A cardiac cycle consists of systolic (contraction) and diastolic (relaxation and filling) phases that are linked closely together for optimal function of the heart. Normal diastolic function allows adequate filling of the heart without an excessive increase in diastolic filling pressure both in the resting state and with stress or exertion. The diastolic phase is remarkably well designed to ensure that the ventricle is optimally filled for a given clinical condition. Basically, at the end of systole, left ventricular (LV) relaxation begins as an initial diastolic process, and LV pressure falls rapidly as the LV expands. This relaxation phase is accompanied by active movement of the mitral annulus away from the apex. The velocity of LV dilatation and mitral annular movement during early diastole correlates well with how fast the LV fills and relaxes, respectively. Myocardial relaxation continues during early diastole to reach the minimal LV diastolic pressure, which helps with “sucking” or “pulling” the blood actively into the LV (Figure 1, online-only Data Supplement Video 1A). The minimal LV diastolic pressure or completion of relaxation normally occurs by 3.5 times the value of tau—the time constant of relaxation (normal <45 ms)—after the mitral opening. LV pressure then rises to be equilibrated with left atrial (LA) pressure, at which time the early diastolic filling decelerates to close the mitral valve until the time of atrial contraction when LA pressure increases to initiate the late filling to complete diastole (Figure 1, online-only Data Supplement Video 1B).

In the healthy young heart, early diastole is responsible for the majority of ventricular filling, providing a good diastolic reserve. As myocardial relaxation becomes less active with aging or abnormally delayed due to a disease process, the rate of LV pressure decline during the early diastole is reduced, and it takes a longer time to reach the minimal LV diastolic pressure. The rate of LV dilatation during early diastole is reduced, and both elongation of the LV and mitral annular motion are reduced (Figure 1), resulting in reduced diastolic filling and a longer time to reach equilibration of LV-LA pressure. Under this circumstance, atrial contraction is responsible for a substantial proportion of diastolic filling. As long as all the necessary filling can be completed through this mechanism with intact atrial contraction and an adequate diastolic filling period, the mean LA pressure remains normal, although it may be increased at the end of diastole if LA compliance is decreased.

A major problem with delayed relaxation, however, is a reduced diastolic reserve. Healthy individuals with normal relaxation are able to increase the rate of myocardial relaxation when there is a need for increased diastolic filling. Faster relaxation allows the achievement of a lower minimal LV diastolic pressure at a shorter time interval than in the resting state. Hence, increased LV filling can occur even with a shortened diastolic filling time. When myocardial relaxation is reduced in the resting state, it cannot be increased as much as necessary to meet the demands of exertion or stress. In this situation with abnormal myocardial relaxation, a reduced diastolic filling period and a lack of atrial contraction compromise LV filling substantially, causing the increase in LA and LV diastolic pressures (hence, decreased diastolic reserve).

As LA pressure increases, the early diastolic filling becomes more dominant despite the impaired myocardial relaxation. Early filling is initiated by the increased LA pressure (by “pushing” as illustrated in Figure 1), and myocardial relaxation actually starts after the opening of the mitral valve. After initial filling, which increases LV diastolic pressure, delayed myocardial relaxation may lower LV pressure during mid-diastole causing the mid-diastolic filling (L wave) followed by late filling with atrial contraction. Although the L wave can occur in healthy, well-conditioned individuals with bradycardia, its peak velocity usually is <20 cm/s in that setting. As diastolic function worsens, LA pressure is elevated and myocardial relaxation is impaired at rest, clinically manifesting as heart failure. In this stage, most of the diastolic filling that occurs during early diastole and LA contraction may not be able to contribute substantially to LV filling because of the increased LV diastolic pressure. In these patients, LA contraction pushes blood back into the pulmonary veins, especially if pulmonary venous diastolic forward flow is already completed at the time of atrial contraction.

Various patterns of diastolic dysfunction can occur with normal as well as abnormal ejection fractions. It has been...
well established that diastolic dysfunction and filling pressure can be assessed by 2D, Doppler, and tissue Doppler (TD) echocardiography. The joint Diastology Working Group from the American Society of Echocardiography and European Association of Echocardiography has published a guideline for the echocardiographic assessment of diastolic function in various clinical conditions. Subsequent sections in this article first will review the established clinical applications of diastolic function assessment and then describe innovative and novel indices of diastolic function that are under investigation for new clinical applications.

