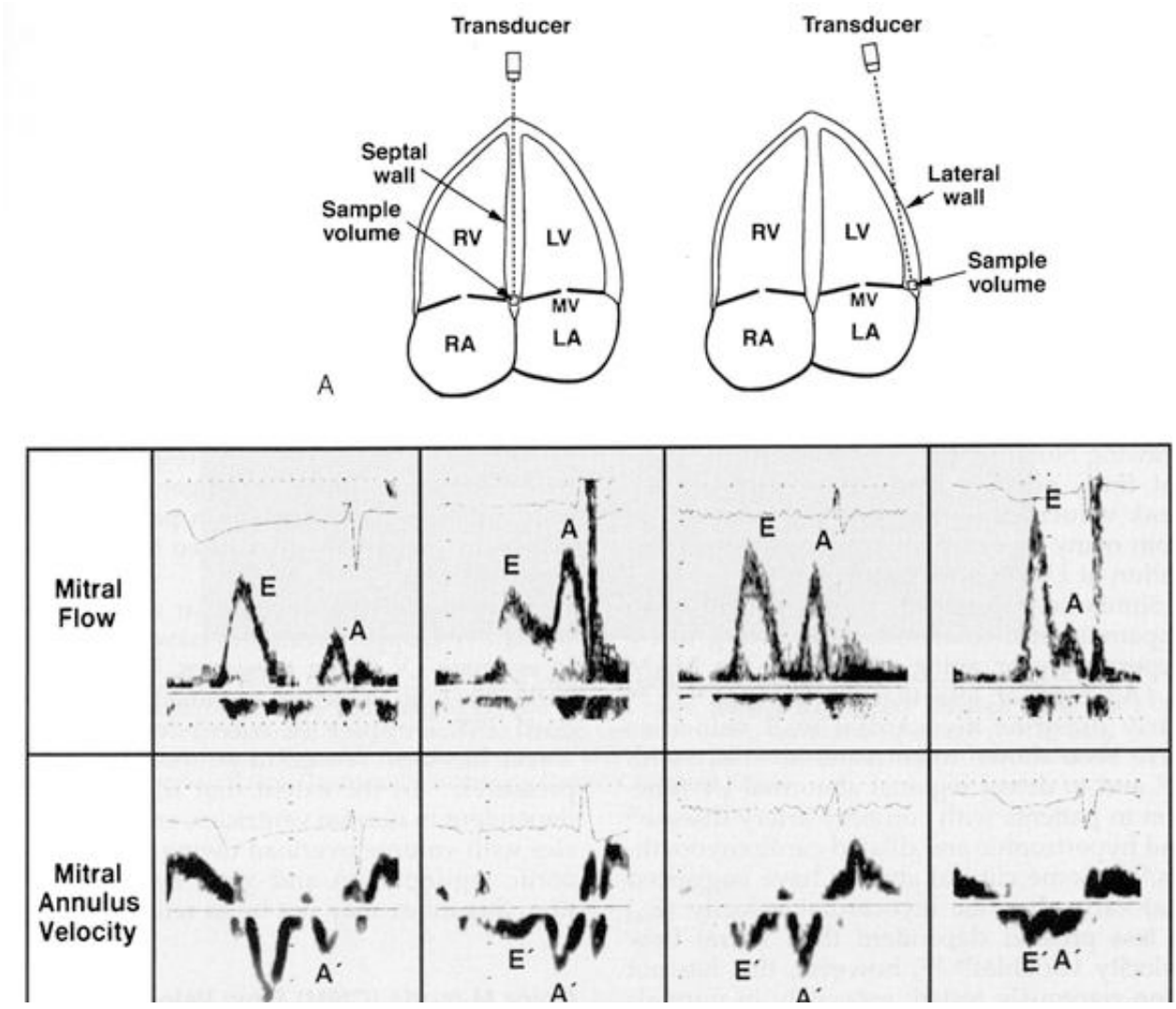


Figure 13. Mitral (*A*) versus pulmonary venous (*B*) A-wave duration. Pulsed-wave Doppler mitral flow velocity and pulmonary

venous flow velocity from a patient with LV hypertrophy and impaired relaxation. In this case, the patient's mitral A-wave duration is 121 ms and pulmonary venous A-wave duration 200 ms so that flow backwards into the pulmonary vein continues for approximately 80 ms after flow into the LV ceases. As shown in the graph when the reverse duration of pulmonary venous compared to mitral A-wave flow exceeds 35 ms, LV end-diastolic pressure is usually >15 mm Hg. *(From Rossvoll O, Hatle LK: Pulmonary venous flow velocities recorded by transthoracic Doppler ultrasound: Relation to left ventricular* ***diastolic*** *pressures (see comments). J Am Coll Cardiol 21:1687-1696, 1993; with permission.)*

Tissue Doppler Imaging

Tissue Doppler imaging (TDI) is a recently developed ultrasound imaging modality that has underlying physics and principles similar to those of conventional PW spectral Doppler. [74] Instead of blood flow, TDI measures the velocity of the myocardium during the cardiac cycle. Blood flow is typically low amplitude and high velocity in nature, whereas myocardial velocities are of higher amplitude and low velocity. Tissue Doppler imaging velocities can be displayed three ways, either as a spectral PW signal (Fig. 14) , as a color velocity encoded M-mode (CMM, Color Fig. 15) , or as a 2D color map (Color Fig. 16) . The limitations of TDI are also similar to standard Doppler in that the PW display, while having a high temporal resolution, only measures velocities at a single point within the heart. Although the CMM has lower velocity resolution, it maintains temporal resolution, while displaying color-coded velocities along an entire scan line. The 2D color map has a lower temporal and velocity resolution, but provides velocity data throughout a sector of the heart. These color displays, especially CMM Doppler and spectral Doppler TDI of MAM, are useful even by qualitative analysis; however, quantitative analysis of all TDI color displays requires digital storage and specialized software.



	E´			
	Normal	Relaxation abnormality	Pseudo-normalization	Restrictive physiology

B

Figure 14. Technique for spectral tissue Doppler imaging of mitral annular motion. *A,* Scan-line orientation for longitudinal axial TDI of the septal (left) and lateral (right) mitral annular velocities (LA = left atrium, LV = left ventricle, RA = right atrium; RV = right ventricle). *B,* Characteristic mitral annular motion spectra compared to normal and abnormal pulsed-wave mitral flow velocity patterns. *(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 30:474-480, 1997, with permission.)*

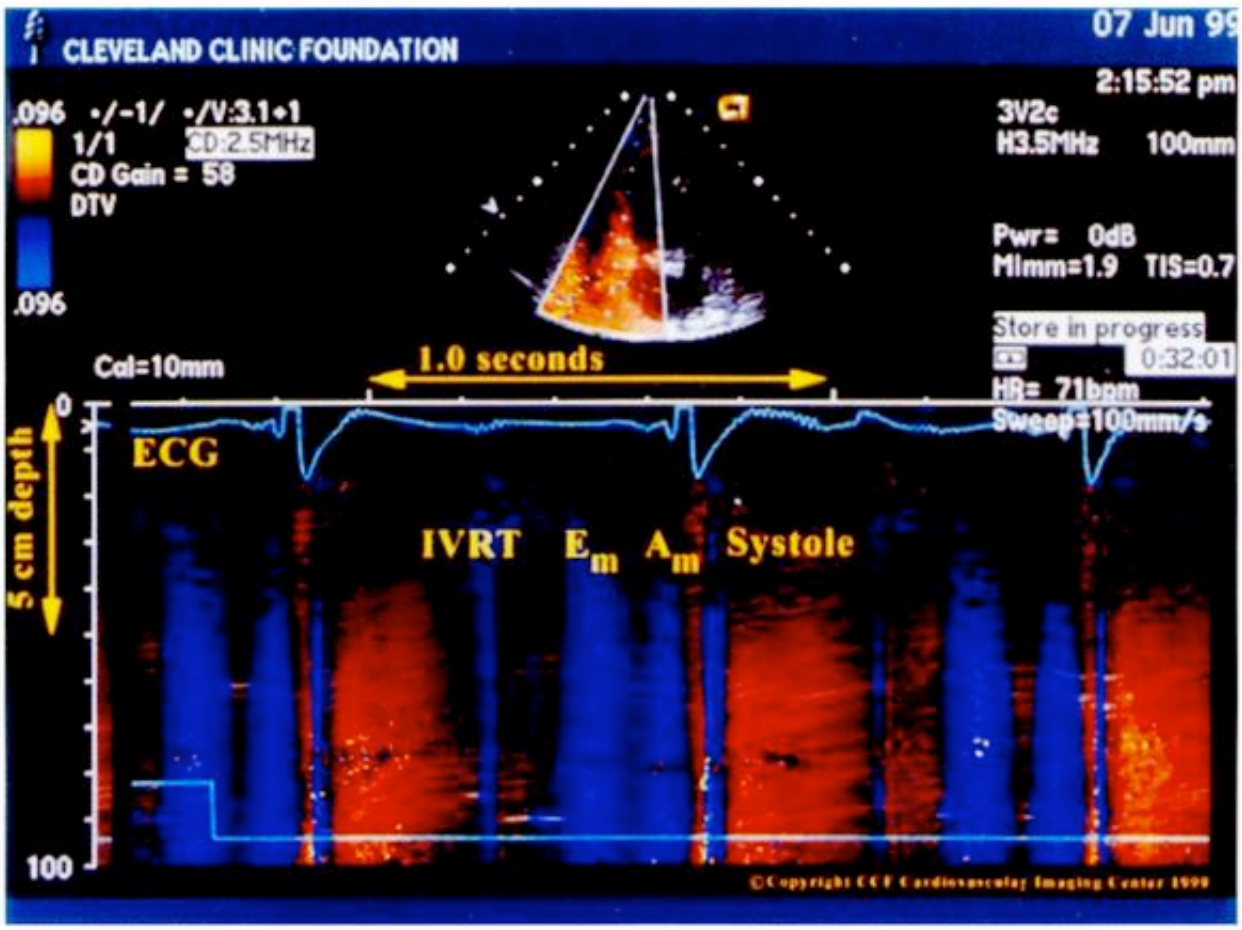
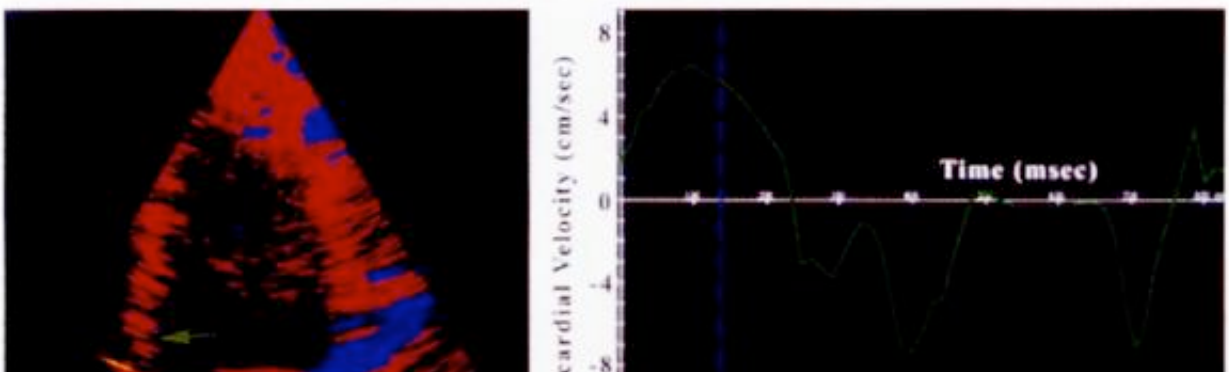


