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Diastolic dysfunction

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Diastolic dysfunction, a syndrome characterized by impaired ventricular filling, is increasingly recognized as an important cause of symptoms and as a prognostic indicator in many patients with congestive heart failure. As many as one-third of patients with congestive heart failure will have preserved left ventricular (LV) systolic function, implicating diastolic dysfunction as the main cause of their symptoms.[1,2] In the 1980s, the emergence of Doppler echocardiography as an important non-invasive method of assessing ventricular diastolic function coincided with the increasing recognition of diastolic heart failure as a true clinical entity. In the 1990s, the field of "diastology" was popularized, defined as the "art and science of characterizing LV relaxation and filling dynamics and integration into clinical practice."

Physiology of diastole

Diastolic function of the heart is a complex sequence of numerous interrelated events, the pathophysiology of which is incompletely understood. The classic approach has been to divide diastole into four distinct phases:

- isovolumic relaxation (period from aortic valve closure to mitral valve opening);
- the rapid filling phase (early diastole);
- the slow filling phase (or diastasis);
- atrial contraction.[3]

A newer approach is to divide the cardiac cycle into three overlapping phases: systolic contraction, relaxation, and diastolic filling.[4-7] Normally, relaxation starts during the second half of contraction and extends into isovolumic relaxation and early rapid filling. Normally, diastolic filling starts with the onset of mitral valve opening and continues until mitral valve closure (Figure 1).

The two major determinants of LV filling are ventricular relaxation and effective chamber compliance.[8] Ventricular relaxation involves the deactivation of contractile elements, beginning during mid-systole and continuing throughout the first third of diastole. It is a complex, energy-dependent process, and is controlled by cellular events which regulate cytosolic calcium ion concentrations. The components of relaxation include inactivation, the load on the ventricle, and the uniformity of relaxation. In disease states, delayed inactivation, diminished load dependence, and increased non-uniformity of relaxation result in impaired relaxation.[4-8] This results in abnormal filling of the left ventricle in early diastole and a compensatory increase in filling with atrial contraction.

The effective chamber compliance refers to the passive properties of the left ventricle during diastole and is energy-independent. During diastole, numerous complex interactions occur affecting effective chamber compliance. These include the ongoing effects of ventricular relaxation, the effect of diastolic 'suction,' passive filling from the left atrium into the left ventricle, the effect of pericardial restraint, the interaction between left and right ventricles, the viscoelastic properties of the left ventricle, and properties of the left atrium, pulmonary veins and mitral valve.[8-11]

The disease processes that result in diastolic dysfunction affect various components that determine LV filling. Myocardial ischemia will delay the energy-dependent deactivation of contractile elements leading to slowed and incomplete ventricular relaxation,[12,13] while myocardial scarring and fibrosis from previous infarction will increase myocardial stiffness and affect the viscoelastic properties of the left ventricle, leading to reduced effective chamber compliance. LV hypertrophy, as a result of systemic hypertension or due to underlying hypertrophic cardiomyopathy, will prolong the action potential, leading to both a delayed and non-uniform relaxation, and the increased myocardial mass

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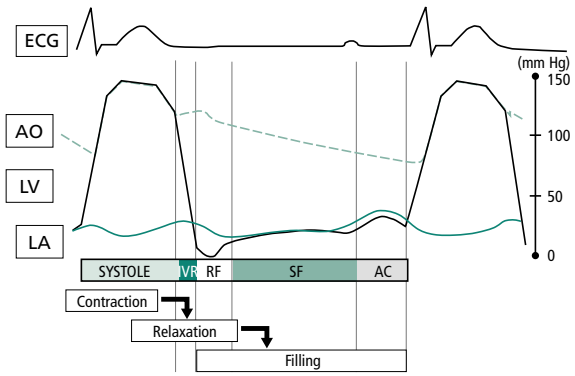
Figure 1: Schematic drawing showing aortic (AO), left ventricular (LV) and left atrial (LA) pressures during the cardiac cycle. The classic 4 phases of diastole are shown; isovolumic relaxation (IVR), rapid fillilng (RF), slow filling (SF) and atrial contraction (AC). In the newer system, the cardiac cycle is divided into contraction, relaxation and filling phases.



and fibrosis will also increase myocardial stiffness and decrease LV compliance. Other disease states cause diastolic dysfunction by similar effects on the components of ventricular relaxation and effective chamber compliance.

