Diastolic Heart Failure Can Be Diagnosed by Comprehensive Two-Dimensional and Doppler Echocardiography

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There are many myocardial and non-myocardial conditions that cause heart failure with normal left ventricular ejection fraction (LVEF). Among them, diastolic heart failure (heart failure due to diastolic dysfunction) is the most common cause of heart failure with normal LVEF. Diastolic heart failure easily can be diagnosed by comprehensive two-dimensional and Doppler echocardiography, which can demonstrate abnormal myocardial relaxation, decreased compliance, and increased filling pressure in the setting of normal LV dimensions and preserved LVEF. Therefore, diastolic heart failure should always be considered when LVEF is normal on two-dimensional echocardiography in patients with clinical evidence of heart failure. The diagnosis can be confirmed if Doppler echocardiography and myocardial tissue imaging provide evidence for impaired myocardial relaxation (i.e., decreased longitudinal velocity of the mitral annulus during early diastole and decreased propagation velocity of mitral inflow), decreased compliance (shortened mitral A-wave duration and mitral deceleration time), and increased filling pressure (shortened isovolumic relaxation time and an increased ratio between early diastolic mitral and mitral annular velocities). Early identification of diastolic dysfunction in asymptomatic patients by the use of echocardiography may provide an opportunity to manage the underlying etiology to prevent progression to diastolic heart failure. (J Am Coll Cardiol 2006;47:500–6) © 2006 by the American College of Cardiology Foundation

A viewpoint paper by Mauer et al. (1) was published in a recent issue of the Journal in which they advanced two positions (1): 1) Doppler-derived diastolic parameters do not provide specific information on intrinsic passive diastolic properties, thus, diastolic dysfunction cannot be diagnosed by Doppler echocardiography; and 2) because delayed relaxation and/or stiffened passive properties may not be the unifying pathophysiologic mechanisms in all patients who present with heart failure and normal ejection fraction (EF), the term “heart failure with normal ejection fraction (HFNEF)” is preferred over the use of the term “diastolic heart failure (DHF)” to describe these patients. They described the basic concepts of diastolic function beautifully and made cogent arguments for their stated views. Their contention was that Doppler echocardiography, which is currently the most practical and reproducible diagnostic modality to identify these patients, reflects mainly diastolic filling pressure rather than the intrinsic diastolic properties of the heart. They further suggested that DHF should be reserved for heart failure caused by an abnormality of intrinsic diastolic function of the heart defined by slowed relaxation or an upward shift of the left ventricular (LV) end-diastolic pressure-volume relation (EDPVR).

In this counter-viewpoint paper, we demonstrate how comprehensive two-dimensional and Doppler echocardiography can assess abnormal relaxation, detect changes in compliance or stiffness, and differentiate the level of filling pressure from the rate of change in pressure during diastole, which together with the structural information obtained from the two-dimensional echocardiography provide a clinically relevant assessment of diastolic function. By demonstrating intrinsic diastolic dysfunction in patients with clinical evidence of heart failure and normal EF, echocardiography can diagnose diastolic heart failure reliably.

NORMAL AND ABNORMAL DIASTOLIC FUNCTION

Normally, the majority of LV filling occurs very rapidly in early diastole as LV pressure falls below left atrial pressure with normal relaxation of the myocardium (2). During exercise, LV filling rates and the total amount of filling can be dramatically increased (3,4). Normally, this increased filling occurs because LV early diastolic pressures decrease with enhanced myocardial relaxation and increased systolic emptying. Thus, substantial increases in filling can occur without left atrial pressure increasing to abnormal levels. For example, high levels of exercise and large amounts of volume loading can occur in young healthy patients without producing pulmonary edema.

The normal response to exercise is lost in heart failure regardless of EF (5,6). Under these circumstances, relaxation of myocardium is slowed with decreased or no ability...
to enhance relaxation with exercise. Thus, LV early diastolic pressure does not decline during exercise but, in fact, increases. In patients with diastolic dysfunction, increases in LV filling in response to exercise are dependent on increases in left atrial pressure. Whether the LV filling is normal with a good myocardial relaxation or LV filling is dependent on left atrial pressure can be easily discerned by two-dimensional and Doppler parameters measured in a daily echocardiography practice, which are used to determine myocardial relaxation, compliance, and filling pressure at rest and with exercise.

