Diastolic heart failure (DHF) and systolic heart failure (SHF) are 2 clinical subsets of the syndrome of heart failure that are most frequently encountered in clinical practice. That these 2 forms of heart failure exist was recognized by Dr. Fishberg almost 70 years ago, as reported by Katz and Zile in a recent editorial. Dr. Fishberg wrote “those forms of cardiac insufficiency which are due to inadequate diastolic filling of the heart (hypodiastolic failure) [and] the far more common ones in which the heart fills adequately but does not empty to the normal extent (hyposystolic heart failure).” However, confusions and controversies regarding the definitions, pathophysiology, prognosis and management of DHF and SHF continue.

Definitions and Diagnosis

In the Webster Dictionary diastole is defined as “the dilatation of the heart with blood: opposed to systole, or contraction.” Conventionally, the closure of the aortic valve is regarded to indicate the onset of diastole as it indicates the onset of ventricular relaxation phase. Because left ventricular ejection influences relaxation and the rapid filling, it has been suggested that these phases should be considered phases of systole. The most commonly accepted view, however, is that the rapid filling phase is part of diastole.

Several definitions of DHF have been proposed. One definition is “a condition resulting from an increased resistance to filling of one or both ventricles leading to symptoms of congestion due to an inappropriate upward shift of the diastolic pressure-volume relation (that is, during the terminal phase of the cardiac cycle).” Another proposed definition is that diastolic heart failure is a condition in which the “ventricular chamber is unable to accept an adequate volume of blood during diastole at normal diastolic pressures and at volumes sufficient to maintain an appropriate stroke volume.” These definitions describe the functional abnormalities, but cannot be applied in clinical practice. Many clinical definitions of diastolic heart failure have been suggested. Zile and Brutsaert proposed a definition, which is “a clinical syndrome characterized...
by the symptoms and signs of heart failure, a preserved ejection fraction (EF), and abnormal diastolic function."

Other definitions such as “heart failure with preserved systolic function” or “heart failure with normal or near normal ejection fraction” have also been used.

Several definitions of systolic heart failure also exist. In 1933, Sir Thomas Lewis defined heart failure as “a condition in which the heart fails to discharge its contents adequately.” In 1980, Dr. Braunwald described heart failure as “a pathophysiological state in which an abnormality of cardiac function is responsible for the failure of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues.” Although these definitions describe the pathologic mechanisms, it is difficult to employ in clinical practice. Thus it is preferable to use the terms “diastolic” and “systolic” heart failure as these definitions describe the principal mechanisms.

Systolic and Diastolic Dysfunction and Clinical Heart Failure

Systolic dysfunction from impaired contractile or pump function and diastolic dysfunction from impaired ventricular relaxation, compliance or filling are not always associated with clinical heart failure characterized by signs and symptoms of low cardiac output or of congestion. Furthermore, in SHF, diastolic dysfunction as assessed by changes in the ventricular filling features is common, particularly in advanced heart failure. In diastolic heart failure, left ventricular systolic performance, function and contractility in general, remain normal. In some studies, long-axis systolic dysfunction has been observed.

Diagnosis

Based on the proposed definitions, it appears that for establishing the diagnosis of DHF or SHF, it is only necessary to measure left ventricular ejection fraction after confirming the presence of heart failure. If ejection fraction is preserved it is DHF, and if reduced it is SHF. It is highly desirable to establish the normal range of ejection fraction for any technique employed, preferably under similar loading conditions. It should be appreciated that signs and symptoms, radiologic and electrocardiographic findings and neurohormonal profile cannot distinguish between DHF and SHF.

Is Cardiac Catheterization Necessary?

Coronary angiography is occasionally indicated when myocardial ischemia is strongly suspected, irrespective of type of heart failure. Similarly, endomyocardial biopsy is rarely necessary to establish the etiology of heart failure. Cardiac catheterization is not necessary to assess ejection fraction, contractile function, or diastolic functions.