Diagnosis

Two definitions of diastolic dysfunction are:

1) impaired capacity of the ventricles to fill at low pressures without a compensatory increase in left atrial pressure;[14]

2) abnormalities of left ventricular filling that would not produce an adequate cardiac output with a mean pulmonary venous pressure of <12 mm Hg.[15]

Clinically, diastolic dysfunction cannot reliably be diagnosed and differentiated from systolic dysfunction on the basis of medical history, physical exam, electrocardiogram, and chest radiograph.

Diastolic dysfunction was initially investigated in the cardiac catheterization laboratory using high fidelity manometer-tipped catheters placed in the left ventricle with direct measurement of filling pressures. Peak negative change in left ventricular pressure over time (dP/dT) and the time constant for relaxation, or tau, are accepted indices of the rate of relaxation, although both have their limitations.[16] The change in volume over the change in pressure, the diastolic pressure-volume curve, has been used to assess changes in effective operating chamber compliance. However, due to the invasive nature, high cost, and limited availability of hemodynamic studies, this remains impractical for widespread use or for serial follow-up examinations.

Diastolic function can be assessed by radionuclide angiogram. Technetium-99m labeled red blood cells are injected into the vascular compartment and once equilibrium is achieved, multigated acquisition (MUGA) is performed. A high-temporal resolution volume curve of the left ventricle is obtained, from which the rate of ventricular filling or peak filling rate (PFR) ,time-to-peak filling rate (TPFR) and the atrial kick percentage (AKP) can be calculated. These parameters are indices of the relaxation properties and compliance of the left ventricle. When there is impaired relaxation, the PFR is reduced, the TPFR is increased, and the AKP is increased. When restrictive physiology is present, the PFR is increased, the TPFR is reduced, and the AKP is decreased. Overall, the need for repeated radiation exposure limits the use of this method for the longitudinal follow-up of patients with diastolic dysfunction.

Doppler echocardiography has become the most widely used and accepted method for the diagnosis and follow-up of patients with diastolic dysfunction. Its reliability, reproducibility, ease of performance, and advances in applications over the past decade make it the ideal tool for the assessment of "diastology."

The basis of the Doppler echocardiographic assessment of diastolic function relies on a careful, integrated approach.[17,19] The mainstay of this approach involves the recording of flow velocities across the mitral valve and within the pulmonary veins to assess filling patterns and estimate left ventricular filling pressures indirectly.[18] Mitral flow velocities are obtained by pulse-wave Doppler echocardiography placing the sample volume located between the tips of the mitral valve leaflet during ventricular diastole. The peak velocity of early rapid filling (E), peak velocity of late filling caused by atrial contraction (A), E/A ratio, the interval from the peak of E velocity to its extrapolation to baseline or the deceleration time (DT), and the interval from aortic valve closure to mitral valve opening or isovolumic relaxation time (IVRT) is measured. As well, the A wave duration (MVa) and the E velocity at onset of A should also be measured. (Figure 2).

Pulmonary venous flow is measured using pulse-wave Doppler echocardiography with the sample volume located

Figure 2: Schematic diagram of a pulsed-wave (PW) Doppler sample volume at the tips of the mitral valve leaflets in the apical 4-chamber view (right) and the corresponding PW Doppler recording (left). AVC (aortic valve closure), MVO (mitral valve opening), IVRT (isovolumic relaxation time), E (early rapid filling), A (atrial contraction), DT (deceleration time), MVa (A wave duration) are shown.

