Diastolic dysfunction: Improved understanding using emerging imaging techniques

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Diastolic heart failure is increasing in prevalence. Although the pathophysiology is incompletely understood and current therapeutic strategies are limited, identification of diastolic dysfunction is important. We review the role of contemporary techniques with echocardiography and cardiac magnetic resonance imaging (CMRI) in the assessment of diastolic dysfunction. Cardiac catheterization is the criterion standard for demonstrating impaired relaxation and filling by making direct measurements; however, echocardiography has replaced it as the most clinically used tool. By evaluating mitral inflow pulsed-wave Doppler with and without the Valsalva maneuver, isovolumetric relaxation time, pulmonary venous flow Doppler, color M-mode velocity propagation, tissue Doppler imaging, and speckle tracking, echocardiography is considered an accurate method for diagnosis and grading diastolic dysfunction. Evaluation of diastolic function can also be performed by CMRI. Mitral valve inflow velocities, early deceleration time, and pulmonary vein flow velocities are diastolic parameters that can be measured by phase-contrast CMRI. Cardiac magnetic resonance imaging steady-state gradient echo can evaluate functional dimensions for time-volume curves; and myocardial tagging can assess ventricular diastolic "untwisting," which may be important for improved pathophysiologic understanding. Studies have compared echocardiography and CMRI for diagnosing diastolic dysfunction in small patient groups with similar results. Cardiac magnetic resonance imaging can now provide clinically relevant data regarding the underlying cause of diastolic dysfunction and offers promise to gain mechanistic insights for therapeutic strategy development and clinical trial planning. (Am Heart J 2010;160:394-404.)

Diastolic heart failure is defined as heart failure (HF) with normal left ventricular ejection fraction (LVEF) in the absence of significant valvular lesions. Diastolic dysfunction has become the dominant form of HF in the community,[1] and the incidence and prevalence has increased with worsening morbidity and mortality.[2] Contrary to HF with decreased LVEF, diastolic HF disproportionately affects women, with a prevalence of 65% to 75% versus 35% to 45% in men.[3] In addition, the presence of diastolic dysfunction portends worse prognosis in patients with systolic HF[4] and likely contributes to the adverse cardiovascular outcomes experienced by women compared with men. Although the pathophysiology of this type of HF is incompletely understood and current therapeutic strategies are limited, identification of diastolic dysfunction is important. There is an urgent need for improved mechanistic understanding to advance therapeutic strategy development and clinical trial planning, as identified recently by the National Heart, Lung, and Blood Institute American Recovery and Reinvestment Act.[5]

The criterion standard for demonstrating left ventricular (LV) diastolic dysfunction is cardiac catheterization to obtain pressure-volume curves to measure the rate of pressure decay during isovolumic relaxation.[6] However, this measurement is imperfect because of the additional effect of transmyocardial pressure on the left ventricle; routine invasive cardiac catheterization is also not feasible. Noninvasive modalities should thus include routine measurements of diastolic function. Although echocardiography is an established and widely available method for assessing filling patterns, cardiac magnetic resonance imaging (CMRI) is an emerging modality for diastolic function analysis. Several studies have compared the 2 modalities and suggest favorable intermodality agreement.

Diagnosis by echocardiography

Measurement of LV pressure decline over time by cardiac catheterization is a useful parameter of impaired diastolic relaxation, but this has largely been replaced by echocardiography to assess diastolic function.[7] Initial

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doi:10.1016/j.ahj.2010.06.040

techniques, such as mitral valve inflow pulsed-wave Doppler, are dependent on loading conditions, systolic function, and heart rate; but recent methods are load independent and have improved assessment of diastolic dysfunction.[8]

Mitral inflow

Doppler mitral inflow velocity is one of the first simple steps in evaluating diastolic filling. Diastole is traditionally described as having 4 phases: isovolumetric relaxation (IVRT), early (rapid) filling phase, diastasis, and late filling phase. Isovolumetric relaxation corresponds to initiation of relaxation when both the aortic valve and mitral valve are closed; it is measured by placing the continued-waved Doppler between the mitral valve and the LV outflow tract to simultaneously interrogate LV outflow and mitral inflow. To evaluate the early and late filling phases, mitral inflow velocities are obtained by placing the pulsed-wave Doppler at the tips of the mitral valve leaflets in the apical 4-chamber view. When the LV pressure falls below the left atrial (LA) pressure, the mitral valve opens and the early rapid filling phase begins; the blood leaves the left atrium and enters the LV passively down a pressure gradient. The peak early filling velocity is termed the *E wave*, which is recorded with the deceleration time (DT) from peak to baseline at the end of the E wave. The LV pressure gradually increases until the LV and LA pressure has equalized and early filling ceases, determining the beginning of diastasis where essentially no net flow occurs. The late phase of diastolic filling occurs with atrial contraction and is represented by the measured A wave.

The normal values for these measurements vary with age, as mitral E and E/A ratio decrease with age, whereas IVRT, DT, and A velocity increase with age.[9] Other factors that affect mitral inflow include heart rate, rhythm, PR interval, cardiac output, mitral annular size, LA function, LV end-systolic or end-diastolic volumes, and LV elastic recoil. Changes in LV relaxation and preload influence the E wave, whereas alterations in LV compliance and LA contractile function affect the A wave. E-wave DT is affected by LV compliance, LV relaxation, and LV diastolic pressures after mitral valve opening. With first-degree atrioventricular block and sinus tachycardia, fusion of the mitral E and A waves is seen, making the DT immeasurable.[10] Left ventricular filling is affected by rapid atrial contractions; therefore, E velocity, E/A ratio, or DT cannot be measured during atrial flutter or fibrillation.