**HOW TO DETERMINE DIASTOLIC PROPERTY AND FILLING PRESSURE BY ECHOCARDIOGRAPHY**

Comprehensive echocardiography in contemporary practice consists of M-mode, two-dimensional, Doppler, color flow imaging, and myocardial (tissue Doppler) imaging, all of which are performed and interpreted collectively in context of clinical findings. Left ventricular relaxation is assessed by isovolumic relaxation time (IVRT), mitral inflow Doppler velocities (Fig. 1), tissue Doppler measurement of mitral annular early diastolic velocity (Ea), and color M-mode measurement of mitral inflow propagation velocity (Vp) (7–9). As myocardial relaxation becomes abnormal, the rate of decrease in the LV pressure is slower and IVRT becomes longer, but LV filling pressure is not necessarily elevated. If LV filling pressure is not elevated, the E velocity of mitral inflow decreases and deceleration time (DT) is prolonged. Even when resting filling pressure is not elevated, patients with abnormal relaxation may develop increased filling pressure with exercise and/or a higher heart rate, which shortens the diastolic filling period and compromises adequate diastolic filling. Patients with normal myocardial relaxation at rest do not develop an abnormally increased filling pressure with stress or exercise. Slowed relaxation also can be identified by a reduction and delay in Ea velocity of the mitral annulus (10), as well as by slower mitral diastolic flow Vp (7), or a reduced rate of early diastolic thinning of LV posterior wall or early diastolic mitral annular motion on M–mode echocardiography. In healthy individuals, longitudinal motion of the mitral annulus (Ea) increases with exercise or increased early diastolic filling (9,11). However, in individuals with abnormal relaxation and reduced Ea, Ea is less influenced by loading conditions (8,12). When myocardial relaxation is markedly abnormal, an early mitral diastolic flow velocity with rapid deceleration is followed by an increased mid-diastolic flow velocity (Fig. 2) as LV mid-diastolic pressure falls with continuing relaxation (13–15). Mid-diastolic “L” velocity also is evident in the mitral annulus velocity recording by tissue Doppler imaging.

With a moderate decrease in compliance, LV pressure with atrial contraction increases abnormally, and transmitral filling during atrial contraction is abbreviated, detected as a shortening of the mitral A-wave duration, whereas the duration of the flow reversal in the pulmonary vein during atrial contraction becomes longer than the mitral A duration.

We do not agree with the statement by Mauer et al. (1) that “these measurements are elaborate, difficult to obtain in many patients, and not routinely performed.” The mitral inflow velocity is and should be recorded routinely, and

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**Abbreviations and Acronyms**

- DHF = diastolic heart failure
- DT = diastolic time
- Ea = mitral annular early diastolic velocity
- EDPVR = end-diastolic pressure-volume relation
- EF = ejection fraction
- HFNEF = heart failure with normal ejection fraction
- IVRT = isovolumic relaxation time
- LV = left ventricular
- LVEF = left ventricular ejection fraction
- Vp = mitral inflow propagation velocity

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**Figure 1.** Pulsed-wave Doppler recordings of mitral inflow velocities from predominant relaxation abnormality (left), normal or pseudonormal (center), and restrictive (right) filling patterns. Abnormal relaxation is the earliest diastolic abnormality with characteristic reduction in early diastolic velocity (E) and prolongation of deceleration time (DT). Usually, filling pressure is not elevated as long as there is adequate diastolic filling time. As diastolic filling pressure increases, E velocity increases, duration of late diastolic velocity (A) becomes truncated (right), and DT becomes shortened. When filling pressure is markedly elevated, there may be diastolic mitral regurgitation (arrow in the right figure). Reproduced with permission from Oh JK, Seward JB, Tajik AJ, editors. Echo Manual. 2nd edition. Philadelphia, PA: Lippincott, Williams, and Wilkins, 1999.
recording of adequate mitral inflow where the duration of
the mitral A-wave can be measured is readily and reproduc-
ibly obtained by all trained sonographers or physicians. A
pulmonary venous recording also can be obtained in the vast
majority of patients, although it may be technically chal-
lenging, especially in patients with marked dilation of both
the LV and left atrium (16). These measurements are not
used “as a surrogate index of diastolic function” but as an
indication of abnormal increase in LV pressure with atrial
contraction, thus a measure of decrease in compliance. With
progressive decrease in compliance, an abnormal increase in
LV pressure occurs earlier in diastole, resulting in the
shortening of the DT and the IVRT and an increase in the
mitral E velocity (Fig. 1).