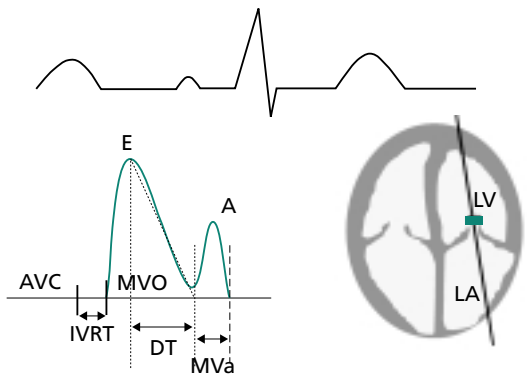
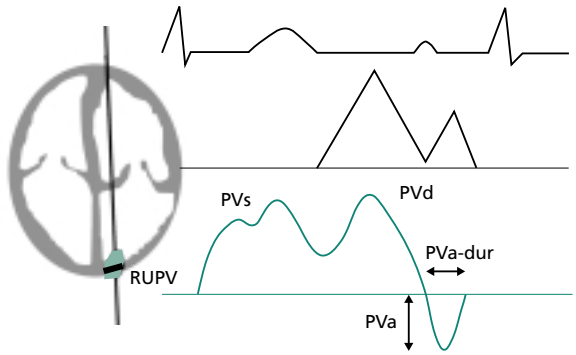


Figure 3: Diagram of a pulsed-wave (PW) Doppler sample volume in the right upper pulmonary vein (RUPV) in the apical 4-chamber view (left), and the corresponding PW Doppler recording (right). The corresponding mitral inflow Doppler recording is shown above. Pulmonary vein systolic (PVs), diastolic (PVd) and atrial reversal (PVa) waves are shown. The duration of pulmonary vein 'a' reversal (Pva-dur) is a useful measurement.



1 to 2 cm into a pulmonary vein, proximal to its insertion into the left atrium. The systolic peak velocity (biphasic flow in 30% of cases) (PVs), diastolic peak velocity (PVd), the S/D ratio, atrial systolic reversal velocity (PVa) and duration (PVa-dur) are measured (Figure 3).

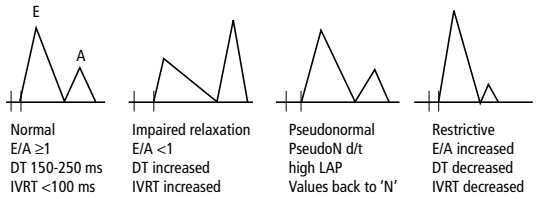
Classification of diastolic filling

Normal

The determinants of LV filling, ventricular relaxation, and effective chamber compliance, change with increasing age. This leads to different diastolic filling patterns for different age groups.[20] In normal young individuals (aged 20s-30s), LV relaxation is rapid, the majority of filling (85-95%) occurring in early diastole and only a small proportion (5-15%) occurring with atrial contraction. This results in mitral inflow parameters of E/A ratio >> 1 (mean 2.2) and relatively short DT (mean 182 msec) and IVRT (mean 71 msec). Pulmonary venous inflow usually shows a slight diastolic predominance (PVd > PVs) with a mean PVa of 0.19 m/sec.[17]

With aging, the rate of LV relaxation decreases with slower and less filling in early diastole and an increased contribution to LV filling by atrial contraction. This leads to a prolongation of the IVRT and DT, a reduction in E velocity, and an increase in A velocity with a subsequent reduction in E/A ratio. Individuals >65 years have the following average parameters: an E/A ratio of 1 or less, a mean DT of 214 msec, and IVRT of 94 msec. As PVd parallels the E velocity, the pulmonary venous flow now shows systolic predominance (PVs > Pvd). As well, the PVa increases slightly, but does not exceed the upper limit of normal (0.35m/sec)[17] (Figures 4 and 5).