Established Applications of Diastolic Function Assessment

Grading of Diastolic Dysfunction

Because one of the earliest abnormalities in diastolic function is myocardial relaxation, we need a reliable parameter to assess myocardial relaxation. The velocity of mitral annular movement during early diastole, designated as e' or E' velocity measured by TD echocardiography, correlates well with invasive measures of the time constant of myocardial relaxation τ." although it is not entirely governed by relaxation. In healthy young individuals, septal e' is >10 cm/s and lateral e' >15 cm/s at rest. These increase with exercise and reflect the ability to achieve a lower minimal LV diastolic pressure to increase early diastolic filling. In individuals with diastolic dysfunction, relaxation or e' is reduced and remains so in all stages of diastolic dysfunction (Figures 1 and 3). Therefore, normal e' velocity is unusual in patients with diastolic dysfunction related to a myocardial abnormality or disease, which is a main reason that the joint Diastology Working Group recommends that an evaluation of diastolic function begins with e' in patients with normal LV ejection fraction.

The next essential parameter for diastolic function assessment is mitral inflow velocities. Normally, the early diastolic mitral velocity (E) is higher than the late velocity (A) with atrial contraction, so that the E/A ratio is >1. The E velocity is determined mainly by myocardial relaxation and LA pressure. Early stage, or grade 1, diastolic dysfunction is characterized by a lower E than A velocity as well as by a prolonged deceleration time (DT) >240 ms. Because myocardial relaxation is reduced with aging, this diastolic filling pattern is most common in elderly individuals, and e' also is reduced. As long as necessary filling can be completed during a given diastolic period, there are no clinical symptoms, but diastolic reserve is reduced, and tachycardia or atrial fibrillation compromise diastolic filling greatly. It should be emphasized that filling pressure usually (but not always especially in the setting of hypertrophy) is normal in patients with grade 1 diastolic dysfunction and is the most desirable diastolic filling pattern in patients with well-treated heart failure as long as underlying myocardial pathology or relaxation abnormality persists (Figure 3B). The most advanced stage, or grade 3, diastolic dysfunction is characterized by an increased E with short DT (usually <160 ms) and decreased A velocity (hence, an E/A ratio ≥2) as well as a reduced e'. Because diastolic filling is restricted to early diastole, this stage is also called the restrictive filling pattern. Between the early diastolic dysfunction predominated by delayed myocardial relaxation and the late or severe dysfunction predominated by increased filling pressure as well as delayed relaxation, there is a stage of moderate, or grade 2, diastolic dysfunction where the mitral inflow velocity pattern may look similar to the normal pattern (so called pseudonormalized), although the duration of antegrade atrial flow usually is shorter than that of pulmonary atrial flow reversal flow, and e’ is reduced.
possible that the LA will not be grossly enlarged in patients with an early stage of diastolic dysfunction, but almost all patients with increased filling pressure have increased LA size. However, the converse is not always true. Individuals with good conditioning and increased stroke volume have increased LA size but normal e’ velocity and myocardial relaxation (Figure 3A). Patients with compensated heart failure also can have increased LA size without increased filling pressure.

**Assessment of Diastolic Filling Pressure**

The isovolumic relaxation time (IVRT) interval is a good screening parameter for LA pressure, regardless of underlying LV ejection fraction. If IVRT is prolonged (>100 ms), LA pressure is not elevated because the delay in mitral valve opening is related to lower pressure crossover between LV and LA in the setting of delayed relaxation. If LA pressure is elevated even with abnormal myocardial relaxation, the mitral valve opens at a high pressure, and IVRT gets shortened. Therefore, it is safe to conclude that LA pressure is elevated if the IVRT is short (<60 ms) in the presence of cardiac disease. However, it is difficult to estimate LA pressure when IVRT is relatively normal.