Valsalva maneuver

The Valsalva maneuver is helpful in clarifying mitral inflow measurements. The process involves forceful expiration against a closed airway, performed to decrease the LV preload during the strain phase and differentiate normal from pseudonormal mitral inflow patterns. The pseudonormal pattern is due to an increase in LA pressure with impaired myocardial relaxation. With the decrease in LV preload produced by the strain phase, pseudonormal mitral inflow will change to a pattern of abnormal relaxation: decrease in mitral E velocity, prolongation of DT, unchanged or increased A velocity, and decrease in the E/A ratio.[11] If the mitral inflow is normal, both E and A velocity will decrease and DT will prolong. The maneuver is helpful when the diastolic function is not apparent after the mitral inflow measurements. Unfortunately, the Valsalva maneuver is not standardized and not always performed correctly. Although pulmonary venous flow assessment and tissue Doppler imaging (TDI) often can accurately estimate LV filling pressure, in cases where the pattern is not clear, the Valsalva maneuver may still be useful.

Pulmonary venous flow

Pulsed-wave Doppler of pulmonary venous flow is a significant tool for diastolic function assessment. The pulsed-wave sample is typically placed 0.5 cm within the right upper pulmonary vein in the 4-chamber view, but the pulmonary vein flow most aligned with the Doppler cursor should be used. The measurements include peak systolic (S) velocity, peak anterograde diastolic (D) velocity, and the peak atrial reversal (Ar) velocity in late diastole. Changes in LV filling and compliance affect D velocity. Ar velocity, and duration are impacted by LV late diastolic pressures, atrial preload, and LA contractility.[12] The S/D ratio and Ar velocities increase with older age, but Ar velocities higher than 35 cm/s suggest increased LV end-diastolic pressure (LVEDP).

Although a reduced systolic filling fraction of <40% correlates to decreased LA compliance and increased mean LA pressure in patients with decreased LVEF, this correlation is not demonstrated in patients with normal LVEF and atrial fibrillation, mitral valve disease, and hypertrophic cardiomyopathy.[13] The Ar-A duration difference is age independent and can differentiate patients with abnormal LV relaxation and normal filling pressures from those with elevated LVEDPs. Although many patients with abnormal relaxation (E/A <0.75) will have normal LVEDP, the isolated increase in LVEDP is the first hemodynamic abnormality seen in diastolic dysfunction and is reflected by an Ar-A duration >30 milliseconds.[14] The Ar-A duration is also useful in those patients with normal LVEF, mitral valve disease, and hypertrophic cardiomyopathy.[15,16]

Few studies have shown the prognostic role of pulmonary venous flow.[17] Obtaining interpretable measurements is technically difficult, as the pulmonary veins are located in the far field of the transthoracic transducer yet can be reliably obtained in most patients. Inconclusive results are often seen in settings such as

sinus tachycardia, first-degree atrioventricular block, and atrial fibrillation.

Color M-mode velocity propagation

Color M-mode and tissue Doppler imaging are less affected by loading conditions and thus provide further assessment of diastolic function. Color flow mapping with M-mode is acquired in the apical 4-chamber view and allows differentiation of normal from restrictive physiology. The measured slowing of mitral-to-apical flow propagation is an intraventricular flow disturbance reflecting LV diastolic dysfunction. The rate of inflow from the mitral annulus to the apex, that is, the flow propagation velocity (Vp), can be computed with M-mode during early filling. A Vp >50 cm/s is considered normal, and the peak E velocity to Vp ratio has been shown to be directly proportional to LA pressure. Therefore, E/Vp can be used to predict LV filling pressure.[18] Propagation velocity also predicts a pulmonary capillary wedge pressure ≥15 mm Hg when E/Vp ≥2.5.[19] The color M-mode Doppler assessment provides prognostic information after an acute myocardial infarction. An E/Vp ratio ≥1.5 is associated with elevated LA pressure and has been found to be a strong predictor of in-hospital HF and survival.[20]

A limitation of color M-mode flow propagation velocity occurs in patients with normal LVEF. In these patients, normal LV volumes and LVEF with abnormal filling pressures can have mistakenly normal Vp.[21] This method is also angle dependent, and the cursor direction needs to be adequately aligned with the LV long axis.

Tissue Doppler imaging

Pulsed-wave TDI performed in the apical view is a useful technique to evaluate LV diastolic function and to measure mitral annular velocities. The primary measurements include systolic, early diastolic e', and late diastolic a' annular velocities. The e' velocity is determined by LV relaxation, preload, systolic function, and LV pressure; a value ≥10 cm/s is consistent with normal function. The main hemodynamic determinants of the a' velocity are LA systolic function and LVEDP. The e' velocity can be used to correct for the effect of LV relaxation on mitral inflow E velocity in patients with cardiac disease. The annular e'/a' ratio and the mitral E velocity to tissue Doppler e' velocity (E/e') ratio can predict LV filling pressures.