Figure 15. Tissue Doppler color M-mode image. Myocardial tissue velocities are color-coded during systole (blues, away from transducer) and diastole (reds, towards transducer). Distance along the scan-line depth and time are indicated. Tissue velocities during isovolumic relaxation (IVRT), early **diastolic** filling (E_m), late **diastolic** filling (A_m), and systole are labeled. *(Courtesy of the Cleveland Clinic Foundation Cardiovascular Imaging Center, Cleveland, Ohio.)*



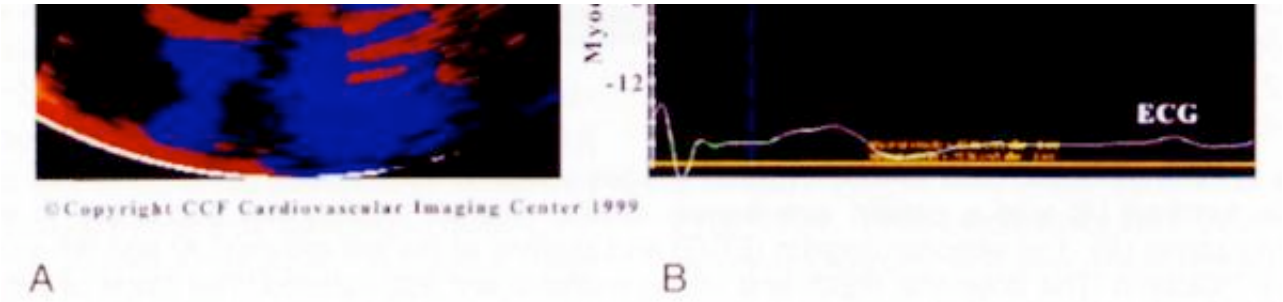


Figure 16. Two-dimensional color tissue image. Myocardial tissue velocities during systole are indicated (*A*). Off-line analysis allows for identification of a single point within the left ventricle (*green arrow*) and the corresponding tissue velocities during an entire cardiac cycle (*B*). Regional changes in **diastolic** and systolic velocities and strain rate can be evaluated. *(Courtesy of the Cleveland Clinic Foundation Cardiovascular Imaging Center, Cleveland, Ohio.)*

Tissue Doppler Imaging Pulsed-wave Spectral Analysis of Mitral Annular Motion

A significant limitation to TDI, particularly with transthoracic parasternal imaging, is that although it provides the velocity of myocardial motion, it cannot separate the translational and rotational components that also occur with myocardial contraction and relaxation. To minimize this limitation, imaging from the longitudinal axial plane (apical window) is performed. From this view, the axial motion of the left ventricle is parallel to the transducer axis and the velocities are primarily related to LV contraction and relaxation. For spectral TDI analysis, a 3 to 7 mm PW sample volume is placed in different segments of the LV (such as the septum and lateral, anterior, inferior, or posterior walls) and regional quantification of segmental velocities is obtained. * For help in recognizing pseudonormal mitral flow velocity patterns, the PW sample volume is usually placed within the septal or lateral regions of the mitral annulus (see Fig. 14) . The TDI function of the ultrasound machine is activated, Doppler gain is markedly lowered (often to 0% power), and wall filters are minimized to display the lower myocardial velocities. Mitral annular velocities are usually less than 20 cm/s. Sweep speed is set at 100 or 200 mm/s.

The normal velocity pattern of MAM obtained from TDI is similar to that of transmitral flow in patients in sinus rhythm. [30] There is a positive (toward the apex) systolic signal (S_m) and negative signal in early (E_m) and late diastole (A_m). In patients with normal ventricular **diastolic** function the peak of the E_m wave tends to occur earlier than the peak of the mitral flow velocity E-wave, suggesting that mechanical relaxation and recoil of the ventricle creates ventricular *suction* drawing blood into the ventricle. At the present time, ongoing research is studying the peak velocities obtained with spectral TDI from many myocardial locations for the evaluation of LV **diastolic** function. [32] [87] [88]

Similar to transmitral profiles, patients with impaired ventricular relaxation owing to LV hypertrophy or aging often have an MAM E_m /A_m ratio of less than 1 (Fig. 14) . [30] [74] [102] Early **diastolic** myocardial wall velocities have been shown to correlate inversely with tau, [87] and to detect regional abnormal LV function in patients with coronary artery disease [11] and hypertrophic and dilated cardiomyopathies. [51] [86] Some clinical studies have suggested that early **diastolic** myocardial velocity (E_m) is less preload dependent than mitral flow velocity variables [76] [102] ; however, this has not been rigorously tested, especially in normals or patients with normal LV systolic function and volume overload owing to mitral or aortic regurgitation. In a study of the effects of preload on TDI MAM velocities in patients with normal and abnormal **diastolic** function, [102] no statistically significant change in E_m was observed in 20 patients with known LV relaxation abnormalities (average baseline mitral deceleration time: 311±84 ms) or in 11 normal individuals following 500 to 700 mL saline infusion. This relative independence to preload has been used to differentiate between constrictive pericarditis and restrictive cardiomyopathy. [29] Despite similar (elevated) PW peak mitral E-wave velocities, all patients with restrictive cardiomyopathy had peak annular E-wave velocities less than 8 cm/s, whereas those with constriction (and normal ventricular relaxation) had peak annular E-wave velocities greater than 8

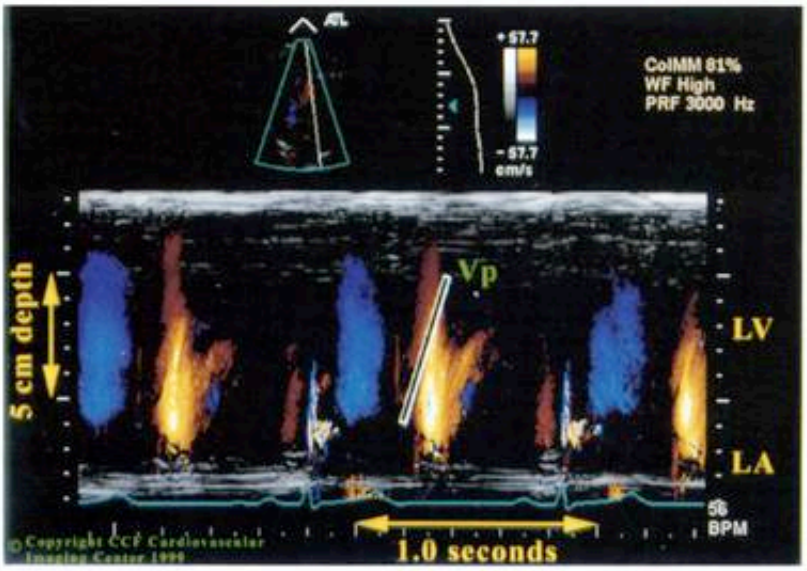
cm/s. Other studies argue against preload independence of MAM where a strong relationship between tissue velocities and LV ejection fraction has been reported. [39] Experimental work has also shown preload dependency in ventricles with normal LV relaxation.

A role for TDI spectral evaluation of MAM in detecting **diastolic** dysfunction associated with rejection in heart transplant patients has been reported in 121 such individuals. [68] The inflammatory reaction and myocardial edema found in transplant rejection result in decreased myocardial compliance and abnormalities in LV ventricular relaxation. Peak E_m waves were lower in patients with moderate rejection and increased following conventional antirejection treatment; however, no association was observed between rejection and systolic TDI velocities. These results need to be confirmed by other investigators, and abnormalities in LV relaxation in patients post-transplant are not always caused by immunologic rejection.