If the E velocity is substantially lower than the A velocity so that the E/A ratio is <0.5 along with a prolonged DT (>240 ms), the mean LV diastolic filling pressure usually is not elevated (Figure 3B). One notable exception is hypertrophic cardiomyopathy in which the mean LA pressure can still be elevated with a filling pattern in which the E/A ratio is <0.5. The other side of the diastolic spectrum is restrictive filling, which can be easily recognized by an increased E/A ratio (>2) along with a very short DT (<160 ms). In this situation, the LA is enlarged, and e’ is reduced (<5 cm/s).

Estimation of filling pressure using mitral inflow velocities is relatively reliable in patients with reduced LV ejection fraction because myocardial relaxation is reduced in almost all of these patients. However, it is more challenging in patients with normal or preserved ejection fraction because the status of myocardial relaxation must be clarified before a reliable assessment of diastolic function and filling pressure can be undertaken. In patients with diastolic dysfunction and increased filling pressure, mitral E velocity increases, and e’ is almost always reduced; hence, the E/e’ ratio increases. Several studies have shown that the pulmonary capillary wedge pressure usually is >20 mm Hg when E/e’ is >15 (e’ from the medial annulus) or >12 (e’ from lateral annuli). However, E/e’ is rather specific, but less sensitive for increased filling pressure. Many patients with increased filling pressure have an E/e’ lower than those values, especially when ejection fraction is preserved (Figure 3C). If E/e’ is <8, LV filling pressure or pulmonary capillary wedge pressure usually is not elevated. When E/e’ is between 8 and 15, other parameters and maneuvers are necessary to estimate filling pressures. The Joint Diastology Working Group recommends using an average value of medial and lateral e’ velocities, especially when there is a regional wall motion abnormality involving the septal basal or lateral basal segment.
The Valsalva maneuver is a technique to assess LV filling pressure when there is uncertainty after using 2D and Doppler echocardiographic parameters in the resting state. However, it is often difficult to perform an adequate Valsalva maneuver, and its use has become less frequently needed after mitral annular velocities are considered. Mullens and his associates reported that E/e' may not be reliable in predicting LV filling pressures in decompensated patients with advanced systolic heart failure. It should be noted, however, that E velocity also depends on stroke volume and may not correlate linearly with increased filling pressure. Additionally, E/e' may not work well in patients with severe mitral regurgitation, intraventricular conduction delay, or pacemaker. A more recent study from 2 medical centers (1 from United States and 1 from Norway) demonstrated that a comprehensive Doppler and tissue Doppler echocardiography were able to estimate reliably pulmonary capillary wedge pressure, pulmonary artery systolic pressure, and right atrial pressure when measured simultaneously with right heart catheterization in patients with decompensated systolic heart failure. Figure 3B demonstrates baseline and posttreatment mitral inflow and annular velocities in a patient with diastolic heart failure who improved dramatically with medical therapy. It is our hope and recommendation that echocardiographic assessment of diastolic filling pressure can be used as “noninvasive Swan-Ganz catheter.”

**Diastolic Stress Test**

Many patients present with exertional dyspnea but have normal LV filling pressures at rest. In these patients, it is important to evaluate filling pressure with exercise. Exercise can be performed using a supine bicycle or treadmill protocol. Because most patients have limited functional capacity, the workload starts at 25 W and increases in increments of 25 W every 3 minutes. We need to record mitral inflow by pulsed Doppler echocardiography at the level of the mitral tips, mitral annular velocities by spectral Doppler echocardiography, and tricuspid regurgitation jet by continuous-wave
Doppler at baseline and after the termination of exercise. Diastolic function parameters can be obtained soon after the assessment of regional wall motion abnormalities, especially when an exercise echocardiogram is performed for the evaluation of dyspnea.

In patients with diastolic heart failure, LA pressure is increased, leading to an increase in mitral E velocity, whereas annular e' velocity remains reduced (Figure 4) given the limited preload effect on e'.9 Moreover, an increase in the pulmonary artery systolic pressure can be detected by the increase in peak velocity of the tricuspid regurgitation jet. On the other hand, in the absence of cardiac disease, e' increases to a similar extent to the increase in mitral E velocity, and the normal E/e' ratio essentially is unchanged with exercise.