Although a E/e' ratio <8 is generally regarded as signifying normal LV filling pressures and a ratio >15 suggests increased filling pressures, there is no clear consensus on whether to use septal or lateral e'.[22] Septal wall e' typically is less than lateral wall e'. However, ratios between these values are less predictive of filling pressure and require other echocardiographic indices for further evaluation. In patients with normal LVEF, lateral tissue Doppler signals have been shown to have the best correlation with LV filling pressures and invasive indices of LV stiffness.[23] The indices have been validated in patients with both reduced and preserved LVEF and have been found to provide a reliable estimate of LV filling pressures compared with invasive diagnostic methods.

Tissue Doppler imaging–derived velocities also have certain limitations. As age increases, the e' velocity decreases; and the a' velocity and E/e' ratio increase.[24] In addition, E/e' ratio is not an accurate index of filling pressure in patients with heavy annular calcification, lateral wall infarction (when septal DTI should be used), mitral valve disease, and constrictive pericarditis.[25] Doppler tissue imaging requires technical experience to produce results, but it is a sensitive and load-independent measure of LV relaxation and should be part on any standard echocardiographic examination.

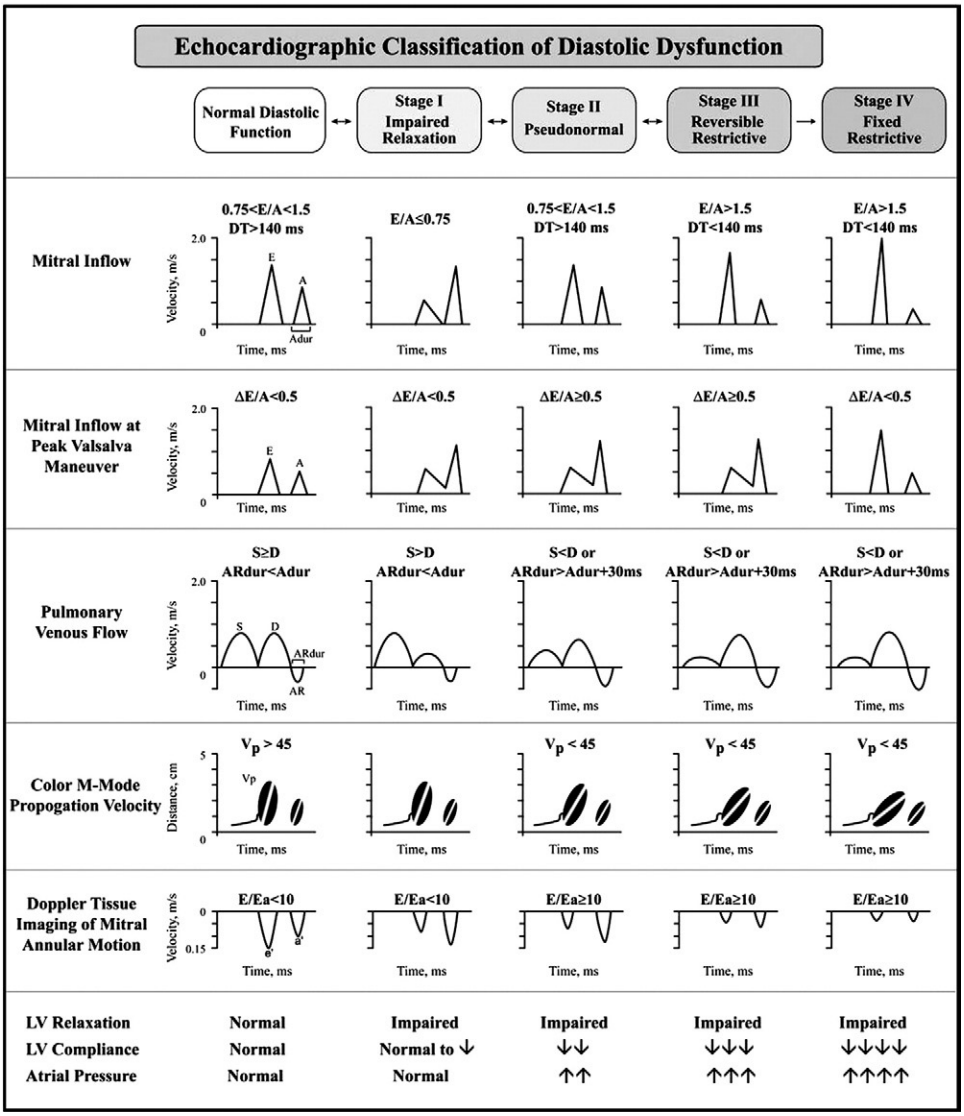
Speckle-tracking echocardiography

Speckle-tracking echocardiography is another method that has emerged to assist with LV function assessment. Speckle-tracking evaluates myocardial deformation and quantifies LV rotation, twist, and untwist, which was previously only possible with the use of CMRI.[26] Speckle analysis also studies radial, longitudinal, and circumferential planes in one data set. Wang et al[27] demonstrated that, in patients with diastolic dysfunction, the LV torsion and peak untwisting rate are preserved, as opposed to patients with systolic dysfunction in which the measurements are reduced. Limitations of this technique include the dependence on 2-dimensional (2D) image quality and frame rates, difficulty of selection of image plane, and the reproducibility and variability of measurements from ventricles with different geometries.[28] The development of 3-dimensional (3D) speckle tracing may assist with these limitations. Future studies will determine if the measurement of LV twist and untwisting rate will be routinely performed for diastolic function evaluation.