Combined TDI mitral annular and conventional PW Doppler variables have been used to estimate LV filling pressures. The ratio of early **diastolic** velocities obtained with standard PW Doppler (E-wave) to MAM E_m waves has been related to pulmonary wedge pressures. [76] To the extent that E_m is preload dependent in normal ventricles, and in ventricles with volume overload owing to mitral or aortic regurgitation and good systolic function, this index may not be as reliable.

Color M-mode (CMM) Flow Velocity Propagation

A limitation to conventional PW Doppler echocardiography is that it only provides the velocity of blood flow at a single point within the heart. CMM recordings overcome this limitation by providing the spatial and temporal velocity characteristics of flow along an entire echocardiographic scan-line (Color Fig. 17) . The advantage of this imaging modality is that it allows for measurement of velocity data in many points along a line in the heart with superior temporal resolution (2.5 to 10 ms), spatial resolution (about 1 mm), and velocity resolution directly proportional to the Nyquist limit. Given the limitations of the autocorrelation technique in color Doppler, this velocity resolution is approximately equal to the forward plus the reverse Nyquist limit divided by 32. Velocity information is mapped to specific colors of a color bar scale, with flow towards the ultrasound transducer represented by shades of yellow and red, while flow away from the transducer is represented by shades of blue. Aliasing occurs when the velocities exceed the upper or lower limits of the color map and *recycle* through the colors again at the opposite end of the spectrum (so that very high velocities away from the transducer may be represented by bright reds and yellows).



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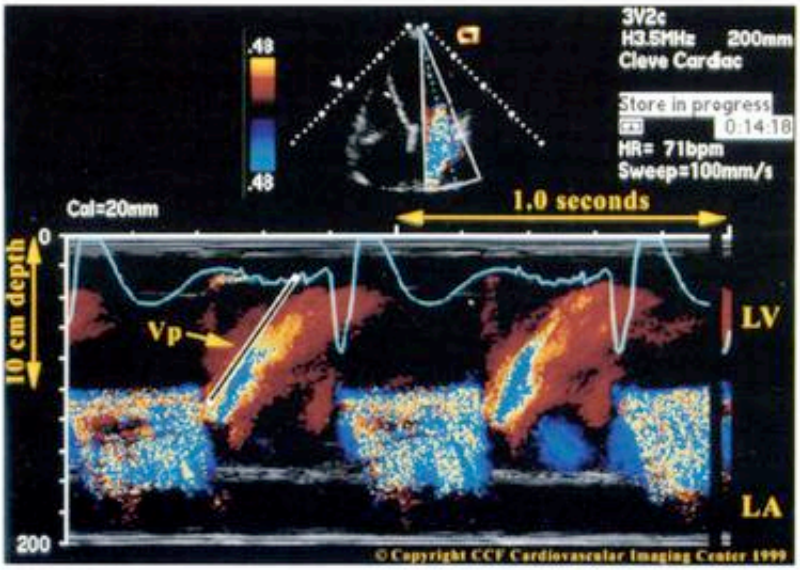


Figure 17. Transthoracic color M-mode (CMM) images obtained from a healthy volunteer with normal **diastolic** function (*A*) and a patient with known severe **diastolic** dysfunction secondary to dilated cardiomyopathy (*B*). The echocardiogram (ECG) and regions of the left atrium (LA) and left ventricle (LV) are indicated. The scan-line depth and timing markers are also labeled. The slope of the early **diastolic** (E-wave) flow propagation (Vp) is identified as a *black on white line*. A steeper (*A*) is associated with faster relaxation and greater "**diastolic** suction" whereas a shallower slope (*B*) is associated with delayed or impaired ventricular relaxation. *(Courtesy of the Cleveland Clinic Foundation Cardiovascular Imaging Center, Cleveland, Ohio.)*

To obtain CMM recordings, the color Doppler function is activated while imaging from the apical four-chamber window. The color sector is placed to include the left ventricle, the mitral valve, and half of the left atrium. The aliasing velocity is initially set between 55 and 60 cm/s. The M-mode cursor is aligned with the mitral inflow (as identified by color Doppler) and passes from the LV apex through the mitral valve and into the left atrium. The M-mode setting is activated at a sweep speed of 100 to 200 mm/s, depending on heart rate. Identification of the flow propagation slope is easier when the velocity scale is adjusted so some aliasing occurs. Similar to PW Doppler, patients in sinus rhythm demonstrate CMM **diastolic** flow that is also characterized by two distinct waves. The first wave correponds to the PW Doppler E-wave and the second follows atrial contraction (A-wave).

The most commonly used variable of CMM Doppler is the propagation velocity of early **diastolic** (E-wave) flow into the left ventricle (Vp). Variation of flow velocity propagation has been demonstrated in normal individuals with aging. [72] The theoretical basis for the Vp slope is temporal (x-axis) and spatial (y-axis) coordinates, which correspond to the maximum velocity of blood flow into the ventricle (see Color Fig. 17) . Despite this simplistic approach, actual measurement of Vp remains a challenge, and no commercial software to determine Vp is presently available. A common research method to obtain Vp is the drawing of a line and measuring of the slope of an isovelocity contour at approximately half the baseline aliasing contour. [37] Another method manually traces the Vp line along the transition zone in which velocity aliasing occurs. [108] Although this approach is more easily applied in routine clinical practice, the validity of the measurement may not be as accurate or reproducible as those obtained using other methods.

In patients with coronary disease and cardiomyopathy, a significant negative correlation between Vp and the time constant of LV relaxation (tau) has been found. [13] [111] Using a different approach, the temporal difference between the point of maximal velocity at the mitral annular level and at the apex has been identified. This time delay is prolonged significantly in dogs during ischemia induced by coronary occlusion [108] and in patients with dilated cardiomyopathy. [107] This time delay is shortened by catecholamine stimulation and prolonged after infusion of beta-blockers, with parallel changes occurring in the rate of LV tau.

Recent clinical studies suggest that CMM Doppler may be useful in distinguishing restrictive cardiomyopathy from constrictive pericarditis in patients with preserved LV systolic function. Although these patients may have similar PW Doppler mitral flow velocity patterns, patients with constrictive pericarditis often have a rapid Vp, whereas patients with restrictive cardiomyopathy show a slower Vp than suggested by their PW peak E-wave velocities. [29] A disparity between PW and CMM Doppler in patients with restriction could be caused either by abnormal generation of vortices owing to functionally reduced mitral valve orifice area or by the reduction of ventricular **diastolic** suction or intraventricular pressure gradients (IVPG). The separation of the two disease entities by propagation velocity is not foolproof, as some patients with adhesive constrictive pericarditis that involves the atrioventricular groove can show reduced MAM and Vp.

CMM Doppler flow propagation velocity, as an index of LV relaxation, may be combined with peak mitral PW Doppler flow velocity to estimate filling pressures. Left atrial pressure and LV relaxation are the main determinants of PW Doppler E-wave velocity. A positive linear relation between E and LA pressure and a negative linear inverse relationship between peak E velocity and tau is reported in animal experiments. [15] Because there is also a negative linear relation between Vp and tau, PW and CMM Doppler data can be combined to try to predict LA pressure using the equation (LAP = 5.27* (E/Vp) + 4.6 mm Hg, r = 0.80, *P* <.001, SEE = 3.1 mm Hg). This equation has been tested in a heterogeneous patient population and benefits from being theoretically sound. [28] [76] Normal individuals with rapid relaxation have increased E and Vp, whereas individuals with impaired relaxation and normal preload have reduced E and Vp, giving similar E/Vp ratios. In contrast, an individual with impaired relaxation but elevated preload will exhibit a higher ratio caused by a higher E-wave velocity with reduced Vp. A simplified application of the relationship between E and Vp suggests that, in patients and healthy normal volunteers, an E/Vp ratio >1.5 indicates an elevated pulmonary artery capillary wedge pressure. These results and confidence intervals remain to be confirmed by other investigators.

In contrast to other PW Doppler mitral filling variables, CMM Vp appears less sensitive to preload. This has been seen in patients with pseudonormal and restrictive LV filling patterns, where Vp is lower than in normals, [111] and in animals undergoing caval occlusion and humans undergoing partial flow cardiopulmonary bypass, [31] where Vp was negatively correlated with LV tau. After examining a variety of hemodynamic conditions and different levels of inotropic stimulation, it appears that the main determinant of Vp is the rate of LV relaxation. Figure 18 summarizes TDI MAM and CMM mitral inflow velocity propagation, which are most commonly seen in normal subjects and patients with abnormal PW Doppler mitral LV filling patterns.