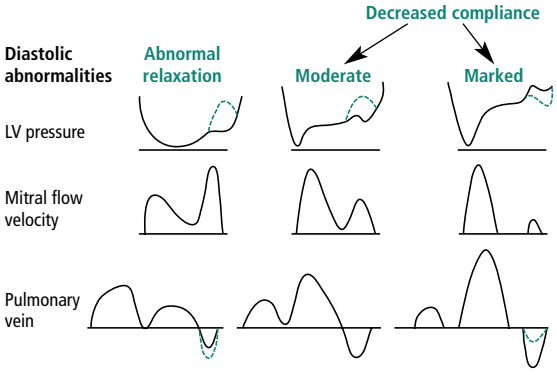
Figure 4: Schematic diagram showing mitral flow velocity patterns in a normal ventricle (first), ventricle with impaired relaxation (second), ventricle with moderate diastolic dysfunction and pseudonormal filling (third) and one with restrictive physiology (fourth). The corresponding changes in mitral inflow parameters are shown below each pattern.



Mild diastolic dysfunction (impaired relaxation)

This likely represents the earliest stage of diastolic dysfunction. There is impaired LV relaxation with initially normal LV filling pressures, leading to decreased early filling and increased filling with atrial contraction. Mitral inflow patterns show an E/A less than 1 and abnormal for age. The IVRT is prolonged (>100 msec), with prolongation of the DT (>200 msec). Pulmonary venous inflow remains normal or shows a systolic predominance (PVs > PVd) with PVa <0.35 m/sec (Figures 4 and 5).When there is impaired relaxation along with an elevation of left ventricular end-diastolic pressure (LVEDP), the mitral inflow parameters are unchanged; however, pulmonary venous flows are affected. Elevated LVEDP (>15 mm Hg) is predicted by

Figure 5: Schematic drawing of the left ventricular pressure tracings (top), mitral inflow velocity (middle) and pulmonary venous Doppler patterns (bottom) in ventricles with abnormal relaxation, moderate and severe left ventricular diastolic dysfunction. The dotted lines represent variations in left ventricular end diastolic pressures and the corresponding changes in Doppler patterns that can occur within each stage.



either a pulmonary venous A wave reversal (PVa) >0.35 m/sec or PVa-dur >Mva.[21]

Moderate diastolic dysfunction (pseudonormal)

As diastolic dysfunction progresses, LV relaxation becomes further impaired and LV stiffness increases. In an attempt to maintain LV filling and cardiac output, the filling pressure, specifically left atrial (LA) pressure, becomes elevated. This increased transmitral pressure gradient leads to increased early filling with the E/A ratio 'normalizing' to a value >1, with shortening of the IVRT and DT back to low normal values. This mitral pattern is similar to the pattern in normal individuals, leading to the term 'pseudonormal.' The differentiation from normal is done on the basis of an abnormal response to the Valsalva maneuver or an abnormal pulmonary venous flow pattern. During the strain phase of the Valsalva maneuver, LV preload is reduced with a reduction in LA pressure. This leads to a reduction in the E velocity and a reversal of the E/A ratio to <1, unmasking the pattern of impaired relaxation. In normal subjects, both E and A velocities will decrease proportionately, with preservation of the E/A ratio.[22] At this stage, pulmonary venous inflow will sometimes show diastolic predominance, with systolic inflow (PVs) blunting (systolic inflow fraction <50% of diastolic fraction) predicting moderately elevated LA pressure (>15 mm Hg).[23] At this stage, LVEDP is usually elevated (unless there is atrial systolic failure or atrial fibrillation), indicated by an increased PVa (>0.35 m/sec) or PVa-dur > MVa (Figures 4 and 5).

Severe diastolic dysfunction (restrictive filling)

As diastolic dysfunction progresses further, LV relaxation continues to be impaired, however, it is masked by rising LV filling pressures and a markedly reduced LV compliance. This mimics the physiology of restrictive cardiomyopathy. The increased LA pressure causes an early mitral valve opening (shortened IVRT) and rapid early filling (increased E velocity). As early rapid filling occurs into a noncompliant LV, there is rapid equalization of LV and LA pressures leading to a shortened DT. Atrial contraction into a noncompliant LV with high diastolic pressure leads to a reduced A velocity. Therefore the E/A ratio is >2, and occasionally >4 to 5. Pulmonary venous inflow shows a marked blunting of systolic inflow (PVs<<PVd) corresponding to the markedly elevated LA pressure and reduced LA compliance (Figures 4 and 5).