Incidence, Prevalence, and Prognosis

The incidence and prevalence of both SHF and DHF is considerable and increasing. The recent epidemic increase in heart failure in older population appears to be related both to increase in the incidence and improved survival. The incidence of systolic and diastolic heart failure has been reported to be 61% to 68% and 16% to 39%, respectively. The cross-sectional population echocardiographic studies have reported that of patients diagnosed with heart failure, 40% to 71% have DHF.

Natural History of Asymptomatic Systolic and Diastolic Dysfunction

Asymptomatic left ventricular systolic dysfunction constitutes Stage B systolic heart failure. The prevalence of Stage B systolic heart failure in the community is between 3% and 6%. The risk of development of symptomatic heart failure is reported to be between 5.1% and 10.5%.

The echo-Doppler studies have reported that patients with asymptomatic left ventricular diastolic dysfunction have a higher incidence of all-case mortality adjusted for age, sex, and ejection fraction. Mild diastolic dysfunction was associated with 8.3-fold, and moderate-to-severe dysfunction with 10.2-fold increased risk of mortality.

Natural History in Symptomatic Patients

The overall mortality of symptomatic patients with DHF or SHF is very similar and is related to the functional class. In patients with New York Heart Association Class II and III DHF, an annual mortality rate of 3.8% was observed. In patients who required hospital admissions for treatment, 1-year all cause death was 27% in DHF and 36% in SHF (Fig. 1).

Mode of Death

In systolic heart failure approximately 50% of deaths are sudden and the rate of sudden death in systolic heart failure is 6 to 9 times higher compared with that in the general population. Interestingly, with the increased severity of systolic heart failure (New York Heart Association IV), incidence of sudden cardiac death decreases. The absolute rates of pump failure death and sudden cardiac death increases with decreasing left ventricular ejection fraction. However, it has been reported that the risk of sudden cardiac death is better correlated to left ventricular mass than to the ejection fraction. The left ventricular mass is increased considerably in both DHF and SHF; thus, the risk assessment for sudden cardiac death based on ejection fraction alone may not be appropriate. In a recent report, the risk of sudden cardiac death was found to be only 7% among 2314 patients, compared with death from other causes, which was 93%.
Risk Factors

Older age, hypertension, diabetes, obesity, and coronary artery disease are risk factors for both DHF and SHF. Although DHF is more common in elderly females, diastolic dysfunction is more common in elderly males. In DHF, hypertension is a more common risk factor. However, a substantial proportion of patients with SHF have a history of hypertension. In SHF, ischemic heart disease is the most common etiology, but many patients with DHF have coronary artery disease. In decompensated heart failure, 63% of patients with systolic and 54% of patients with diastolic heart failure have coronary artery disease. Thus, for prevention, modification of the same risk factors should be employed in both DHF and SHF.

Remodeling

The distinctive features of remodeling in DHF and SHF are summarized in Table 1 and illustrated in Fig. 2. In SHF, the left ventricular cavity size is increased with an increase in both end-diastolic and end-systolic volumes, decreased or unchanged wall thickness, increased wall stress, and reduced ejection fraction. The mass is increased, but the mass/cavity ratio remains unchanged or is decreased. In SHF, there is an alteration in ventricular shape and geometry with a greater increase in transverse than in long axis, and mechanical dyssynchrony with or without electrical dyssynchrony occur in a substantial number of patients. In DHF, the cavity size remains unchanged or may even decrease, and the end-diastolic and end-systolic volumes remain normal or decrease. In DHF, there is usually an increase in wall thickness and mass; however, mass/cavity ratio is substantially increased. In DHF, end-diastolic wall stress is increased and systolic wall stress remains normal and ejection fraction remains normal or may even be higher than normal. The left ventricular morphologic and functional changes in DHF and SHF compared to controls as evaluated by echocardiographic studies are summarized in Table 2.