Furthermore, filling pressure can be estimated by echo-
cardiography in most patients. Mitral inflow DT correlates
well with pulmonary capillary wedge pressure when EF is
reduced (17,18). When filling pressures are markedly ele-
vated, the mitral inflow velocity pattern becomes “restrictive,” with shortened IVRT, increased E velocity, decreased
A velocity, and shortened (<140 ms) deceleration time. It is
ture that mitral inflow velocity pattern of restrictive physi-
ology is largely determined by the increased filling pressure,
but myocardial relaxation is almost always abnormal (i.e.,
decreased Ea and Vp) in patients with the restrictive mitral
inflow velocity pattern (8,19,20).

Because mitral E velocity increases and relaxation-related
parameters (Ea and Vp) are reduced when filling pressure is
increased, the E/Ea or E/Vp ratio can estimate ventricular
filling pressure or pulmonary capillary wedge pressure with
a reasonable accuracy over a wide range of EFs (19–23). In
intensive care unit patients, E/Ea was found to have a better
correlation than B-type natriuretic peptide with pulmonary
capillary wedge pressure (24). Mitral inflow velocities from
the patients with moderately increased filling pressures may
appear similar to those of healthy individuals because of the
opposing effects of abnormal relaxation and increased filling
pressure on the mitral inflow velocity signal, but the mitral
A-wave is abbreviated, and their two-dimensional echocar-
diography, Ea, and Vp are distinctly different (Figs. 1 and 3).
A reversal in E/A or E/A less than 1 in mitral inflow
indicates impaired myocardial relaxation without significant
elevation of left atrial pressure, which suggests that the
increased \( \tau \) or impaired relaxation alone is not sufficient
to produce symptomatic heart failure. However, a subset of the
patients normal resting left atrial pressure and impaired
relaxation can increase their left atrial pressure with exercise,
increased heart rate, or increased afterload (12,25). Al-
though many Doppler diastolic parameters are influenced by
filling pressures (preload dependency), which is used as a
criticism of the technique by some, this preload dependency
is, in fact, a strength because the ratio between mitral inflow
velocity and relatively preload independent Ea or Vp allows
echocardiography to estimate filling pressures (19,20). An-
other important clinical contribution of Ea and Vp is to help
identify patients with constrictive pericarditis and to differ-
entiate it from DHF due to a myopathy (26–28).