Grading diastolic dysfunction

Stage I diastolic dysfunction occurs when there is impaired relaxation characterized by a reduction in early diastolic mitral flow velocity (decrease in the E wave) and an increase in late diastolic filling (increase in the A wave). Therefore, the E/A ratio becomes <0.75 with the prolongation of DT and IVRT.[29] The S wave is dominant in the pulmonary venous inflow tracing; and lateral e' is <10 cm/s, but with E/e' ≤8. The Ar-A duration is also normal, that is, <30 milliseconds. Although there is impaired relaxation, there is no evidence of increased filling pressures at rest. Stage I diastolic dysfunction is often seen in patients with ischemic heart disease and hypertension, and with aging. Stage II diastolic dysfunction is defined by a pseudonormal filling pattern. In these patients, the mitral inflow resembles a normal

Figure 1



Echocardiographic classification of diastolic dysfunction. *Adur*, Duration of A wave; *ARdur*, peak pulmonary venous atrial reversal flow velocity duration; *Ea*, peak early diastolic myocardial velocity. Reprinted with permission from S. J. Khouri.

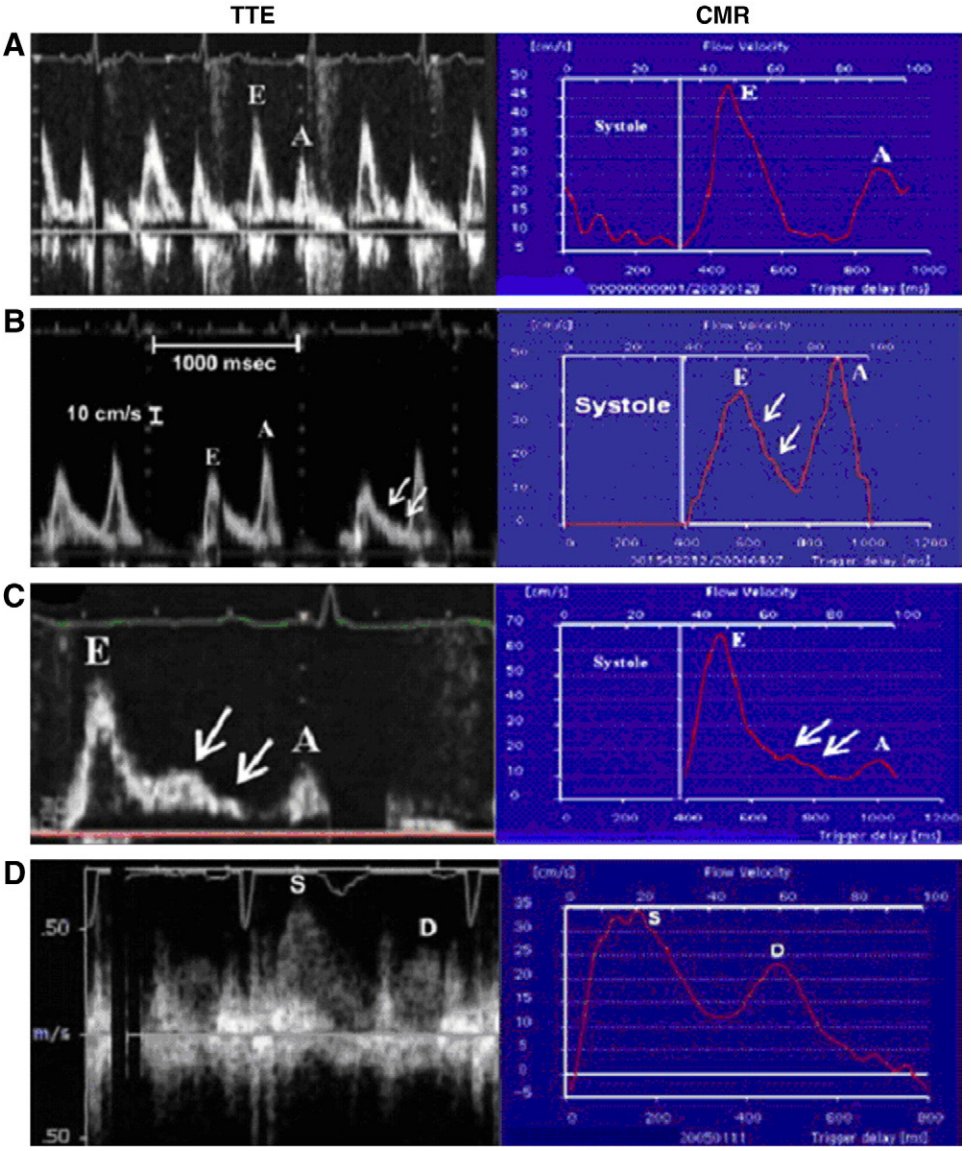
pattern (normal E/A ratio, normal DT); but there is decreased LV compliance and increased LA pressure at rest.[30] The D wave in the pulmonary venous inflow tracing will be dominant, that is, E/e' often 8 to 15, but may be greater; and the Ar-A duration is prolonged (≥ 30 milliseconds).

Restrictive LV filling, also known as *stage III to IV diastolic dysfunction*, is defined by impaired relaxation with markedly elevated filling pressures. Left ventricular compliance is also severely impaired. The restrictive pattern is characterized by an increased E/A ratio (>1.5) and shortening of the IVRT and DT (<150 milliseconds). The E/e' is >15, and the S wave in the pulmonary venous inflow is markedly reduced or absent (Figure 1).