The differences in the structural changes in systolic and diastolic heart failure are summarized in Table 3 and illustrated in Fig. 3. In SHF there is myocyte lengthening and an increase in myocyte length/width ratio. The sarcomeres are replicated in parallel. In DHF there is an increase in the myocyte cross-sectional area with little or no change in its length/width ratio. The sarcomeres are replicated in parallel. The abnormality in calcium regulation occurs in both types of heart failure. Increased collagen volume and fibrosis occur in both but the character and degree of fibrosis appear to be different. In animal models, in SHF, there is degradation and disruption of fibrillar collagen; in contrast, in the pressure-overloaded hypertrophy which is associated with diastolic failure, there is an increase in collagen with increased width and continuity of the fibrillar collagen. The collagen cross links are decreased in SHF and increased in DHF. In general the matrix metalloproteinases

![Fig. 1. One-year mortality morbidity in patients with severe systolic (open bar) and diastolic (closed bar) heart failure. Although the mortality morbidity rate in patients with preserved systolic function is lower than that of patients with reduced systolic function, the mortality rate in both groups with severe heart failure was high. (Published with permission of Dauterman KW, Go AS, Rowell R, Gebretsadik T, Gettner S, Massie BM. Congestive heart failure with preserved systolic function in a statewide sample of community hospitals. J Card Failure 2001;7:221–8.)](image-url)

Table 1. Morphologic and Functional Changes in Diastolic vs Systolic Heart Failure

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Diastolic Heart Failure</th>
<th>Systolic Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular cavity size</td>
<td>Normal or decreased</td>
<td>Increased</td>
</tr>
<tr>
<td>Left ventricular mass</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Mass/cavity</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Wall thickness</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>End-diastolic stress</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>End-systolic stress</td>
<td>Normal</td>
<td>Increased</td>
</tr>
<tr>
<td>End-diastolic volume</td>
<td>Normal</td>
<td>Increased</td>
</tr>
<tr>
<td>End-systolic volume</td>
<td>Normal or decreased</td>
<td>Increased</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Mechanical dyssynchrony</td>
<td>May be present</td>
<td>May be present</td>
</tr>
<tr>
<td>Left ventricular shape and geometry</td>
<td>Usually remains</td>
<td>Spherical</td>
</tr>
</tbody>
</table>


are increased in SHF and decreased in DHF. In contrast, their endogenous tissue inhibitors tend to decrease in SHF and increase in DHF.\textsuperscript{37,38} Other biochemical evidences for abnormal collagen metabolism such as increased circulating levels of amino-terminal propeptide of Type III procollagen have been reported in systolic heart failure.\textsuperscript{39} The titin isoforms N2BA/N2B ratio is decreased in systolic failure and it is increased in diastolic failure.\textsuperscript{5} Left ventricular endomyocardial biopsy studies have reported an increase in myocyte diameter and less decrease in myocyte volume in DHF compared with SHF, whereas collagen volume fractions increased in both types.\textsuperscript{40}

The initiating stimuli for remodeling in SHF and DHF have not been clearly delineated. In SHF, after acute myocardial infarction, the extent of myocardial injury and the magnitude of left ventricular systolic dysfunction appear to be the major determinants. A small infarct and relatively preserved ejection fraction is not usually associated with ventricular remodeling.\textsuperscript{41,42} Abnormal neurohormonal activation has also been implicated as a major mechanism for progressive remodeling in systolic heart failure.\textsuperscript{43}

In DHF, the stimuli for ventricular remodeling remain unclear. The pressure overload resulting from hypertension

Table 2. Echocardiographic Left Ventricular Morphologic and Functional Characteristics in Primary Systolic and Diastolic Heart Failure Compared With Controls