Limitations and pitfalls

Despite recent advances in the noninvasive assessment of diastolic dysfunction, a number of technical and physiologic factors still limit the integrated approach to the Doppler echocardiographic evaluation of diastolic function. In order to obtain useful and reproducible measurements, a careful standardized approach is important, attention being given to sample volume size and location, filter settings, and signal quality. With a consistent and structured approach, good quality mitral inflow and pulmonary venous flows can be reliably obtained in the majority of patients.

Physiologic variables affecting the Doppler evaluation of diastolic function include abnormalities of preload and afterload, LV systolic function, and the presence of atrial arrhythmias, mitral valve, and pericardial diseases. These must be considered in the interpretation of parameters of LV diastolic function. The presence of tachycardia or a prolonged PR interval will result in fusion of E and A velocities, leading to higher A velocities. If the E velocity at onset of the A is higher than 20 cm/sec, both the A velocity and E/A ratio will be affected.[24] Finally, age will affect the parameters used to assess LV diastolic function and needs to be accounted for in the assessment and reporting of diastolic dysfunction in individuals at the extremes of age.

Newer Doppler echocardiographic modalities

Due to the limitations of standard pulsed Doppler indices of mitral inflow and pulmonary venous flow, with significant overlap between normal and abnormal values, there remain many instances when the information obtained is either inconclusive or contradictory. This has spurred the development of newer modalities to assess diastolic function, including color M-mode Doppler echocardiography and tissue Doppler echocardiography.

Figure 6: Schematic drawing of two newer modalities used to assess diastolic function. On the left is an M-mode cursor aligned along the mitral inflow color region parallel to flow and the corresponding color-M mode recording. Vp is the slope of the leading edge of the color wave front of the initial wave. On the right is a pulsed wave Doppler sample volume placed over the basal-lateral segment of the left ventricular myocardium in the apical-4 chamber view and the corresponding spectral display. This consists of a systolic signal directed towards the apex (Sm), an early diastolic signal directed away from the apex (Em) and a late diastolic signal directed away from the apex with atrial contraction (Am).

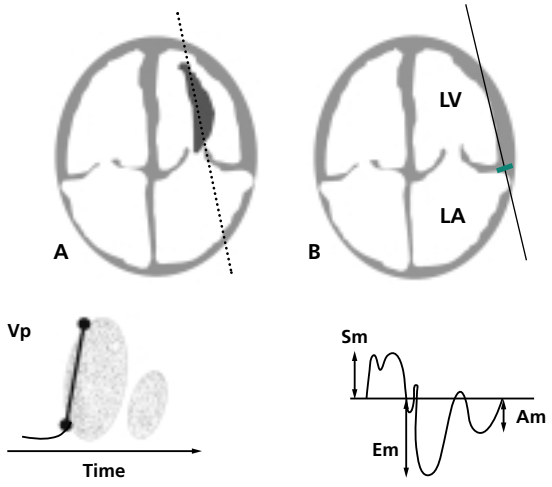
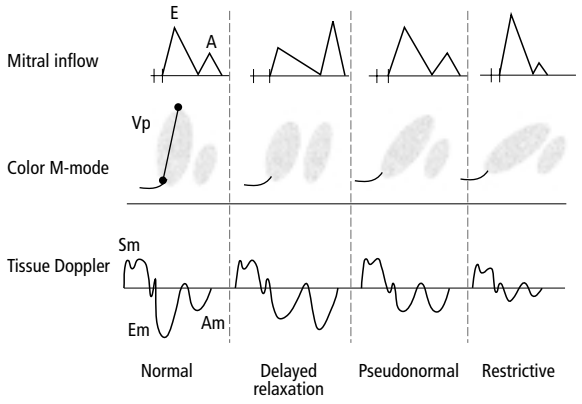


Figure 7: Schematic drawing of correspoinding mitral inflow velocity patterns (top), color M-mode recordings (middle) and tissue Doppler recordings (bottom) in situations of normal diastolic function (left), delayed relaxation (second from left), moderate diastolic dysfunction with pseudonormal filling (third from left) and restrictive physiology (right).