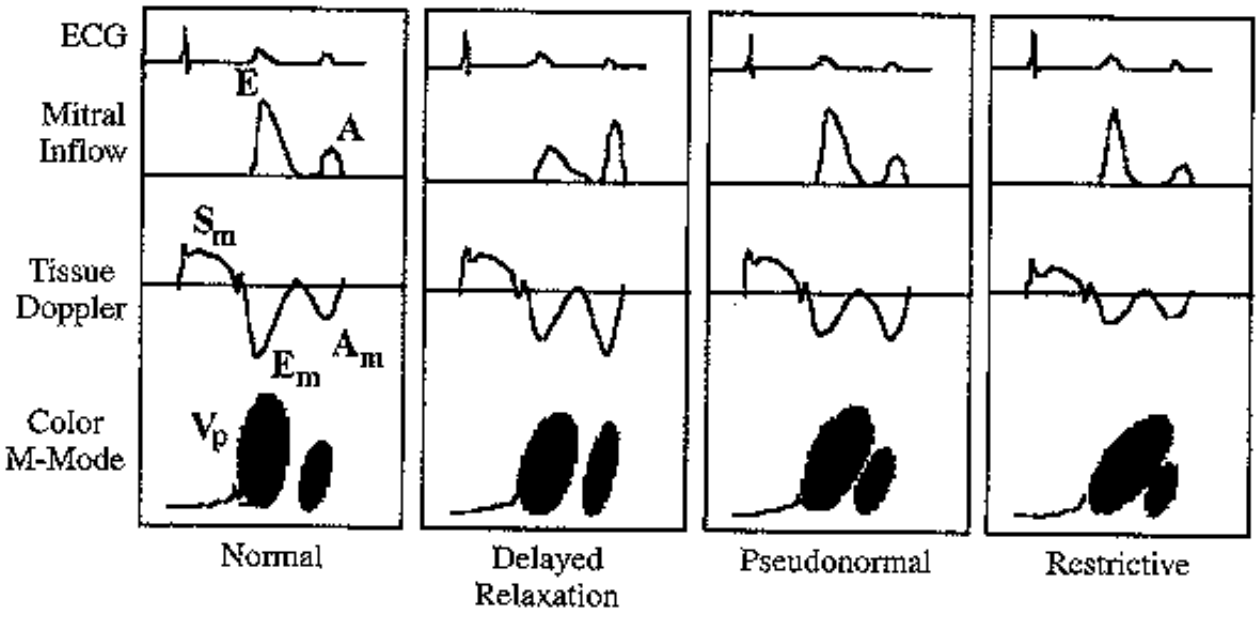


Figure 18. Representative transmitral, myocardial tissue, and CMM patterns expected in patients with normal and abnormal **diastolic** function.

Color M-mode TDI

To obtain a 2D TDI image, a sample box is placed over the region of interest (usually the entire left ventricle) and the TDI function is activated. Overall 2D gains are reduced to remove most grayscale imaging except that needed for identification of myocardial landmarks. To obtain a CMM TDI, a scan-line cursor is placed over the region of interest, usually the interventricular septum or the LV free wall. The M-mode function is activated at sweep speeds of 100 to 200 cm/s. Once the M-mode is activated, the grayscale can be further decreased to eliminate background noise. At the present time, these CMM recordings of myocardial TDI (see Color Fig. 15) are being investigated for clinical application.

Future Applications of CMM and TDI

More complex interpretation of CMM flow propagation images can also be performed by applying basic concepts from the physics of fluid dynamics. The Euler equation (Equation 1) forms that basis for the relationship between the temporal (∂t), velocity (∂v), and spatial (∂s) distribution of fluid flow across a pressure gradient along a streamline (rho = density of blood).

$$\rho\left[\frac{\partial v}{\partial t} + v\frac{\partial v}{\partial s}\right] = -\frac{\partial p}{\partial s}$$

When the Euler equation is integrated the result is the Bernoulli equation (Equation 2). The complete form of the Bernoulli equation describes the inertial

$$\Delta p(t) = \tfrac{1}{2}\rho(v_2^2 - v_1^2) + M\frac{dv}{dt} + R(v)$$

, convective {½ rho(v_2^2 - v_1^2)}, resistive {R(v)}, and gravitational forces that each contribute to a pressure gradient {Deltap(t)}. In routine clinical application, the gravitational and resistive forces are assumed to be negligible.

$$\Delta p(t) = \tfrac{1}{2}\rho(v_2^2 - v_1^2) + M\frac{dv}{dt} + R(v) \qquad \text{[Eq. 2]}$$

For high-velocity flow across a stenotic valve, such as in mitral stenosis, a simplified version of the Bernoulli equation {Deltap(t)= ½ v^2 }, which only considers convective forces, has been shown to be accurate. (When the units are changed to mm Hg and m/sec, the familiar Deltap=4V^2 relation emerges). Unfortunately, for low flow through less restrictive orifices, such as across a normal mitral valve, the simplified Bernoulli equation does not consider the significant contribution of inertial forces. [25] The spatio-temporal and velocity characteristics of flow as derived from CMM flow propagation analysis can be used to solve the Euler equation and separately determine the convective and inertial forces that define a pressure gradient. Analysis of CMM images has been successfully applied to estimating IVPG and more accurately measuring transmitral **diastolic** total pressure gradients and the role of inertial forces. [24]

Left ventricular IVPG that facilitate filling are present after mitral valve opening, with lower LV minimum pressure seen in the apex compared to the LV base. [19] [64] It had also been shown that these IVPG decrease during acute ischemia induced by acute coronary occlusion. [18] It is believed that IVPG are the result of the elastic recoil or *suction* mechanism in normal ventricles during diastole that allows for normal ventricular filling and cardiac output in the presence of near-zero LA pressure. Unfortunately, little work has been done measuring and estimating the determinants of IVPG in humans. In one recent study of eight normal volunteers, positional changes resulted that increased end-diastolic and stroke volumes were also associated with an increase CMM derived intraventricular pressure gradients and a more spherical LV geometry. [23] This insight into the normal relationships between IVPG and acute changes in LV filling and **diastolic** geometry may lead to further research into the role of IVPG and **diastolic** dysfunction.

Myocardial Strain

A unique application of color TDI is the noninvasive determination of myocardial strain and strain rate. Myocardial strain epsilon is defined as the change in segment length (L) relative to the resting length (L_0) of muscle: epsilon = (L - L_0)/L_0 . Strain rate (depsilon/dt) is mathematically identical to the rate of change of tissue velocity over distances within the myocardium (dv/ds), which can be calculated directly from the TDI velocity map (Fig. 16) . A theoretical advantage of strain rate over TDI velocities is that it eliminates some of the translational effects caused by the combined contraction and twisting during systole. Emphasis has typically been directed toward examining the strain rate between the basal and apical septum or the velocity gradient across the septum or posterior wall as viewed from the parasternal window. Regional strain rates between the epicardium and endocardium (myocardial velocity gradient) correlate with regional ventricular contractility. [116] When similar techniques were applied to peak **diastolic** gradients, patients with hypertensive heart disease (peak: -3.9±1.3 per second) and dilated cardiomyopathy (peak: -4.4±1.4 per second) had significantly lower **diastolic** gradients than normal patients (peak: -7.7±1.5 per second, $P < .01$) versus both disease groups. [100]

Although much of the preliminary work investigating strain rate has focused on systolic function, its usefulness in evaluation of LV **diastolic** function remains unknown. Part of this uncertainty is because myocardial thinning can be the result of active relaxation or passive shape changes of the left ventricle. Further research is needed to clarify whether these two circumstances can be differentiated.

A limitation to using TDI as indices of global LV **diastolic** function is that they only measure velocities in one region of the myocardium. Although these characteristics may be desirable in evaluating regional differences in myocardial function, particularly in patients with segmental wall motion abnormalities, regional myocardial function may not accurately reflect global function.

Model-Based Image Processing of Doppler E- and A-Waves

One limitation of current methods of **diastolic** function assessment by analysis of the shape and size of the E- and A-waves stems from the fact that determination of certain mitral parameters (E/A, acceleration time [AT], deceleration time [DT]) requires that only one or two points of the entire E- and A-wave contour be used. It is easy to envision two similar E-waves having the same E_{max} and DT, but having different curvilinear contours connecting E_{max} and the end of the E-wave. A one- or two-point derived index cannot differentiate between these E-waves.

Model-based image processing (MBIP) is a novel method that uses the entire E- and A-wave contour as input in order to solve the *inverse problem* of diastole (for details see the article by Kovacs and colleagues, elsewhere in this issue). A kinematic lumped-parameter model motivated by the mechanical suction-pump attribute of the heart is used to predict transmitral flow velocity as a function of time. The model's predicted

solution for flow velocity is iteratively fit to the E- and A-wave contour by an automated algorithm. [40] [41] The result of the fitting process generates the model parameters (including measures of goodness of fit). For the E-wave, the model has three parameters (x_o , k, and c) accounting for E-wave amplitude, width, and rate of decay, respectively. The physiologic meaning of these parameters has been determined. The time-velocity integral is given by x_o , chamber stiffness is linearly related to k, and the chamber viscoelastic constant can be defined by way of c. The model also specifies the relative balance between k and c to generate the observed Doppler contour.

Application of the model in the clinical arena has allowed determination of chamber stiffness from the E-wave, [62] differentiation of E-waves of hypertensive subjects from those of normal controls, [61] and derivation of an index (having the greatest + and - predictive value) of 1-year mortality in elderly subjects hospitalized with CHF. [94] The MBIP method is generalizable for the discovery of new physiology and has played a role in explaining the mechanism of third heart sound (S3) and fourth heart sound (S4) generation (see the article by Kovacs and colleagues, elsewhere in this issue for additional details regarding additional applications of MBIP). [69] [70]

PERFORMING A PRACTICAL ECHO-DOPPLER EVALUATION OF LEFT VENTRICULAR DIASTOLIC FUNCTION

The assessment of LV **diastolic** function requires high quality echo-Doppler images and recordings of mitral and pulmonary venous flow velocity. Although beyond the scope of this article, a practical guide for optimizing these recordings and avoiding pitfalls is available. [10]

Organizing an echo-Doppler assessment of LV **diastolic** function into a standard routine helps the sonographer and the physician improve their interpretive skills. [17] [83] [93] Our laboratories start with standard M-mode and 2D anatomic imaging to obtain measurements of chamber sizes, LV mass, LV relative wall thickness, [60] and LV systolic function (preferably calculated by volume technique). At the same time, a visual assessment is made of the movement at the atrioventricular groove in the parasternal long axis and apical views. Observing this and mitral and tricuspid annular movement from an apical four-chamber view helps identify the cardiac rhythm and also whether the left atrium appears to have normal size and contractility compared with the right atrium. A normal-sized left atrium that appears *hypercontractile* indicates reduced filling in early diastole and an impaired relaxation pattern. *Hypocontractility* with LA enlargement is usually associated with elevated pressures and pseudonormal or restricted mitral filling patterns. At the same time, symmetry in the rate of LV and RV contractility and relaxation is assessed along with the magnitude of AV longitudinal plane movement. With practice, this visual interpretation of 2D anatomic and LV filling will usually indicate what Doppler LV filling patterns are subsequently seen.