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Systolic Heart Failure</th>
<th>Diastolic Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV (mL)</td>
<td>102 ± 12</td>
<td>192 ± 10*</td>
<td>87 ± 10</td>
</tr>
<tr>
<td>LVESV (mL)</td>
<td>46 ± 11</td>
<td>137 ± 9*</td>
<td>37 ± 9</td>
</tr>
<tr>
<td>LVEF %</td>
<td>54 ± 2</td>
<td>31 ± 2*</td>
<td>60 ± 2\textsuperscript{1}</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>125 ± 12</td>
<td>232 ± 9*</td>
<td>160 ± 9\textsuperscript{1}</td>
</tr>
<tr>
<td>LV mass/volume</td>
<td>1.49 ± 0.17</td>
<td>1.22 ± 0.14</td>
<td>2.12 ± 0.14\textsuperscript{1}</td>
</tr>
<tr>
<td>NE pg/mL</td>
<td>169</td>
<td>287</td>
<td>306; (P = .007)</td>
</tr>
<tr>
<td>BNP pg/mL</td>
<td>3</td>
<td>28</td>
<td>56; (P = .02)</td>
</tr>
</tbody>
</table>

Adapted from Kitzman DW, et al. JAMA 2002;288:2144−50.\textsuperscript{11} LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction; LV, left ventricle; NE, norepinephrine; BNP, B-type natriuretic peptide.

\*Systolic heart failure vs. controls, \(P < .001\).

\textsuperscript{1}Diastolic heart failure vs. controls, \(P < .001\).

\textsuperscript{1}Diastolic heart failure vs. controls, \(P < .002\).

Table 3. Diastolic and Systolic Heart Failure Remodeling: Myocyte and Matrix Changes

<table>
<thead>
<tr>
<th></th>
<th>Systolic Heart Failure</th>
<th>Diastolic Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocyte</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertrophy</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Apoptosis</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Necrosis</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Myocardial fibrosis</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Calcium regulation</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>MMPs/TIMPs</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Collagen cross-links</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>Titin isoforms N2BA/N2B</td>
<td>−</td>
<td>+</td>
</tr>
</tbody>
</table>

+, increased; −, decreased or impaired; MMPs, matrix metalloproteinases; TIMPs, tissue inhibitors of metalloproteinases.
and obesity associated with concentric hypertrophy is likely to be an important contributing factor. Neurohormonal abnormalities, similar to those observed in systolic heart failure, occur in DHF. Thus neurohormonal abnormalities do not explain differences in ventricular remodeling in DHF and SHF. It is possible that neurohormonal abnormalities produce different substrate response in DHF and SHF.

### Functional Changes

In SHF, impaired contractile function is the principal functional derangement and is the major mechanism for reduced ejection fraction (Fig. 3). The other mechanism for reduced ejection fraction in SHF is increased wall stress. Diastolic function, as assessed by echo-Doppler studies, is frequently abnormal in patients with overt SHF. Impaired left ventricular relaxation and increased passive stiffness is the principal functional derangement in DHF. The pressure-volume relation during diastole shifts upward and to the left (Fig. 4); as a result there is a disproportionately greater increase in diastolic pressure for any increase in volume.

The hemodynamic profile may be similar in SHF and DHF. In SHF, reduced ejection fraction results in a decrease in stroke volume and cardiac output. Increased left ventricular end-diastolic volumes and often associated abnormal

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**Fig. 3.** Changes in myocytes (left) and in extracellular matrix (right) in systolic heart failure resulting from dilated cardiomyopathy, and diastolic heart failure resulting from pressure over load compared with normals in animal models. In systolic heart failure, the myocyte length is increased without any change in the cross-sectional area; in diastolic heart failure, the cross-sectional area of the myocyte is increased without a significant change in its length. In systolic heart failure, collagen degradation and disruption occur; in diastolic heart failure, there is increased width and continuity of fibrillar collagen. (Reprinted with permission.)