Ha et al20 were the first to introduce the concept of the diastolic stress test. Subsequently, exercise E/e' ratio was validated against invasive measurements.21 Importantly, exercise septal E/e' ratio was an important determinant of exercise capacity, and its decline with age was noted in a large series of patients referred for exercise echocardiography.22 Furthermore, a recent study showed the incremental prognostic value of exercise E/e' ratio over clinical variables and exercise wall motion score index.23 Collectively, there is growing evidence that the diastolic stress test can provide important diagnostic findings that can be helpful in the management of patients presenting with dyspnea of an unclear etiology. Because dobutamine is a vasodilator as well as an inotrope, the hemodynamic response to dobutamine is very different from that of exercise. It is unusual for a diastolic filling pattern to improve with exercise, but it is not uncommon with dobutamine. However, diastolic filling that becomes worse with dobutamine is a very poor prognostic sign.24

**Diastolic Function in Atrial Fibrillation and Constriction**

Atrial fibrillation is a challenging clinical situation for non-invasive as well as for invasive hemodynamic assessment. However, it has been shown that a short DT (<130 ms) is associated with a poor prognosis, presumably because of
increased filling pressure and advanced heart failure. There are few studies showing that E/e' might be used to estimate LV filling pressure in atrial fibrillation.

Constrictive pericarditis is a unique, potentially curable, and currently underdiagnosed condition in patients presenting with heart failure and normal ejection fraction, which can be readily identified by diastolic function assessment. Combined parameters from mitral inflow, mitral annular velocities, and hepatic vein velocities have made the diagnosis of constriction and its differentiation from myocardial disease much easier than ever before (Figure 5). Constrictive pericarditis must be considered if a patient with heart failure demonstrates normal or increased mitral medial e' (≥8 cm/s) and restrictive mitral inflow velocity with or even without respiratory variation.

**New Diastolic Indices and Their Clinical Applications**

A number of novel indices of regional and global LV diastolic function were developed in recent years. Some are based on TD imaging (TDI), whereas others are obtained using speckle tracking echocardiography (STE). TDI measures velocities of myocardial tissue using the Doppler principle. Hence, it highly depends on minimal angulation (<15°) between the ultrasound beam and the plane of motion while having the advantage of a high temporal resolution. To achieve its high temporal resolution, it is essential to have a high frame rate of >100/s, which necessitates imaging of individual walls. Signals derived by color TDI are processed off line and can be displayed either as color 2D images or reconstructed time versus distance or deformation (ie, strain) curves.

STE is based on tracking myocardial “speckles” from frame to frame in grayscale images. Speckles are very small structures in the image that can be recognized after filtering out noise. STE can be used to determine myocardial velocity and strain. The technique does not have the limitations of angle dependency as TDI and is obtained from images acquired at a frame rate of 50 to 80/s. Velocity vector imaging is based on the same concept, and deformation measurements by velocity vector imaging have been validated against sonomicrometry.

Using these techniques, it is possible to measure displacement (cm), velocity (cm/s), strain (a dimensionless parameter expressed in %), and strain rate (SR) (s^-1). SR is the rate of change in length calculated as the difference between 2 velocities normalized to the distance (d) between them: (V_a – V_b)/d, where V_a – V_b is the instantaneous velocity difference between points a and b. Strain is the percent change in length during a given time period. It is obtained by integrating the SR over time or by the following equation: (L – L_o)/L_o, where L is the final length, and L_o is the original length. It is possible to measure strain by STE in the longitudinal, circumferential, transverse, and radial directions.

**Assessment of Regional Diastolic Function**

Assessment of regional diastolic as well as systolic dysfunction in coronary artery disease is an old concept but is feasible now with TDI and strain imaging. Experimental studies have shown a decrease and delay in myocardial velocities in the setting of acute coronary occlusion, and subsequent clinical studies have shown that a delay in expansion or persistent compression in early diastole can be used to diagnose coronary artery disease with good accuracy. Likewise, diastolic deformation measurements have been applied to identify viable myocardium. Experimental studies have shown that longitudinal and radial early diastolic SR with dobutamine reflect the cellularity/collagen mix in a given segment and relate well to interstitial fibrosis. There are also clinical studies that support the use of segmental early LV filling period (SRF) for identifying myocardial viability.