Mauer et al. (1) stated that “the Doppler filling profile
does not provide any insights into the relative position of
EDPVR”, and “abnormal diastolic Doppler pattern provide
Figure 3. (A) End-diastolic pressure and volume relationship (EDPVR) curve. Modified from Mauer et al. (1). The EDPVR is shifted left-upward for diastolic dysfunction or diastolic heart failure and is shifted right-downward for remodeled heart. Inserted in the figure are mitral inflow and mitral septal annulus velocity recording for normal, diastolic dysfunction, and remolding groups. Mitral inflow velocity may appear similar in all three groups, but myocardial relaxation (hence, mitral annulus early diastolic velocity) is almost always reduced in patients with diastolic dysfunction or remodeling. Patients with diastolic dysfunction or remodeling may not be distinguished by mitral inflow and mitral annulus velocities, but the distinction is obvious when interpreted with two-dimensional echocardiography, as shown in (B). Top panel shows three mitral inflow velocity recordings from normal subject (center), a patient with diastolic heart failure (left), and a patient with left ventricular (LV) remodeling after myocardial infarction (right). In the first two, it is difficult to tell their diastolic function or filling pressures by mitral inflow velocity pattern alone. On the right, both deceleration time and atrial flow duration were shortened indicating marked elevation of LV diastolic pressure. The middle panel shows tissue Doppler velocity recording from the septal corner of respective individuals with mitral inflow velocities shown on the top panel. In the middle column, mitral annulus early diastolic velocity (Ea) is normal (11 cm/s), indicating that myocardial relaxation is normal with normal filling pressure (E/Ea = 80/11 = 8). In the left column, Ea is markedly reduced to 5 cm/s with E/Ea of 20 (100/5). On the right, Ea is delayed and fused with late diastolic velocity occurring after biphasic isovolumic velocities. On the basis of mitral inflow velocity and tissue Doppler mitral annulus velocity, the patients in the left and right column were found to have increased filling pressure and abnormal relaxation of LV. However, their underlying reason for increased filling pressure is not clear without structural information, shown at the bottom. Two-dimensional echo shows completely normal cardiac structures for normal subject at the center, abnormal heart (increased wall thickness and enlarged left atrium), but normal LV size and ejection fraction (in real time) in the left typical of diastolic heart failure with leftward/upward-shifted EDPVR and abnormal heart (enlarged LV size and reduced ejection fraction in real time) on the right typical of remodeling with rightward/downward-shifted EDPVR.
no insight into changes of EDPVR.” It should be noted, however, that the mitral inflow velocity is not analyzed in isolation; instead, it should always be interpreted in conjunction with information from two-dimensional and M-mode echocardiography such as LV size, wall thickness and motion, and LA volume. As for the relative position of the EDPVR (for example, restrictive cardiomyopathy compared with dilated cardiomyopathy, or leftward/upward-shifted EDPVR vs. rightward/downward-shifted EDPVR), it is not difficult to appreciate the difference in EDPVR in these conditions with the additional information from two-dimensional echocardiography. The schematics shown in Figure 3 of the Mauer et al. paper (1) only show the changes that appear with no shift in the EDPVR; therefore, it is not what it is in real life with a variable degree of abnormal relaxation in most, combined with no, or mild-to-marked decrease in compliance. The interplay between the basic diastolic properties and the filling pressure can be appreciated by the combined assessment of mitral inflow, tissue Doppler, and two-dimensional imaging. Mauer et al. (1) fail to recognize the difference between measuring an elevated level of diastolic pressure and assessment of abnormal pressure increase during diastole indicating reduced compliance.

Limitations also exist when using EDPVR, which Mauer et al. (1) use as the index to define diastolic dysfunction. Although the EDPVR describes a very important diastolic property of the ventricle, it is not the only determinant of filling. The diastolic P-V trajectory frequently is very different from the EDPVR. In the intact circulation, the diastolic trajectory is subject to substantial shifts. In this regard, slow relaxation, subendocardial ischemia, and external constraints can change LV pressure throughout diastole, not just during late diastole. The operating stiffness of the LV (change in pressure/change in volume) may have a greater impact on LV filling than the absolute position of the EDPVR curve (29), and it can be assessed by Doppler as discussed previously. There also are practical limitations to the EDPVR curve. It is difficult, if not impossible, to determine the EDPVR accurately in a patient. Furthermore, there is no clear determination of what a normal end-diastolic P-V relation actually is.

Finally, no patient has ever come into a physician’s office complaining of a slow τ, reduced Ea, or an abnormal end-diastolic P-V relation. However, their symptoms may be direct consequences of being unable to augment cardiac output without an elevated left atrial pressure, which can be demonstrated by echocardiography. The relative position of EDPVR cannot be defined by Doppler echocardiography alone, as suggested by Mauer et al. (1), but the position of the EDPVR is obvious if Doppler parameters are interpreted in the context of other echocardiographic as well as clinical information (Fig. 3).

### Table 1. Examples of Heart Failure With Normal Left Ventricular Ejection Fraction

<table>
<thead>
<tr>
<th>Type of Heart Failure</th>
<th>Example</th>
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<tbody>
<tr>
<td>Diastolic heart failure</td>
<td>Hypertension</td>
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<td>Restrictive cardiomyopathy</td>
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<td>Infiltrative cardiomyopathy</td>
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<td>Hypertrophic cardiomyopathy</td>
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<td>Noncompaction cardiomyopathy</td>
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<td>Right heart failure</td>
<td>Severe pulmonary hypertension</td>
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<td>Right ventricular infarct</td>
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<td>Arterialgenic right ventricular dysplasia</td>
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<td>Atrial septal defect</td>
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<tr>
<td>Valvular heart diseases</td>
<td>Severe valvular stenosis</td>
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<td></td>
<td>Severe valvular regurgitation</td>
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<td>Pericardial disease</td>
<td>Cardiac tamponade</td>
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<td></td>
<td>Constrictive pericarditis</td>
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<td>Intracardiac mass</td>
<td>Atrial myxoma</td>
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<td></td>
<td>Apical eosinophilic thrombus</td>
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<td>Pulmonary vein stenosis</td>
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<td>Congenital heart diseases</td>
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### DHF or HFNEF