Diagnosis by CMRI

Cardiac magnetic resonance imaging can be used to evaluate diastolic function and provides advantages over echocardiography in selected patients. The ability to image the whole chest without limitation of the echo window permits visualization of the entire heart, with excellent spatial and temporal resolution. In addition to anatomical imaging, measurement of blood flow velocity can be performed at any location; and this can produce

Figure 2



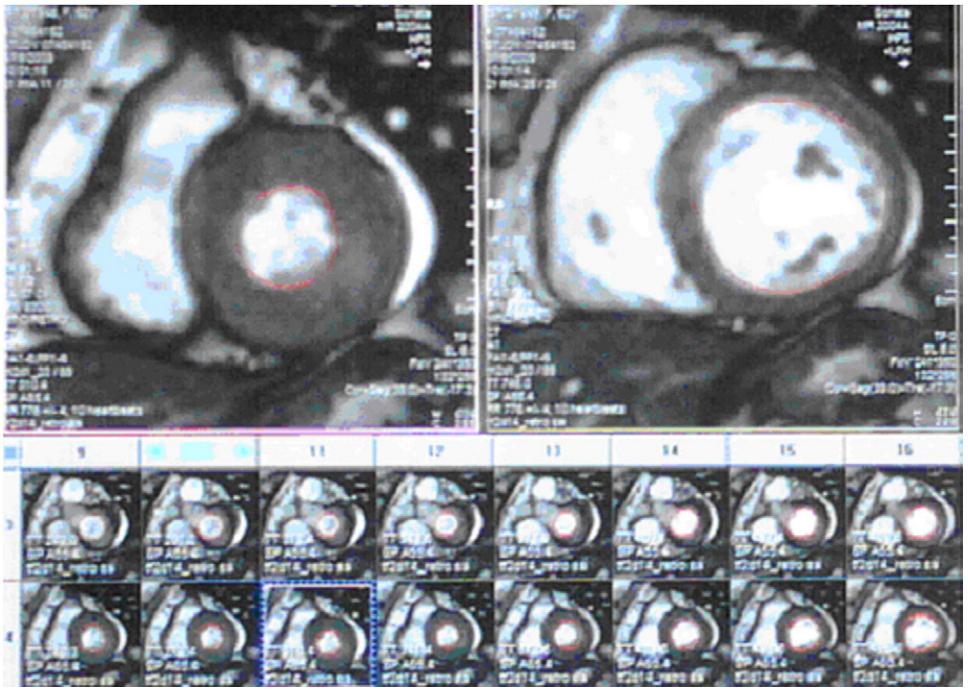
Velocities obtained by echocardiogram and phase-contrast CMR. **A**, Normal E/A and DT. **B**, Impaired relaxation with prolonged DT and a high A wave. **C**, Restrictive pattern with short DT and an elevated E/A. Diastasis points (arrows) illustrate similarities in depiction of flow features. **D**, S (systolic) and D (diastolic) waves of the pulmonary vein are similar in both CMRI and echocardiography. Reprinted with permission from V. K. Rathi.

inflow velocity data for the mitral valve and pulmonary veins, akin to echocardiography. Unique properties of the magnetic field imaging permit placement of myocardial tag markers for imaging and analysis of myocardial strain and torsion recovery rate.

Phase-contrast CMRI

Phase-contrast CMRI allows quantitative measurement of blood flow at any selected location within the chest. This technique is possible by measurement of signal intensity change when flowing blood is exposed to gradients that are applied in equal and opposite directions. The resultant image data are usually displayed as a phase map that defines both velocity and direction of flow during the cardiac cycle. This can be performed in parallel to the direction of flow to provide qualitative information about turbulence. Transmitral and pulmonary vein flow can thus be measured similar to Doppler

Figure 3

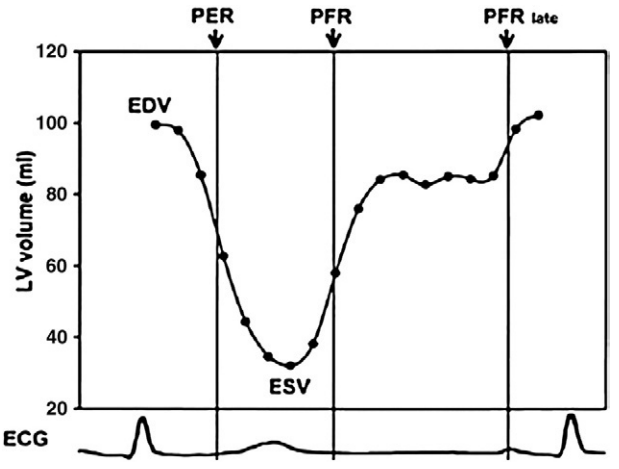


Analysis of volume-time curve. Peak ejection rate and peak early filling rate were determined as peak incremental volume changes. *PER*, Peak ejection rate; *PFR*, peak early filling rate; *ESV*, end systolic volume; *ECG*, electrocardiogram. Reprinted with permission from T. Buck.

echocardiography.[31] Localization scout images identify the LV in the long-axis 4-chamber view and visualize the mitral valve leaflets and right superior pulmonary vein. Short axis cine imaging is then performed parallel to the mitral valve annular plane and perpendicular to the pulmonary vein to capture mitral valve and pulmonary vein flow. Phase-contrast velocity-encoded images are obtained using retrospective electrocardiographic gating over a complete cardiac cycle, ensuring data sampling throughout diastole (Figure 2). Contours of the cross section of the mitral valve leaflets or pulmonary vein are used to create velocity-time graphs, yielding mitral E and A waves and pulmonary diastolic S and D waves.