When anteroapical segments in patients with myocardial...
infarction were compared with those with apical ballooning syndrome, the early diastolic SR and post-systolic shortening were greater in patients with apical ballooning syndrome despite a larger area of akinetic walls, demonstrating a systolic and diastolic functional paradox. Another exciting application of diastolic function assessment by STE is to identify ischemic area by detecting delayed relaxation. Ishii and his associates showed that myocardial relaxation is delayed for a substantial amount of time after transient myocardial ischemia (or wall motion abnormality) resolves, and the delay in relaxation can be readily detected by diastolic strain display (Figure 6). This technique appears to be promising and ideal for evaluation of acute chest pain or stress-induced myocardial ischemia if the technique proves to be feasible in most patients.

Assessment of LV Global Diastolic Function

In most patients, it is possible to obtain reasonable estimates of LV diastolic function using the established Doppler echocardiographic methods. However, there are a number of clinical settings that pose challenges for these methods. These include normal subjects and patients with mitral valve dis-

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\( E \) indicates early diastolic velocity; \( e' \), medial mitral annulus early diastolic velocity; EDP, end-diastolic pressure; EF, ejection fraction; IVR, isovolumic relaxation; LA, left atrium; \( T_{e^{-}}-E \), time interval from the onset of \( e' \) to that of \( E \) velocity.
ease, constrictive pericarditis, left bundle branch block, and heavy annular calcification. Accordingly, additional indices can be of value in these settings (Table).

**Time Intervals From Pulsed Doppler Echocardiographic Recordings of the Mitral Annulus**

With myocardial dysfunction, LV long-axis expansion and relaxation are delayed, and the delay in e’ velocity detects this abnormality. In heart failure and coronary artery stenosis models, e’ was reduced and delayed such that it occurred after onset of mitral inflow (Figure 7).49,50 This finding is in contrast to normal ventricles when e’ can precede mitral E velocity. The delay in e’ was significantly related to the time constant of LV relaxation and LV minimal pressure.49,50 Furthermore, it is possible to estimate LV filling pressures when $T_{e'-E}$ (time interval from the onset of e’ to that of E velocity) is combined with IVRT. This method was evaluated in patients with mitral regurgitation and mitral stenosis.51 The ratio of IVRT/$T_{e'-E}$ was inversely related to mean wedge pressure (and LA pressure) in this setting and was accurate in identifying patients with high filling pressures. The concept was evaluated in patients with mitral disease and atrial fibrillation, and its initial results appear promising.51

The major limitation to this method is the need to measure 3 time intervals from different cardiac cycles. Accordingly, the recent report on the higher accuracy of a single-cycle E/e’ ratio in predicting mean wedge pressure in patients with atrial fibrillation using a dual Doppler echocardiographic probe40 opens the door for a more practical approach to acquiring cardiac timing intervals.

**Myocardial Deformation Measurements**

Earlier studies reported that segmental early diastolic strain and SR were lower in patients with slow LV relaxation46 and in patients with hypertrophic cardiomyopathy with increased LV end-diastolic pressure.52 However, there can be problems in extrapolating global diastolic function from segmental performance in patients with heterogeneous LV function. Accordingly, approaches to obtain global parameters41,42 were developed using SR during the IVRT (SR$_{IVR}$) and during SR$_{e}$. Both SR measurements are not affected by mitral valve disease or annular calcification, which can alter mitral annulus velocities. Furthermore, deformation measurements take into account resting length, which is not the case for velocity measurements. Finally, SR$_{IVR}$ occurs during the isovolumic relaxation period when the mitral valve is closed; therefore, it is not affected by the transmitral pressure gradient. These theoretical advantages were tested in an animal model where LV relaxation was altered using dobutamine and esmolol and loading conditions were manipulated.