Color M-mode Doppler analyzes the phase shifts of a series of paired ultrasound pulses and obtains the velocities along a scanline. The velocities are color encoded and displayed, placing time along the x-axis (increasing to the right) and depth from the transducer along the y-axis (increasing away from the transducer). This provides a spatio-temporal distribution of these velocities across a vertical line. Thus a color M-mode recording with the M-mode cursor placed at the center of the mitral inflow region (parallel to flow) in the apical 4-chamber view gives a representation of the velocities of blood at different levels from the mitral orifice to the LV apex. The typical pattern in sinus rhythm consists of two waves: the first wave propagates from the mitral orifice to the LV apex during early filling and the second wave follows with atrial contraction. The velocity at which flow in early diastole propagates within the LV (Vp) is given by the slope of the leading edge of the color wavefront of the initial wave (Figure 6). Other color M-mode parameters are being investigated.[25,26] Preliminary clinical studies suggest that there is a strong negative correlation between color M-mode Vp and tau, the time constant of relaxation (measured invasively). Thus, as diastolic function worsens the velocity of propagation (Vp) decreases (Figure 7), a correlation that is preload independent.[26, 27]

Tissue Doppler echocardiography is a new application which provides accurate quantitative information about myocardial tissue velocities during the cardiac cycle. Moving myocardium reflects low velocity, very high amplitude Doppler signals, in contrast to red blood cells which reflect high velocity, low amplitude signals. Thus, in order to display these tissue velocities, the high filter is bypassed (keeping the low velocity signals) and a lower gain amplification is used (eliminating the weaker intensity, low amplitude blood flow signals). Once these adjustments are made, various methods are used to obtain tissue Doppler velocities. One approach measures the axial motion of the LV by placing the pulsed wave sample volume on the basal-lateral segment near the mitral annulus from the apical 4-chamber view.[28,29] As the position of the apex is relatively fixed in this window and the motion of the base is close to parallel with the Doppler cursor, the tissue velocities obtained are representative of the motion of the basal myocardium during the cardiac cycle. A typical spectral display consists of three distinct velocity signals; a signal directed towards the LV apex during systole (Sm), and two signals directed away from the apex during early systole (Em) and atrial contraction (Am) (Figure 6). In clinical studies, abnormal LV relaxation, indicated by a prolonged tau (measured invasively), was associated with a low Em (30,31) (Figure 7). This inverse correlation was independent of preload.

Both these newer techniques have potential advantages over standard Doppler techniques for assessment of diastolic function. They are both independent of preload. As well, the patterns of normal and abnormal filling have far less overlap than mitral inflow and pulmonary venous flow (pseudonormal filling), a significant limitation of standard pulsed Doppler techniques. A color M-mode velocity of propagation (Vp) less than 45 cm/sec and a tissue Doppler early diastolic velocity signal (Em) less than 8 cm/sec appears to correlate with the presence of diastolic dysfunction.[32] These and other promising applications, such as color kinesis and automated border detection, are still evolving. Further studies to refine and standardize the methods, protocols, and measurements, to establish ranges of normal values and to identify and overcome potential limitations are needed before incorporation into routine clinical practice.[32]

Clinical importance and prognosis

Many common cardiovascular diseases are characterized by LV diastolic dysfunction with or without systolic dysfunction. These include myocardial ischemia and infarction,[33,34] left ventricular hypertrophy due to hypertension,[35,36] aortic stenosis[37] or hypertrophic cardiomyopathy,[38] diabetes mellitus,[39] dilated[40] and restrictive cardiomyopathy,[41] constrictive pericarditis,[42] heart transplant recipients,[43] and valvular diseases.

Congestive heart failure due to diastolic dysfunction, with preserved systolic function, is now a well recognized clinical entity. The incidence appears to rise significantly with age.[44] The diagnosis of diastolic heart failure has important implications on the prognosis and management of these patients. The prognosis of patients with congestive heart failure due to diastolic dysfunction is generally better than patients with systolic dysfunction. The annual mortality is approximately 8% in patients with diastolic heart failure compared to 19 % with systolic heart failure.[45,46] In certain disease states, abnormalities of diastolic function have important prognostic implications, with worsening diastolic function signifying an adverse prognosis.