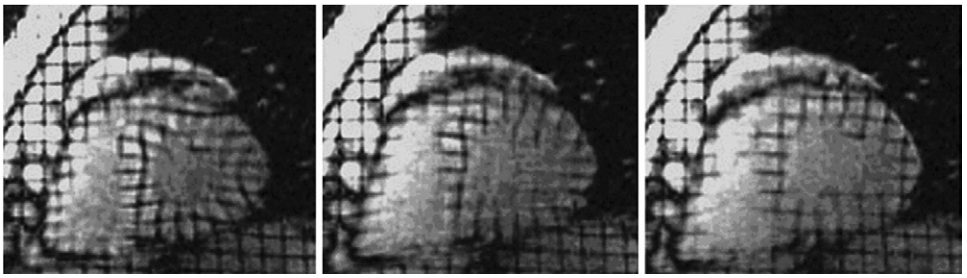
Transmitral flow is a dynamic phenomenon that may be affected by intramyocardial properties, and phase-contrast CMRI can also be used to inspect myocardial tissue velocity. The influence of myocardial relaxation on E wave can be evaluated by mitral septal tissue velocity, which may be useful in patients with LV hypertrophy. Paelinck et al[32] measured mitral inflow and septal mitral annular velocities with phase-contrast CMRI and Doppler echocardiography to calculate E/E' and compare the data to pulmonary capillary wedge pressure. Cardiac magnetic resonance imaging correlated with Doppler, and both measurements of E/E' had strong correlations to invasive pulmonary capillary wedge pressure. However,

Figure 4



Subendocardial contouring of the LV, using serial short-axis images obtained from steady-state free precession gradient echo CMRI. Images courtesy of Louise E.J. Thomson, MBChB, FRACP, S. Mark Taper Foundation Imaging Center, Los Angeles, CA.

Figure 5



Cardiac magnetic resonance imaging K-space–tagged images from systole to diastole, displaying LV deformation and restoration that can be quantified. Reprinted with permission from V. K. Rathi.

the CMRI measurements had a tendency to underestimate A velocity.

The advantages of phase-contrast CMRI include the ability to acquire velocity profiles at any arbitrary position within the chest, with less variability and difficulty compared with Doppler echocardiography, which is limited by beam angle, multiple velocity directions, and eccentric blood flow. Data acquisition is performed with either breath-held or free-breathing techniques. As with all CMRI sequences, increases in spatial and temporal resolution result in longer scan time, which must be limited for breath-hold imaging. Imaging performed with free breathing allows improved spatial and temporal resolution at the expense of respiratory motion artifact. To overcome this limitation, some centers use a prospective respiratory gating technique to suppress respiration artifacts. Correction for bulk tissue motion can also be performed during postprocessing based on subtraction of global translation velocities from the local velocity components.[33]

Gradient echo CMRI

Gradient echo CMRI uses radiofrequency pulses gated to the electrocardiogram, which permits imaging at multiple phases of the cardiac cycle so that a cine display can be generated. Spoiled-gradient echo CMRI has largely been replaced by balanced steady-state free precession (steady-state gradient echo) CMRI to generate a higher contrast to delineate the endocardial borders. From multiple short-axis images of LV volume during diastole, global ventricular filling can be analyzed. Cardiac magnetic resonance imaging has previously been confirmed as having superior accuracy of LV volume measurements.[34] Endocardial contouring of the entire LV allows measurement of the LV volume, which is then used to generate time-volume curves (Figures 3 and 4).[35] Peak filling rate can be determined from the maximal change of ventricular volume during early diastole; time to peak filling rate from end-systole is also calculated. Diastolic dysfunction is associated with decreased peak filling rate and increased time to peak filling rate. In a study of 15 healthy participants, volume-time curves were successfully generated in all participants by 3D echocardiogram and CMRI, with individual volume-time curves showing great uniformity. The diastolic filling parameters (peak filling rate, time to peak filling rate) of CMRI agreed with those of echocardiography.[36]

Steady-state gradient echo CMRI sequences are prone to off-resonance banding artifacts caused by local field inhomogeneities, so a very uniform magnetic field is required to avoid artifacts. In addition, because the volume-time curves do not provide any information regarding LV filling characteristics and do not fully represent LV compliance because of external contributions from the right ventricle or the pericardium, volume-time curves are less commonly used in the diagnosis of diastolic dysfunction.

Tagged CMRI

Tagged CMRI allows the visualization of systolic and diastolic myocardial deformation, which is characterized by LV torsion and strain. Tagged CMRI labels the myocardium with selective radiofrequency saturation prepulses in planes perpendicular to the imaging plane. A grid of radiofrequency tags of the myocardium reveals the deformation and displacement of the myocardium, which allows accurate analysis of any diastolic strain and 3D motion (including rotation and torsion) of the heart[37] (Figure 5). Unlike volume-time curves, flow velocity, and myocardial velocity, LV strain rate and torsion recovery rate directly reflect diastolic dysfunction. The deformations are measured using units of strain (percentage S) or torsion (degree). Left ventricular torsion represents the clockwise and counterclockwise rotation of the apex and base, promoting a more complete ejection of LV blood. In systole, twist of the subendocardial fiber matrix creates storage of potential energy, whereas subsequent recoil of twist deformation results in a release of energy that creates diastolic