**Fig. 4.** Schematic diagram of pressure-volume relations in normals, systolic and diastolic heart failure. In systolic heart failure, a downward and rightward shift of the end-systolic pressure-volume line indicates decreased contractile function, which is the principal cause of reduced ejection fraction and forward stroke volume. In primary diastolic heart failure, diastolic pressure-volume relation (dashed line) shifts upward and to the left, indicating a disproportionate and a greater increase in diastolic pressure for any increase in diastolic volumes. If there is also a decrease in end-diastolic volume, then a decrease in stroke volume also occurs. (Reprinted with permission.)
diastolic filling result in increased left ventricular diastolic pressure, a passive increase in left atrial and pulmonary venous pressure, and postcapillary pulmonary arterial hypertension. Right ventricular failure and systemic venous hypertension and its hemodynamic and clinical consequences occur.

In DHF, because of the disproportionate increase in left ventricular diastolic pressure, there is an increase in left atrial and pulmonary venous pressure that is associated with symptoms and signs of pulmonary venous congestion (Fig. 5). Postcapillary pulmonary hypertension resulting from increased pulmonary venous pressure may precipitate right heart failure. Left ventricular stroke volume and cardiac output may also decline because of decreased end-diastolic volume (preload dependent). Chronic elevation of pulmonary venous pressure may be associated with increased pulmonary vascular resistance from secondary pulmonary vasoconstriction, which may occur in both SHF and DHF.

**Does Left Ventricle Dilate in Diastolic Heart Failure?**

Left ventricular dilation always occurs in SHF. In DHF, however, left ventricular dilation does not appear to occur without an additional insult such as myocardial infarction. In some patients with DHF without coronary artery disease, serial assessment of ventricular volumes and pressures and stiffness have been performed; end-diastolic volumes and ejection fraction remain unchanged, but end-diastolic pressure and stiffness index increase, suggesting that in DHF ventricular dilatation does not occur and worsening diastolic function is the mechanism for development and progression of heart failure (Table 4). Thus left ventricle size remains unchanged and it does not dilate without an ischemic insult.

**Differences in Therapeutic Options**

Although there have been considerable advances in the treatment of SHF, very little progress has been made in the management of DHF. The improvement in prognosis in SHF is most likely related to the therapeutic discoveries that have been observed to attenuate adverse remodeling and improve hemodynamic abnormalities. The neurohormonal modulators such as renin-angiotensin-aldosterone and adrenergic antagonists clearly improve symptoms and quality of life and decrease mortality. So far no such therapies have been discovered for improving prognosis in patients with DHF. Angiotensin receptor blocking agents have the potential for decreasing morbidity but not mortality. It has been reported that statin therapy has the potential to decrease mortality of patients with DHF. Statin therapy is also associated with lower mortality in SHF.

Chronic resynchronization therapy with or without implantable cardioverter defibrillator improves prognosis of patients with SHF. However, chronic resynchronization therapy has not been shown to produce beneficial effects in DHF. Cardiac transplantation is likely to benefit selected patients either with SHF or DHF.

**Conclusion**

Established clinical systolic and diastolic heart failure appear to be 2 distinct syndromes of chronic heart failure. The myocardial structural and primary functional derangements are distinctive in these 2 syndromes, although hemodynamic consequences, clinical presentations, signs and symptoms, and prognosis are similar. The neurohormonal abnormalities are also similar in both of these syndromes. Although there have been considerable advances in the
management of systolic heart failure, the management of DHF remains primarily to relieve symptoms. Because of inadequate knowledge of the molecular and biochemical mechanisms of the structural remodeling and principal functional derangement in diastolic heart failure, treatments to improve prognosis have not evolved. Thus further basic science and clinical research is urgently required. However, potential exists for discovery of therapeutic agents to improve fundamental abnormalities of the cytoskeleton and myocardial architecture and thereby decrease myocardial stiffness—the principal functional derangement in diastolic heart failure. Until then the treatment of diastolic heart failure will remain empirical.

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