Following the above, an apical four-chamber color Doppler screen is performed to check for valvular regurgitation. CMM of mitral inflow and LV outflow is then used to preview the LV filling pattern, E-wave flow velocity propagation (Vp), and whether there is IVRT flow [98] or systolic LV intracavitary gradients. Pulsed-wave Doppler mitral inflow velocity, mitral velocity inflow with Valsalva maneuver, and PW Doppler analysis of pulmonary venous flow are then performed. If confusion still exists regarding the normalcy of LV filling pattern, TDI spectral Doppler of MAM is assessed. Before leaving the left side of the heart, any LV intracavitary gradients or IVRT flow seen on the CMM screen are located and quantified by PW Doppler. The transducer is then moved medially toward the sternum and PW Doppler of tricuspid inflow along with estimation of PA systolic pressures using peak tricuspid regurgitant velocity is performed. Finally, PW analysis of Doppler hepatic veins and SVC flow during apnea and inspiration is recorded.

With practice, the above components of a **diastolic** function examination can be done with an additional 5- to 10-minute time commitment. The information derived not only helps assess LV **diastolic** function and filling pressures, but also aids patient management decisions.

Using Echo-Doppler Information for Individual Patient Management

If the only information available from examining LV filling patterns was whether the patient had an elevated LA pressure, this can usually be ascertained from the patient's history, physical examination, and chest radiograph. Unique information available from the echo-Doppler study is relating LV **diastolic** function to systolic function, identifying which **diastolic** property is most abnormal and which parts of diastole are most affected and seeing whether the patient's heart rate is well matched to the physiology present. Once ascertained, a short-term treatment plan can be devised to immediately help the patient by manipulating loading conditions and sometimes heart rate. A long-term therapeutic plan is determined by treating the underlying cause of the LV systolic or **diastolic** function.

After the echo-Doppler study is completed, the first question is to identify the main cardiac abnormality present: systolic dysfunction, **diastolic** dysfunction, or valvular heart disease. In patients with a reduced LV ejection fraction, **diastolic** dysfunction is expected and is usually *matched* to the reduction in LV ejection fraction. For example, if there is a mild reduction in LV systolic function, an impaired relaxation filling pattern is expected. Similarly, patients with a moderate reduction in LV ejection fraction (30% to 35%) often have pseudonormal mitral filling patterns. Patients with severe reduction in LV ejection fraction (<20%) commonly demonstrate restrictive filling. A *mismatch* between these expected relations is notable. For instance, if only mild systolic dysfunction is present, a pseudonormal or restrictive mitral filling pattern indicates either volume overload or worse LV compliance than expected. Coronary artery disease, diabetes, or some other associated disease process should be suspected. Conversely, patients with moderate and severe LV systolic dysfunction may have an impaired LV filling pattern without evidence for increased LA pressure. Such individuals often have excellent exercise tolerance, a favorable prognosis, [92] and do not tolerate the indiscriminate use of diuretics. Why patients with severe LV systolic dysfunction have such variability in LV compliance remains a key enigma that requires further investigation.

When LV systolic dysfunction is equal to or greater than **diastolic** dysfunction, treatment of the systolic function is emphasized using diuretics, afterload reduction, and sometimes beta-blockers and digoxin. If LV systolic dysfunction is severe, even small decreases in afterload will improve **diastolic** function. [22] In severe four-chamber dilated cardiomyopathies ventricular interdependence may be seen as shortening of the mitral deceleration time on inspiration during increased RV filling. In these cases diuretics may be particularly helpful along with afterload reduction. The effect of beta-blocker therapy on mitral flow velocity variables in patients with dilated cardiomyopathies has been studied. Interestingly, an improvement in mitral DT and symptoms occurred within 3 months while the maximum increase in systolic performance was not seen until months later. [1]

In patients with symptoms of CHF or exercise intolerance who have normal LV systolic function, attention is focused on assessing LV **diastolic** function. Questions to be answered include whether the LV **diastolic** properties of relaxation or compliance are abnormal, which (if either) predominates, and during what part(s) of diastole the abnormalities are present. This gives an idea of the best approach for short-term therapy and whether altering the heart rate is likely to improve the patient's symptoms. Although classifying patients as having one of the three abnormal filling patterns is often useful for this purpose, there are variations of LV filling patterns that do not easily fit into this scheme. Furthermore, similar mitral filling patterns may have markedly different combinations of LA pressure and rates of LV relaxation. Therefore, the most reliable information regarding **diastolic** function and what treatments might benefit the patient are still best available by carefully examining the mitral flow velocity pattern and its individual Doppler variables.

Let Ventricular Isovolumic Relaxation Time Interval

Isovolumic relaxation time (IVRT) is the interval from aortic valve closure to mitral valve opening (MVO) and the start of mitral inflow. The IVRT interval is helpful when it is at its extremes, being either short (<60 ms) or long (>110 ms). It is less useful in between these values. A normal IVRT for a middle-aged adult is approximately 80 ms. A short IVRT (<60 ms) indicates an early mitral valve opening. This can be seen in young, healthy, normal individuals, or in patients with elevated mean LA pressure. This clinical distinction is easily made by the 2D anatomic findings, especially LA size and function. When the IVRT is long (>110 ms), mitral valve opening is delayed. This is seen in patients with impaired relaxation and normal pressures, and is an early indicator of LV **diastolic** dysfunction. LV IVRT intervals between 60 and 100 ms are seen in a variety of different LV filling patterns. [7] [77]

Mitral Flow Velocity Integral

Because LV **diastolic** dysfunction is a disorder of LV filling, it is useful to examine the IVRT interval along with the entire mitral flow velocity integral. This integral (in the absence of significant mitral regurgitation or aortic insufficiency) multiplied by mitral valve cross-sectional area is the LV stroke volume. Cardiac output is obtained by multiplying stroke volume by the heart rate. At normal heart rates, an increased mitral flow velocity integral in early diastole will (by necessity) be associated with a lesser flow velocity integral at atrial contraction. Conversely, when the early **diastolic** flow velocity integral is decreased, a corresponding increase in late flow velocity integral (A-wave) is present. If the heart rate is relatively rapid or, if first degree AV block is present, early- and late-diastolic filling may be partially fused (E at A velocity >20 cm/s), or seen only after atrial contraction. In these cases, the E/A ratio is decreased and peak A-wave velocity and velocity time integral are significantly elevated because of the increased stroke volume (see Fig. 6) .

Examining the variations in LV filling patterns helps determine if the heart rate is well matched to the LV **diastolic** abnormalities that are present. Current evidence suggests that maximizing early- and mid-diastolic filling through LV relaxation and elastic recoil leads to the most physiologic LV function and the least symptoms. [54] [79] In patients who have impaired relaxation patterns, the resting heart rate needs to be slow enough so the mitral filling velocity at atrial contraction has decreased to less than 20 cm/s. If greater than 20 cm/s, the fusion of early- and late-diastolic filling may limit increases in LV end-diastolic volume and reduce functional aerobic capacity. [54] Drugs that slow the heart rate without prolonging the PR interval often reduce these patients' symptoms and increase their exercise ability. The same comments apply to a patient who has filling only at atrial contraction. First-degree AV block resulting in partial E- and A-wave fusion is more difficult to treat. Negative chronotropic agents such as beta-blockers or calcium channel blockers will slow the heart rate in these patients, but may also prolong the PR interval. The result may be that the overall filling pattern is not improved, and **diastolic** mitral regurgitation may occur. [5] [99] If symptoms remain after normalizing preload and afterload, or, if a dilated or hypertrophic cardiomyopathy is present, a dual-chamber pacemaker that shortens the PR interval and increases the filling in early diastole may reduce symptoms. [77] [80] In patients with pseudonormal and restricted mitral flow velocity patterns, reducing preload often improves the patient's symptoms and reverts the filling pattern back to impaired relaxation. A slower heart rate may then be needed to allow the ventricle to fill maximally before atrial contraction. The goal is to slow the heart rate to offset the impaired LV relaxation and maximize early- and mid-diastolic filling. This keeps the mean LV **diastolic** filling pressure normal and confines any potential pressure increase to the interval following atrial contraction.

Peak Mitral E-Wave Velocity

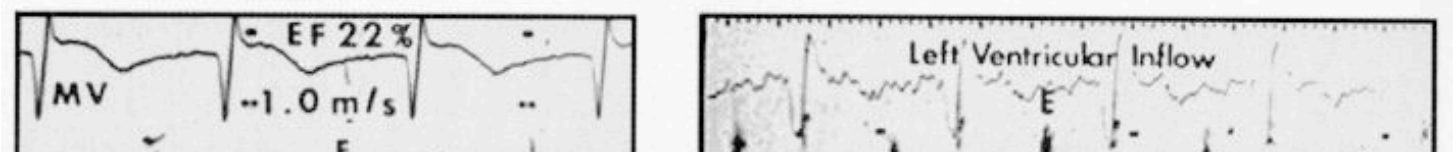
Peak mitral E-wave velocity is determined by the early **diastolic** TMPG (see Fig. 2) . An increased peak E-wave velocity is seen in four circumstances: 1) normal individuals with vigorous elastic recoil create a low LV minimum pressure that increases the early TMPG; 2) mitral stenosis where the reduced valvular orifice causes an increase in the TMPG throughout diastole; 3) pseudonormal and restrictive LV filling with the increase in early **diastolic** TMPG the result of reduced LV compliance and increased LA pressure; and 4) significant mitral regurgitation with its increased volume returning through the regurgitant mitral valve.