The severity of diastolic dysfunction has been shown to be an important predictor of survival in patients with cardiac amyloidosis. The combination of a shortened deceleration time and an increased E/A ratio, indicative of restrictive phys-

iology, were strong predictors of cardiac death compared to those with relatively normal diastolic filling.[47]

One of the first hemodynamic changes seen with myocardial ischemia or infarction is that of diastolic dysfunction. In patients presenting with acute myocardial infarction, a restrictive filling pattern at presentation predicted the presence or subsequent development of congestive heart failure, perhaps identifying the patients at increased risk who may benefit from early intervention.[48,49]

Patients with dilated cardiomyopathy (ischemic and non-ischemic) and LV systolic dysfunction commonly have abnormalities of LV diastolic filling. There appears to be a progression, from mild diastolic dysfunction in patients with early stage congestive heart failure, to a restrictive filling pattern in the symptomatic decompensated stage of dilated cardiomyopathy. A short deceleration time (<130 msec) has been shown to be strongly predictive of an increased mortality in patients with dilated cardiomyopathy.[50] As well, studies have shown that if the restrictive filling pattern is reversible (prolongation of DT, reduction in E/A ratio) with optimization of heart failure therapy, these patients have a more favorable prognosis.[51,52]

Treatment

The treatment of patients with diastolic dysfunction remains problematic. Therapy should focus on the management of the underlying disease process, in particular, hypertension and coronary artery disease. However, control of symptoms and relief of precipitating factors are also very important.

Medical therapy for myocardial ischemia and coronary revascularization have been shown to improve diastolic dysfunction in patients with coronary artery disease.[53-55] Similarly diastolic dysfunction appears to normalize late after aortic valve replacement for aortic stenosis.[56] Treatment of underlying systemic hypertension is important in regression of left ventricular hypertrophy and improvement in diastolic dysfunction. However, studies showing that this improvement leads to improved symptoms and prognosis in these patients are lacking. In patients with hypertrophic cardiomyopathy, measures taken to relieve left ventricular outflow tract obstruction (medical,[57] dual-chamber pacing, non-surgical septal reduction,[58] septal myectomy), can lead to regression of hypertrophy and improvement in diastolic dysfunction. Other management strategies for disease-specific cases of symptomatic diastolic dysfunction include surgical procedures to relieve pericardial constriction in constrictive pericarditis and therapy to limit cardiac infiltration in certain causes of restrictive cardiomyopathy.

The mainstay of pharmacologic therapy for patients with diastolic heart failure includes diuretics, nitrates, calcium channel blockers (CCBs), beta-blockers (BBs) and angiotensin-converting enzyme inhibitors (ACEI). Diuretics are useful in relieving symptoms of pulmonary congestion. However, as these patients rely on higher filling pressures to maintain cardiac output, overdiuresis can reduce stroke volume and cardiac output, leading to fatigue, postural hypotension, and renal failure. Nitrates may be useful in enhancing relaxation by reducing right ventricular pressure and volume, leading to reduced pericardial restraint and improved LV filling.[59] As well, animal models have shown an improvement in LV relaxation with endogenous nitric oxide.[60] The negative inotropic and chronotropic properties of the CCBs make them likely to be effective in treating diastolic dysfunction. Studies have yielded conflicting results with many showing improved relaxation,[57,61] but others showing no change in the rate of relaxation.[62] BBs have no direct effects on myocardial relaxation, however , they may be effective by slowing heart rate and reducing myocardial demand and ischemia. ACEI have not been as well studied, but may hold some promise.[63] They may be particularly effective in the settings of hypertension with left ventricular hypertrophy and in the situation of concomitant systolic dysfunction.[64]

Other general therapy includes simple dietary measures such as salt and fluid restriction and heart rate control in situations of tachycardia. The maintenance of sinus rhythm and atrioventricular synchrony is very important, atrial fibrillation being poorly tolerated in these patients and a common precipitating cause of diastolic heart failure.