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**Figure 8.** Examples of LV twist and its time derivative from 3 clinical situations (control, DHF, and SHF). Shown from left to right, top to bottom are twist curves from a subject in the control group (twist = 17°) and a patient with diastolic dysfunction and normal EF (twist = 16°); reduced twist (5°) from a patient with depressed EF; and the time derivatives of LV twist from a normal subject (untwisting rate = -90°/s), a patient with diastolic dysfunction and normal EF (untwisting rate = -90°/s), and a patient with systolic dysfunction (untwisting rate = -50°/s). Another tracing at the bottom of each image is a simultaneous ECG recording. DHF indicates diastolic heart failure; EF, ejection fraction; SHF, systolic heart failure. Other abbreviation as in Figure 1. Reprinted from Wang et al60 with permission from Lippincott Williams & Wilkins. Copyright © 2007 from the American Heart Association.
using inferior vena caval occlusion. SR_IVR had good correlations with the time constant of LV relaxation and −dP/dt and was not affected by changes in preload. SR_e had similar hemodynamic determinants as mitral annulus e'. The ratio of mitral E velocity to SR IVR (ratio units in cm because E is in cm/s and SR IVR is in s⁻¹) was used as an index of mean wedge pressure and had a good accuracy in identifying patients with increased filling pressures. It was particularly useful in patients with normal ejection fraction and regional dysfunction and when E/e' ratio was in the indeterminate range. Similar to segmental SR_e, global SR_e had significant inverse correlations with mean wedge pressure and the time constant of LV relaxation but with wider scatter that limits its clinical utility. There are a number of limitations to these measurements, including the need for high-quality signals, adequate myocardial visualization in the apical views, experience in acquisition and analysis, and longer time to obtain and measure strain and SR versus the online measurement of velocities, and the lower frame rate for STE can lead to underestimation of SR, although the latter limitation would not invalidate the clinical application.

Recently, the prognostic power of these novel indices was examined in 371 patients with acute ST-elevated myocardial infarction. Global SR IVR by STE provided incremental information over baseline clinical, angiographic, and other echocardiographic variables (including ejection fraction and TD velocities). Patients with SR IVR ≤0.24 s⁻¹ had a significantly higher event rate than those with a higher SR IVR.

**Evaluation of LV Relaxation by LV Intraventricular Pressure Gradient**

Using color flow M mode from the apical long- or 5-chamber view, Yotti and associates were able to obtain the waveform of the LV apex-outflow tract instantaneous pressure difference, which was validated against invasively measured intracavitary pressures in the LV. Because myocardial relaxation decelerates systolic flow to stop and generates negative pressure gradient from the apex to the outflow tract, the peak reverse ejection intraventricular pressure difference between the LV apex and the outflow tract obtained by Doppler echocardiography was found to correlate well with tau and to improve noninvasive assessment of LV relaxation in combination with e' velocity. It was also shown to improve correlation with pre-A LV pressure over the use of e'. It is very feasible that technical development for semiautomatic processing of color flow M-mode information to derive the
LV intracavitary pressure gradient will allow more-reliable assessment of diastolic function easily in clinical practice.

**LV Twist and Untwisting**

Twisting and untwisting of the LV are important aspects of cardiac mechanics and function. Viewed from the apex, the apical portion of the LV normally twists counterclockwise and the basal segment twists clockwise during systole, storing potential energy. The LV untwists immediately after systolic contraction, contributing to generating an intraventricular pressure gradient. LV torsion is the summation of the apical and the basal twisting. It is now possible to measure twist using TDI and STE from short-axis images of the LV.55,56 Under normal circumstances, apical rotation exceeds basal rotation and accounts for most of the observed twisting.

Several studies evaluated LV mechanics in patients with diastolic heart failure or diastolic dysfunction.43,57 These studies showed that torsion and circumferential strain are normal in patients with diastolic heart failure (Figure 8),43,57 whereas longitudinal and radial deformation are reduced. In fact, torsion is increased during the initial stage of diastolic dysfunction (Figure 9) so that it may be helpful in identifying patients with mild diastolic dysfunction. The findings can be explained as follows. Rotation is determined by the helical radius, and the larger radius of the subepicardial fibers results in these fibers being the dominate force for rotation. The subendocardial torque counteracts this effect. Accordingly, subendocardial and subepicardial disease can lead to an imbalance between the 2 helical torques and a change in twist. Because subendocardial function is impaired in patients with diastolic heart failure, the subepicardial torque plays the dominant role in determining LV twist and explains the presence of normal torsion in this disease. In contrast, myocardial dysfunction involves the midwall and subepicardial layers in patients with systolic heart failure and leads to a reduction in circumferential strain and torsion.43 It is likely that the normal circumferential strain and torsion are responsible for maintenance of a normal ejection fraction in patients with diastolic heart failure, compensating for the abnormally depressed longitudinal function.