The 2D findings of normal LA size and vigorous LV and right ventricular contractility indicate the normal individuals. If there is a question between normal and pseudonormal filling, the distinction can be made by the multiple ancillary methods previously described. In patients with an elevated E velocity caused by mitral regurgitation, mitral DT should remain normal. This shift of the LV P-V curve to the right is the normal adaptation of the ventricle to volume overload that helps keep left-heart filling pressures normal. With moderate or severe mitral regurgitation, a shortened mitral deceleration time (<160 ms) indicates either acute mitral regurgitation (evident as rapidly decreasing late systolic velocity in the MR continuous wave Doppler signal), or some co-existent disease process that reduces LV compliance. In patients with an elevated E-wave velocity who have pseudonormal or restricted mitral flow velocity patterns, a Valsalva maneuver (see Fig. 12) or sublingual nitroglycerin [48] reveals the degree of preload sensitivity. Generally, reduction in preload by diuresis will lower mean LA pressure and improve the patient's symptoms, although a slower heart rate may be needed if they improve to an impaired relaxing filling pattern. If mitral E- at A-wave velocity is elevated it should be reduced to less than 20 cm/s if possible. Whether a heart rate of 70, 60, or 50 beats/min is adequate can be determined by follow-up echocardiographic examinations.

Mitral Deceleration Time

In adult patients with symptomatic heart disease, mitral deceleration time (DT) is generally related to the mean LA pressure and LV compliance. [67] [114] A relatively short DT (130 to 160 ms) can be seen in healthy, young, normal individuals and is recognized by the patient's age and 2D echo findings. A short DT (<140 ms) in association with LV systolic dysfunction or isolated **diastolic** dysfunction indicates markedly reduced LV compliance. Patients who are volume overloaded have an elevated central venous pressure on physical exam, or a dilated IVC and hepatic veins that do not collapse normally with respiration on 2D echo. Volume overloaded patients improve with diuresis. If a patient is not greatly volume overloaded but their mitral flow velocity becomes more normal with the Valsalva maneuver, mild diuresis may be beneficial.

In some patients, afterload is significantly increased and lowering blood pressure may also improve LV relaxation, filling pattern, and functional aerobic capacity. [120] Patients who have normal preload and afterload and yet maintain their abnormally short mitral DT have a less favorable prognosis in a wide variety of heart diseases, including restricted and dilated cardiomyopathies, [57] [90] [124] first acute myocardial infarctions, [84] and atrial fibrillation. [48] In patients with restrictive cardiomyopathy, slowing the heart rate may have adverse consequences if the majority of filling occurs in early diastole so that stroke volume is fixed. The response in patients with dilated cardiomyopathy is more variable, with some patients improving by slowing the heart rate, perhaps because of a negative restitution phenomenon with their relative (80 to 100 beats/min) tachycardia. Because the response to beta-blockers is unpredictable in advanced cardiomyopathies, they should always be initiated at very low doses. Persistence of a restrictive LV filling pattern in dilated cardiomyopathy after maximum medical therapy is an ominous prognostic sign. [91] Examples of patients with dilated and restrictive cardiomyopathy are shown in Figure 19 .



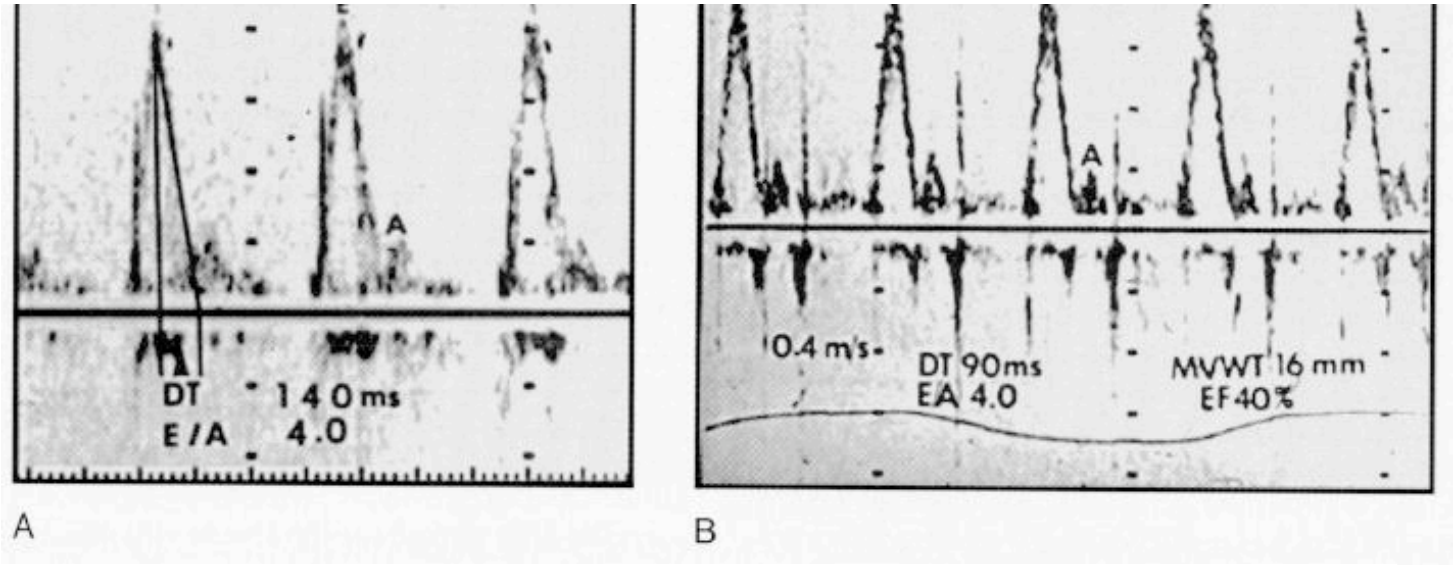


Figure 19. Pulsed-wave mitral flow velocity recordings from patients with dilated cardiomyopathy (DCM; *A*) and restrictive cardiomyopathy (RCM) to amyloid heart disease (*B*). In both cases there is a restrictive filling pattern with increased E- to A-wave ratio and a shortened deceleration time (DT). The small A-wave flow velocity integral reflects increased filling pressures and left atrial systolic dysfunction. In the patient with RCM a slower heart rate may be deleterious as the majority of LV filling occurs in early diastole, therefore making cardiac output heart rate dependent.

Mitral Flow Velocity at the Start of Atrial Contraction (E- at A-Wave Velocity)

In general, an effort should be made to keep the heart rate slow enough to keep this velocity at less than 20 cm/s. This maximizes early- and mid-diastolic ventricular filling and reduces the proportion of filling associated with atrial contraction. If this velocity is more than 20 cm/s at rest, patients have a decreased reserve to increase their mitral flow velocity integral and LV end-diastolic volume when they exercise. Slowing the heart rate with calcium channel or beta-blockers in these patients is usually beneficial, unless they have a first degree AV block.

Peak Mitral A-Wave Velocity

The mitral A-wave is determined by the late **diastolic** TMPG. An elevated A-wave velocity and velocity time integral are expected in patients with impaired relaxation and reduced E-wave velocity time integral, and are necessary to maintain a normal LV end-diastolic volume. When LV relaxation is slowed, the reduced filling in early diastole results in less LV pressure increase relative to minimum LV pressure, so that the atrium contracts into a relatively low-pressure, compliant chamber. By 2D echo, the left atrium appears *hypercontractile* with exaggerated MAM toward the pulmonary veins. The A-wave peak velocity is increased, the A-wave flow velocity integral is relatively large, and the flow duration is increased, usually greater than 125 ms. If A-wave velocity is greater than 1 m/s or, if the atrial deceleration time unusually short (<110 ms), this often indicates an increase in LV end-diastolic pressure.

Mitral A-Wave Duration

Comparing the duration of mitral and pulmonary venous A-wave reversal distinguishes which patients with impaired relaxation of LV filling have an elevated LV A-wave pressure and end-diastolic pressure, the earliest hemodynamic abnormality seen with **diastolic** dysfunction. When pulmonary venous A-wave reversal duration is greater than 35 ms compared with mitral A-wave duration, LV pressures increase at atrial contraction, and LV end-diastolic pressures are elevated, [14] [97] [125] even in the pediatric age group. [89] When it is difficult to measure the A-wave durations accurately, referencing the end of each to the ECG QRS complex may be helpful, as pulmonary venous flow duration does not normally exceed that of the mitral A-

wave.