Table I. Echo and CMRI modalities and their parameters of diastolic function

Echocardiography	CMRI
Mitral inflow velocities E wave, A wave, E/A ratio, DT, and IVRT	Phase-contrast CMRI Mitral inflow, pulmonary venous flow
Valsalva maneuver Differentiate normal and pseudonormal	Gradient echo CMRI Peak filling rate, time to peak filling rate from end-systole
Pulmonary venous flow S velocity, D velocity, S/D ratio, Ar-A duration	Tagged CMRI LV untwisting during diastole
Color M-mode velocity propagation Vp, E/Vp	
Pulsed-wave Doppler tissue imaging e' velocity, a' velocity, e'/a' ratio, E/e' ratio	

suction. Diastolic suction enhances mitral valve opening, and the untwisting contributes to LV diastolic relaxation and early diastolic filling.[38] Diastolic torsion usually is completed in the first third of diastole, and the LV diastolic untwisting rate is independent of preload. Delay and prolongation of diastolic untwisting may be related to a decrease in relaxation and early diastolic filling velocity, which is seen with aging and in LV hypertrophy.[39,40] Diastolic untwisting is also shown to be delayed and prolonged in anterolateral infarction, hibernating myocardium, and transmural ischemia.[41]

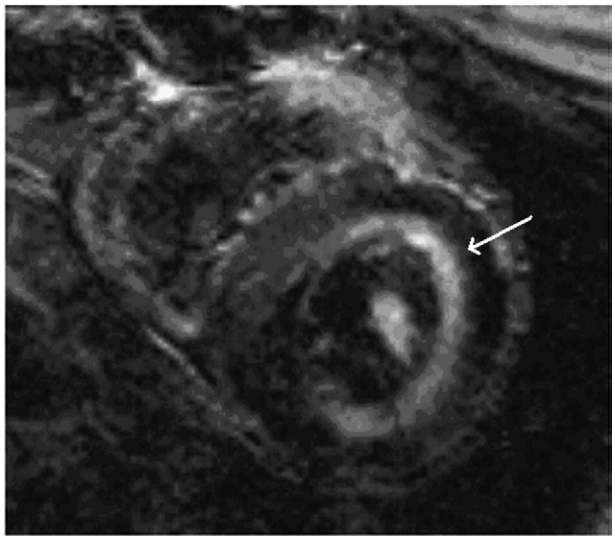
Diastolic strain rate characterizes deformation patterns based on circumferential, longitudinal, or radial strain. Novel techniques have been developed to facilitate and speed the acquisition and postprocessing of tagged CMRI, which can be a long process. The highly automated harmonic phase method tracks regional myocardial function by filtering harmonic peaks of tag patterns[42] and is currently the most widely used method for strain quantification.[43] Using the highly automated harmonic phase method, the Multi-Ethnic Study of Atherosclerosis studied circumferential strain in asymptomatic participants with LV hypertrophy and preserved systolic LV function; LV hypertrophy was found to be associated with reduced regional diastolic strain rate ($P < .001$) regardless of age or sex.[44] Another recent development has been cine displacement encoded with stimulated echoes CMRI, which measures strain without the need for tagging and may allow higher temporal and spatial resolution for strain mapping.[45]

Comparing echocardiography and CMRI

Both echocardiography and CMRI have unique methods to diagnose diastolic dysfunction (Table I). Echocardiogram has important disadvantages, including limited field of view and calculation errors relative to flow direction. Interferences from bone or lung on the acoustic window are limitations of echocardiogram. Small changes in LA or LV volumes and mass can be detected by CMRI as opposed to echocardiography; these small changes may be important when evaluating disease progression or therapy response. Cardiac magnetic resonance imaging, which is the criterion standard for measuring volumes and LV mass due to its image quality and high spatial and temporal resolution, has been compared with echocardiography for diagnosis of diastolic dysfunction in a limited number of studies. Rubinshtein et al[46] compared echocardiography and CMRI in a study evaluating 38 patients with diastolic dysfunction. They concluded that CMRI measurements of mitral inflow peak velocities, DTs, and E/A ratios correlated well with echocardiographic measurements. In another study of 31 patients, phase-contrast CMRI measurements of mitral valve and pulmonary vein flow correlated with echocardiography measurements.[47] These studies suggest that CMRI is a feasible method for diagnosis of diastolic dysfunction, with reproducible and reliable data.

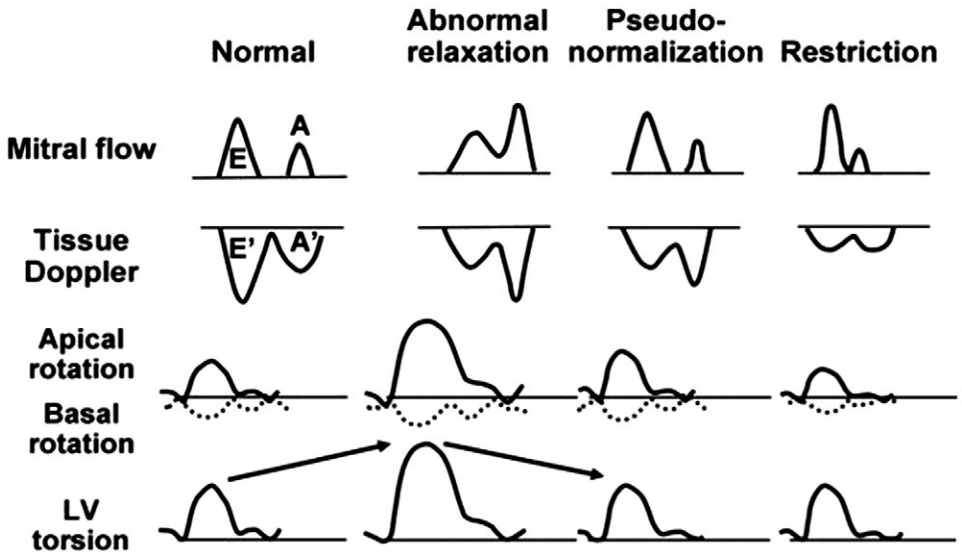
Although CMRI may be a comparable tool to echocardiography for the diagnosis of diastolic dysfunction, further studies with a larger series of patients are required to confirm the validity of these findings. According to one report, CMRI diagnosed diastolic dysfunction with reasonable accuracy; but the study found an underestimation of the degree of diastolic