Most of these therapeutic recommendations for treating diastolic heart failure are empirical and based on the results of small clinical studies with surrogate endpoints. There are, as yet, no randomized, controlled clinical trials evaluating the effects of these treatments on patient outcomes and prognosis.

Conclusion

Diastolic dysfunction remains a common problem, and with the routine use of echo-Doppler can be reliably assessed in up to 85% of patients. As the newer techniques to assess diastolic function, including tissue Doppler echocardiography and color M-mode, are refined and developed, the assessment of diastolic function can be made in virtually all our patients. Despite these advancements in the diagnosis of diastolic dysfunction, there remain many unresolved issues. These include the need for an increased physician awareness of the magnitude of the problem, a better understanding of the underlying pathophysiology, and most importantly, the need for long term outcome studies on the various therapies for diastolic dysfunction and diastolic heart failure.

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Abstracts of Interest

Propagation velocity of left ventricular filling flow measured by color M-mode Doppler predicts prognosis of patients with left ventricular systolic dysfunction

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To determine whether the Doppler diastolic indexes predict prognosis of the patients with left ventricular systolic dysfunction, we studied 41 patients (old myocardial infarction, n=25, and dilated cardiomyopathy, n=16). Between 1992-1995, pulsed-Doppler and color M-mode Doppler echocardiography were performed in these patients to measure the early (E) and late (A) diastolic peak velocities of transmitral flow, E/A ratio, deceleration time (DT) of the E wave, isovolumic relaxation time (IRT), propagation velocity of left ventricular rapid filling flow (PVE) and PVE/E ratio. After that, their clinical course was followed until March, 1999. During a mean follow-up period of 47±4 months, 4 of 41 patients (10%) died of cardiac events and 16 (39%) suffered from cardiovascular events (hospitalization due to heart failure, ventricular tachycardia or cerebral infarction). Among the Doppler diastolic indexes PVE/E was the strongest predictor of the cardiovascular events by univariate Cox model analysis (chi-square 4.12, p=0.04). When the patients were divided into 21 patients with PVE/E <0.60 (Group 1) and 20 patients with PVE/E ≥0.60 (Group 2), the cumulative event-free ratio determined by the Kaplan-Meier method was significantly greater in Group 2 than in Group 1 (p=0.005). No cardiac death was observed in Group 2. In conclusion, PVE/E determined using color M-mode Doppler echocardiography is a powerful predictor of cardiac events and prognosis of the patients with left ventricular systolic dysfunction.

Left ventricular wall thickness and mass do not explain normal variation in left ventricular diastolic function

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Objectives: To evaluate the relationship between LV mass and diastolic parameters in the normal population.
Background: Left ventricular (LV) diastolic abnormalities are associated with hypertension and LV hypertrophy, presumably because of decreased LV compliance. However, it is not known if diastolic abnormalities are related to LV mass.
Methods: We measured blood pressure and used M-mode echocardiography to estimate LV mass index (LVMI) by the Penn convention in 194 population volunteers, from whom we excluded 23 subjects with known cardiovascular disease. To evaluate diastolic function, the E/A ratio, DT, IVRT, S/D ratio, and PVA-MVA were obtained from mitral inflow and pulmonary venous Doppler recordings.
Results: Although LVMI was significantly (P <0.0001) greater in men (81.3 g/m^2, IQR: 67-94) than women (59.7 g/m^2, IQR: 49-74), no gender differences were observed in diastolic indices. There was a significant decline in LV diastolic function with increasing age and diastolic variables correlated significantly with both blood pressure and heart rate. However, no diastolic parameters correlated with LVMI in either univariate or multiple regression analyses that adjusted LVMI for variations in heart rate and blood pressure. After adjustment for blood pressure, heart rate and sex there remained a highly significant correlation between E/A ratio and age (r = -0.59. P<0.0001).
Conclusion: In a healthy population, LV mass does not correlate with LV diastolic function and does not explain the decline in LV diastolic function with age. These results suggest that intrinsic qualities rather than the quantity of myocardium determine LV diastolic function.

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