Mitral A-wave duration is also determined by the TMPG but several other factors affect its duration that need to be considered during interpretation. The age-related changes in peak mitral A-wave velocity are also present for A-wave duration, with shorter values in younger individuals and a progressive increase throughout life. In middle-aged patients, a peak E- at A-wave velocity of less than 20 cm/s with a relatively long A-wave duration (>130 ms) usually indicates that LV compliance and filling pressures are normal. Early **diastolic** filling predominance, an E- at A-wave velocity of less than 20 ms, and a shorter mitral A-wave duration (<120 ms) can be seen in healthy normal patients or in patients with pseudonormal or restrictive filling. Normal hearts have normal LA and LV size and contractility and a pulmonary venous A-wave reversal that is the same or less than mitral A-wave duration. In pseudonormal or restricted filling patterns, the mitral A-wave duration is shortened because the reduced LV compliance results in an excessive rise in LV pressure with atrial contraction, which abruptly terminates transmitral flow. [71] This is often indicated by an asymmetrical A-wave whose deceleration time is shorter than acceleration time. [113]

Even in cases where the atrium is enlarged, markedly hypokinetic, and failing, the pulmonary venous A-wave duration continues to be longer (>35 ms) than the abbreviated mitral A-wave duration. Variation in cardiac cycle length caused by sinus arrhythmia or premature atrial beats also effects mitral A-wave duration. Longer cycles result in more mid-diastolic LV filling and pressure increase so that A-wave duration and velocity integral are reduced. Short R-R intervals result in longer A-wave durations (Fig. 20) . A lengthening of A-wave duration after medical intervention is helpful in confirming if an increase in peak E-wave velocity represents improved LV relaxation, and not increased LA pressure. [82]

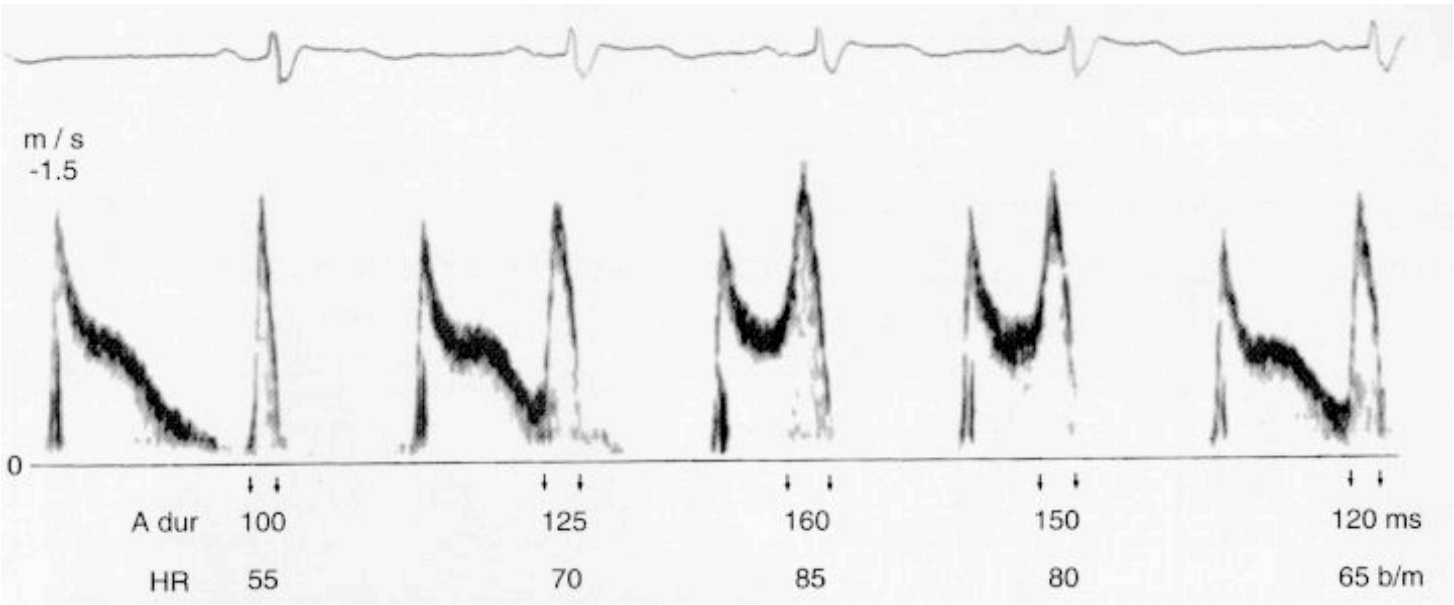


Figure 20. Changes in pulsed-wave Doppler mitral A-wave duration (A dur) owing to variation in heart rate (HR). With longer R-R intervals and slower heart rates, more ventricular filling occurs in mid-diastole so that LV pressure is higher at the time of atrial contraction. This results in smaller atrial stroke volume and shorter A-wave duration. With faster heart rates, less time is available for ventricular filling in mid-diastole, so the atrium contracts when LV pressure and volume are lower. The result is an increased atrial stroke volume, longer A-wave duration, and a higher E- at A-wave velocity.

The interpretation of mitral A-wave duration is different if the E- at A-wave velocity is greater than 20 cm/s. In these cases, the A-wave duration is usually longer than normal to accommodate the increased atrial stroke volume that is present. This makes the comparison of mitral and pulmonary venous A-wave durations less reliable, especially when atrial contraction occurs before PV **diastolic** velocity has decreased to the zero velocity baseline (Fig. 21) . With higher peak A-wave velocities, A-wave duration is also larger because the deceleration of flow takes longer to decrease to the zero velocity baseline. A *pseudo*-increase in mitral A-

wave duration can sometimes be seen in patients who have mid-diastolic filling that is fused with filling at atrial contraction. This can occur in young, normal individuals and also in patients with markedly impaired LV relaxation who have mid-diastolic filling caused by markedly prolonged relaxation (Fig. 22) . Therapeutically, patients with an E- at A-wave velocity greater than 20 cm/s usually benefit from slowing the heart rate to allow more ventricular filling to occur in early diastole.

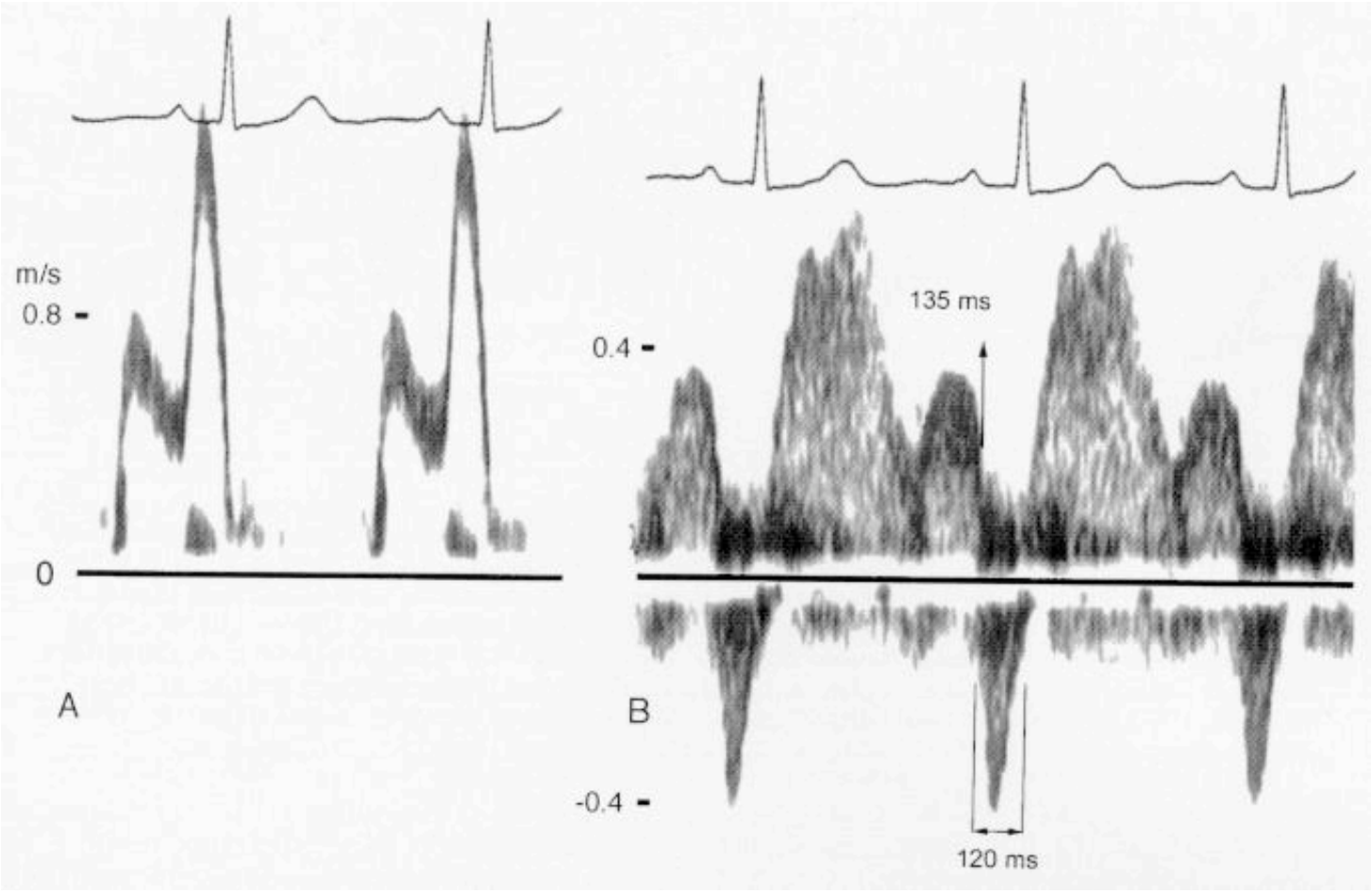


Figure 21. Pulsed-wave Doppler mitral and pulmonary venous recordings from a patient with hypertension and LV hypertrophy that illustrate the effect faster heart rates can have on mitral (*A*) and pulmonary venous (*B*) flow velocity variables. Pulmonary venous flow velocity at atrial contraction (PVa) is abnormally large (40 cm/s), suggesting an increase in LV end-diastolic pressure, but PVa duration (125 ms) is less than mitral A-wave duration (135 ms). In this case factors that contribute to a mitral A-wave duration greater than PVa include a mitral E at A velocity of greater than 20 cm/s (which increases mitral A-duration) and a pulmonary venous **diastolic** velocity at the start of atrial contraction that is significantly above the zero velocity baseline (35 cm/s, *arrow*). With a slower heart rate, mitral A-wave duration would be shorter and PVa duration would be longer.