Twisting leads to storage of potential energy that is released in early diastole during untwisting. Untwisting depends on restoring forces that are, in part, generated from the sarcomeric protein titin. Titin isoforms and phosphorylation status are important determinants of the restoring forces.58 Earlier experimental studies with cardiac magnetic resonance reported a strong inverse correlation between the time constant of LV relaxation and peak untwisting rate.59 Other studies showed that loading conditions strongly influence the untwisting rate. Wang and his associates60 conducted canine experiments where load was altered by inferior vena caval occlusion, and LV lusitropic (relaxation) state was altered by dobutamine and esmolol. During all experimental stages, the untwisting rate tracked best the changes in LV end-systolic volume rather than the time constant of LV relaxation. Indeed, when experimental stages were matched by LV end-systolic volume, untwisting rate was very similar in these stages despite large and significant differences in the time constant of LV relaxation.60 It was noted that LV end-systolic volume is among the important determinants of untwisting rate in patients with heart failure, irrespective of LV ejection fraction.60 Park and her associates44 also noted significant changes in measures of LV torsion and the rate of untwisting as well as of twisting during changes in loading conditions. All these parameters were augmented in the setting of drug-induced vasodilation, indicating substantial load dependence of these measures.

The abnormalities in LV torsion and untwisting can be uncovered with exercise in patients with diastolic heart failure. In normal subjects, exercise leads to an increase in both torsion and untwisting. However, in patients with heart failure, there is minimal augmentation of torsion and untwisting with a detrimental impact on LV filling during exercise.45

**Figure 10.** Example of LA strain curves. Septal LA strain is shown in yellow, and lateral strain is shown in blue. LAA indicates LA strain during atrial contraction; LAS, LA strain during the systolic phase of the cardiac cycle. Other abbreviation as in Figure 1. Reprinted from Kurt et al47 with permission from Lippincott Williams & Wilkins. Copyright © 2009 from the American Heart Association.
LA Function

The measurement of maximum LA volume is an essential component of the comprehensive assessment of LV diastolic function. More recently, LA volumes have been obtained by 3D echocardiography. It is possible to gain insight into LA and LV function by measuring the changes in LA volume from mitral valve opening to its closure. However, it can be technically challenging to determine LA volumetric changes during diastole. Accordingly, the direct assessment of LA function is preferable and is now feasible by measuring LA strain by TDI and STE. In general, sampling of several LA walls and regions is needed to draw conclusions about global LA function. The number of sites sampled varies between 2 and 12. Several indices of LA function can be derived from strain/SR time curves. These include maximal strain during LV systole (LAs), which corresponds to LA reservoir function; strain during early diastole, which corresponds to LA conduit function; and strain (LAA) during atrial systole, which corresponds to LA booster pump function (Figure 10). LAs appears to be 1 of the important predictors of maintenance of sinus rhythm after cardioversion. In addition, LAS relates significantly with LV diastolic pressures such that LAS decreases in the presence of increased LV filling pressures. The relation between LV end-diastolic pressure and LAS appears stronger in patients with depressed ejection fraction than in those with normal ejection fraction.

Furthermore, it is possible to use LAs along with LA pressure or its Doppler echocardiographic surrogate (E/e’ ) to calculate LA chamber stiffness. We noted that this measurement (wedge pressure/LAs or E/e’/LAs) relates well to pulmonary artery systolic pressure and is significantly higher in patients with cardiovascular disease (diastolic dysfunction, diastolic heart failure, and systolic heart failure) than in normal controls. Importantly, LA stiffness has good accuracy in identifying patients in diastolic heart failure versus those with only diastolic dysfunction when diastolic heart failure is defined using invasive criteria. Therefore, LA strain is a potentially important measurement of LA and LV diastolic function, but additional experience and more data from a large number of normal subjects are needed to have relatively narrow confidence intervals of LA strain measurements.

Disclosures

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