Figure 6



Left ventricular hyperenhancement in a patient with cardiac amyloidosis. Delayed gadolinium enhancement images demonstrate a circumferential pattern of subendocardial hyperenhancement (arrow), rather than the segmental pattern of hyperenhancement seen with myocardial infarction due to coronary artery disease. Images courtesy of Louise E.J. Thomson, MBChB, FRACP, S. Mark Taper Foundation Imaging Center, Los Angeles, CA.

Figure 7



Assessment of diastolic dysfunction based on mitral inflow, mitral annular velocity, and LV torsion. Reprinted with permission from J. Oh.

dysfunction in 70% of patients evaluated by CMRI compared with echocardiography.[48] Furthermore, CMRI may be limited by its availability in clinical centers, cost, and individual patient settings, such as the presence of pacemakers or claustrophobia.

Cardiac magnetic resonance imaging can enhance insight into the cause of diastolic dysfunction in certain clinical situations. In many patients, the cause of diastolic dysfunction may be readily apparent (eg, longstanding hypertension); but in situations with diagnostic uncertainty, CMRI can provide information not provided by echocardiography. In selected patients, CMRI may better define cardiac and extracardiac morphologic characteristics with contrast delay enhancement.[49] Amyloidosis, a process in which infiltration with fibrillar proteins causes a loss of LV compliance, may be detected by delayed-enhancement CMRI, which is validated for detection of the typical diffuse global enhancement pattern in amyloidosis (Figure 6). Myocardial T2* CMRI has been validated for myocardial iron load quantification in patients with β-thalassemia major and can also show response to therapy.[50,51] Cardiac magnetic resonance imaging can also play an important role in distinguishing between constrictive pericarditis and restrictive cardiomyopathy, as CMRI is the tool of choice for demonstration of pericardial thickening, adherence, inflammation, and cardiac constriction, with high diagnostic accuracy.[52] Cardiac magnetic resonance imaging stress testing can detect subendocardial ischemia that is missed by other imaging techniques and may be important in diagnosing microvascular coronary dysfunction in patients with persistent chest pain and open coronary arteries.[53]

Future directions

With the increased national attention to the management of HF with normal LVEF, the diagnosis has also remained fundamental. Measurement of diastolic parameters to determine response in treatment has been investigated. Doppler echocardiographic measurements of diastolic dysfunction are dependent on preload, afterload, and sympathetic tone, which can vary on a daily basis.[14] Measurements that are adjusted for sex, weight, and blood pressure have been reported; but the cutoff values for normal and abnormal are difficult to nationalize. Diastolic dysfunction is also often coexistent with systolic dysfunction, and their relationship has been further described in the studies of LV untwisting and suction.[54] In fact, Tan et al[55] recently revealed that patients with HF with normal LVEF had complex abnormalities of both systolic and diastolic LV function. Systolic abnormalities included reduced systolic longitudinal and radial strain, systolic mitral annular velocities, and apical rotation, whereas diastolic dysfunction is present with reduced and delayed untwisting, reduced LV suction at rest, and higher LVEDP during exercise. Previously evaluated primarily by CMRI, LV strain measurements are now assessed by 2D echocardiographic speckle tracking and may provide additional useful analysis regarding the mechanism of diastolic dysfunction (Figure 7).[56] A major limitation of CMRI has been the

routine study of patients with pacemakers or automatic internal cardioverter-defibrillators, and further investigation of the effects of CMRI on leads placed in the coronary sinus needs to be done. Evaluation of diastolic strain rate has been limited because of the availability of computer software; and myocardial tag density decreases exponentially as a function of time, limiting diastolic assessment during late diastole.[57] The advent of 3D echocardiography will very likely improve the echocardiographic assessment volumes and mass. Furthermore, 2D speckle tracking, although requiring specialized software, is easy to acquire and may in the future prove important for detection of early diastolic dysfunction.

Conclusion

The assessment of diastolic function is now essential on routine testing for HF. The noninvasive nature of echocardiography has allowed an increase in diagnosis and awareness of diastolic dysfunction, whereas or the unique features of CMRI allow for the detailed evaluation of diastolic dysfunction. Both modalities offer insights into the mechanism of diastolic dysfunction in HF with normal LVEF. The increased and rising prevalence of HF with normal LVEF, along with the absence of effective therapeutic strategies, is an urgent call for improved mechanistic understanding of diastolic dysfunction to plan clinical trials for innovative therapy development.

Disclosure

No extramural funding was used to support this manuscript. The authors are solely responsible for the drafting and editing of the paper and its final contents.

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