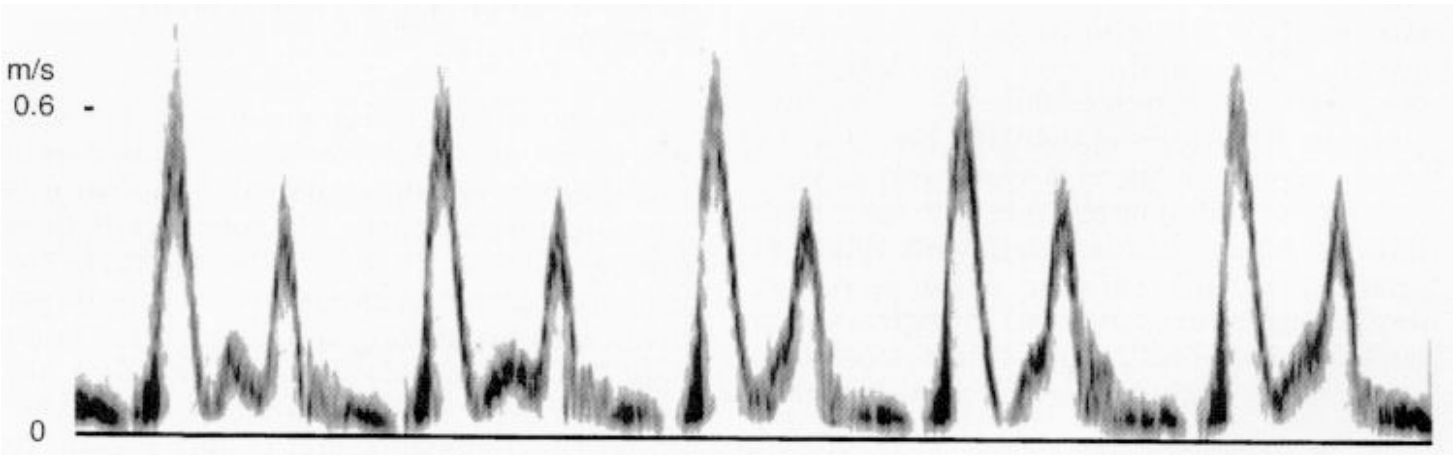


Figure 22. Pulsed-wave Doppler mitral flow velocity recording from a patient with LV hypertrophy and coronary artery disease. The first beat demonstrates a shortened mitral DT (120 ms), indicating a decrease in early **diastolic** LV compliance. In mid-diastole flow resumes owing to markedly impaired LV relaxation. This is followed by a mitral A-wave whose duration of flow is 115 ms. In the subsequent beats there is minimal change in R-R interval, but the mid-diastolic filling blends to varying degrees with the mitral A-wave, giving the false impression that its duration is increased.

E- to A-Wave Ratio

This ratio has been used to help characterize the overall mitral flow velocity pattern. Although this is generally true, when E- at A-wave velocity is greater than 20 cm/s the E- to A-wave ratio is reduced because the A-wave velocity is higher than it would be at a slower heart rate or shorter PR interval. This information is useful because fusion or partial fusion of E- and A-wave velocities indicates that a slower heart rate or reduced PR interval may improve **diastolic** function and patient symptoms.

Less Common Mitral Flow Velocity Patterns

Variations in LV filling patterns are seen where impaired LV relaxation persists into mid-diastole or where altered compliance is present only in early diastole rather than throughout the **diastolic** filling period. For instance, as shown in Figure 23 (Figure Not Available) , elderly patients with severe long-standing hypertension may have very delayed LV relaxation but demonstrate a short initial mitral DT and reduced LV compliance that is only present in early diastole. The initial mitral E-wave velocity is relatively high and is followed by a short mitral DT. At lower heart rates, continued filling with a less steep slope is seen in mid-diastole with normal filling at atrial contraction. Comparing pulmonary venous and mitral flow velocities in such patients shows that the changes in the ventricle precede those in the pulmonary veins. The predominant abnormality present is markedly impaired LV relaxation, which causes a severe decrease in LV compliance (the short initial mitral DT), but one that is confined to early diastole, perhaps because of inadequate actin-myosin cross-bridge detachment. If the heart rate is slow enough, relaxation, although markedly prolonged, may continue so the left ventricle can fill with little elevation in end-diastolic pressure. In these patients, faster heart rates are likely to result in exercise intolerance and pulmonary congestion.

Figure 23. (Figure Not Available) Unusual pulsed-wave Doppler mitral flow velocity recording showing three forward filling and one reverse filling wave. The initial early **diastolic** velocity has a very short mitral (*A*) DT because of a rapid increase in LV pressure (*B*). This not only abruptly decelerates mitral flow but results in transient **diastolic** mitral regurgitation (*arrow*). Forward flow then resumes in mid-diastole with a decrease in LV pressure. The last forward velocity peak is a result of atrial contraction. This is an example where transient restrictive-like physiology exists in early diastole (perhaps because of inadequate contractile element disassociation), but thereafter the delayed relaxation and more compliant ventricle as the ventricle undergoes delayed LV relaxation. This is an example of restrictive physiology during early diastole that is transient rather than fixed, and with continued relaxation the majority can occur in mid- and late diastole. *(From Hatle L: Doppler echocardiographic evaluation of **diastolic** function in hypertensive cardiomyopathies. Eur Heart J 14(suppl):88-94, 1993; with permission.)*

In summary, looking at each component of the mitral flow velocity pattern helps in deciding what therapies may benefit a symptomatic patient. Although it is generally true that normalizing preload and afterload will improve the rate of LV relaxation and operating LV chamber compliance, the examination of the components previously outlined helps with interpretive pitfalls in assessing mitral and pulmonary venous flow velocity patterns and suggesting what heart rate may be most beneficial to the patient. In all patients, the underlying cause of the **diastolic** dysfunction should be determined, as this needs to be treated to make long-term improvements in LV **diastolic** function. The ability to decide whether a relaxation abnormality or compliance problem is foremost, and during which parts of the cardiac cycle it is present, how preload sensitive it is, and whether the patient's heart rate is well matched to their **diastolic** abnormalities is unique to an echoDoppler examination and information unavailable by any other current modality.

INTERPRETATION OF RIGHT VENTRICULAR DIASTOLIC FUNCTION

The same Doppler analysis used for mitral flow velocity can be applied to tricuspid inflow and right ventricular filling. Because inspiration increases right ventricular filling, changes in tricuspid flow velocity are seen throughout the respiratory cycle, whereas on the left side of the heart, Doppler mitral variables vary only about 5%. [4] This increase in inspiratory right ventricular filling can be used, in conjunction with hepatic and superior vena cava flow velocities, to assess the **diastolic** properties of the right ventricle.

PW Doppler tricuspid DT is about 25 ms longer than its mitral counterpart. With normal right ventricular **diastolic** function this value changes little with the increased flow during inspiration, and hepatic A-wave reversals decrease in velocity and duration. With a decrease in late **diastolic** right ventricular compliance hepatic venous A-wave velocity and duration increase with inspiration. An inspiratory shortening of tricuspid DT, **diastolic** predominance of hepatic venous flow [75] with prominent V- and A-wave reversals are signs of a marked decrease in right ventricular compliance and increased **diastolic** filling pressures. The **diastolic** slope and A-wave decrease in velocity in pulmonary regurgitation Doppler signals can also be used to assess early and late **diastolic** right ventricular compliance.

LIMITATIONS

The greatest limitation to the echo-Doppler assessment of LV **diastolic** dysfunction is the experience to discern from the information available which of the key **diastolic** properties (LV relaxation or compliance) are most abnormal, how these are related to LV systolic function, and how both interact to affect the overall LV filling pattern. When first learning to interpret LV **diastolic** function using echo-Doppler techniques there is a tendency to try to make all variables fit into one abnormal LV filling pattern or another, when in reality there are nearly endless variations and exceptions to defined *criteria*. This is why the authors believe examining the mitral filling pattern together with all available 2D and Doppler information is the most helpful in patient management. This approach acknowledges that the variables used are imperfect indicators of individual **diastolic** filling properties or pressures, but in aggregate usually give enough information to be clinically useful in patient management.

Another common limitation to echo technique is the lack of technical experience in acquiring high-quality Doppler recordings so that all variables are accurately measured. It can be expected that even when performing a routine **diastolic** function examination on every patient undergoing echocardiography, it may take at least 6 months for sonographers [10] and physicians to master these skills.

Several pitfalls that make a **diastolic** function examination more difficult to interpret were previously mentioned. Fusion of E- and A-waves makes the assessment of the relationship of mitral and pulmonary venous A-wave duration more difficult because the mitral A-wave is increased in duration, whereas a pulmonary venous flow reversal at atrial contraction is often narrowed because its starting point is above the zero of velocity baseline. Atrial fibrillation presents its own unique problems. In this case, there are no mitral or pulmonary venous A-waves to assess. It can be expected that deceleration time is shortened approximately 20 ms in patients in atrial fibrillation. Recognizing increased filling pressures is not precise in these patients, although an increase of early mitral flow velocity of grater than 1 m/s is usually abnormal. In addition, a shortened mitral deceleration time (<130 ms) has the same adverse prognostic value that it does in other cardiac disease states in which patients are in normal sinus rhythm. [48]

Some of the newer techniques discussed in this article, such as TDI for MAM and wall velocities or MBIP

for automated **diastolic** function assessment, require new generation ultrasound machines, and specialized software. Late generation machines also help the routine performance of a **diastolic** function examination because they have greater sensitivity in their Doppler functions and better color flow Doppler to help align signals and identify sample volume placement for pulmonary venous flow. Pediatric patients present their own challenges. Isolated **diastolic** dysfunction is rare in this group, and there is much less literature available to establish when abnormal **diastolic** properties are present.

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