There is a considerable debate regarding the use of the term DHF to describe the patients with a normal LVEF who have symptoms and signs of heart failure (1,30,31). Mauer et al. (1) argued against using the terminology of DHF in their viewpoint and suggested using the term “heart failure with normal ejection fraction” (1). There are many clinical conditions that cause heart failure with normal EF (Table 1). However, abnormal diastolic function is the most common cause of heart failure with normal EF, which is easily diagnosed by echocardiography in a patient with a preserved LVEF with an evidence of abnormal relaxation, decreased compliance, and increased filling pressure and normal LV dimensions. This is what we term DHF.

Diasstolic heart failure has multiple potential etiologies, such as systolic hypertension, restrictive cardiomyopathy, coronary artery disease, cardiac amyloidosis, and genetically determined cardiomyopathy. Once DHF is diagnosed by two-dimensional and Doppler echocardiography, additional diagnostic procedures usually are necessary to identify its underlying etiology. The management of DHF requires a treatment of the underlying etiology as well as symptoms. For management of patient’s symptoms, comprehensive echo/Doppler evaluation may point to rational therapy. If the main diastolic abnormality is impaired myocardial relaxation, the treatment may be focused on improving relaxation and providing an adequate diastolic filling period not only at rest but also with exercise. The use of an angiotensin-converting enzyme inhibitor, an angiotensin receptor blocker, or an aldosterone antagonist, which also may regress hypertrophy and reduce fibrosis is attractive (32–34) but needs to be validated in large clinical trials. Ultimately, a therapy to improve myocardial relaxation without producing other untoward effects should be an ideal...
agent, but such medication is not yet available clinically. However, if reduced compliance is a major component of heart failure, a patient may not tolerate reduction in heart rate because stroke volume is usually fixed.

Because it has been shown that the presence of even a mild form of diastolic dysfunction in asymptomatic subjects indicates a five-fold increase in mortality compared with the asymptomatic subjects with normal diastolic function (35), underlying etiologies for diastolic dysfunction should be aggressively sought and treated. Ongoing and future clinical trials will guide us in selecting an optimal treatment strategy. Echocardiography is the most widely available and comprehensive diagnostic tool to identify such populations with intrinsic diastolic dysfunction who are at increased risk of morbidity and mortality on a routine basis noninvasively.

We agree with Mauer et al. (1) that DHF should be reserved for heart failure caused by an abnormality of diastolic function of the heart but, contrary to their view, a great deal of evidence exists in support of the fact that echocardiography indeed can reliably detect and grade the severity of diastolic dysfunction, estimate filling pressure, and provide prognostic insights for DHF as well as for systolic heart failure (18,33,36–38). To date, no other diagnostic modality has provided so much practical and clinically relevant information about DHF that echocardiography has provided in the past two decades.

CONCLUSIONS

Heart failure with normal EF includes many non-myocardial, as well as myocardial abnormalities, which can cause heart failure with normal EF. On the other hand, DHF accurately denotes the patient population who presents with symptoms and signs of heart failure, normal EF, increased filling pressure, and evidence of diastolic dysfunction, but without other non-myocardial abnormalities responsible for heart failure. In patients with clinical evidence of heart failure, normal EF on two-dimensional echocardiography immediately suggests the potential diagnosis of DHF. Doppler, color flow imaging, and myocardial tissue imaging can confirm or exclude the diagnosis of DHF by assessing intrinsic diastolic function and estimating diastolic filling pressure. Early identification of diastolic dysfunction in asymptomatic patients by echocardiography may provide an opportunity to manage the underlying etiology appropriately to prevent its progression to DHF.

REFERENCES


