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Diastolic and Systolic Heart Failure — Similarities and Differences – Part I

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Diastolic and systolic heart failure, the two clinical subsets of the syndrome of heart failure (HF), are frequently encountered in clinical practice. There are considerable similarities, as well as some important differences between the two entities in terms of their pathophysiology and clinical profile. In this issue of *Cardiology Rounds*, Part 1 of this topic focuses on the definition and diagnosis, incidence and prevalence, and prognosis and natural history of diastolic and systolic HF. It will conclude by introducing a section describing the changes in ventricular function, hemodynamics, and remodeling. Part 2, in the next issue, will continue the discussion, describing matrix architectural changes, abnormalities in collagen synthesis, and the therapeutic options available for diastolic heart failure.

Definitions and diagnosis

Diastolic heart failure

There are controversies, not only regarding the definition and diagnosis of diastolic HF, but also the onset, duration, and phases of diastole. Conventionally, closure of the aortic valve is regarded to indicate the onset of diastole.¹ However, left ventricular (LV) ejection is completed before the aortic valve closes and it has been suggested that the isovolumic relaxation and rapid filling phases should be considered phases of systole, rather than of diastole.² The other view is that the onset of diastole coincides with the opening of the mitral valve and that, therefore, the rapid filling phase is part of diastole.³

There is also considerable controversy about how to define diastolic heart failure. Both pathophysiologic and clinical definitions have been proposed. For example, Brutsaert et al proposed this pathophysiologic definition: “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).”²⁷ Another pathophysiologic definition was proposed by Zile and Brutsaert: “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.”⁴

It is apparent that, although these pathophysiologic definitions describe the functional abnormalities, they cannot be applied during everyday clinical practice. Many clinical definitions of diastolic HF have also been suggested. Zile and Brutsaert⁴ proposed this clinical definition: “a clinical syndrome characterized by the symptoms and signs of HF, a preserved ejection fraction (EF), and abnormal diastolic function.” Other definitions such as “HF with preserved systolic function” or “HF with normal or near-normal EF” have also been proffered.

Systolic heart failure

Several definitions of systolic HF have also been suggested. In 1933, Sir Thomas Lewis defined HF as “a condition in which the heart fails to discharge its contents adequately.”⁵ In 1980, Professor Eugene Braunwald described HF 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.”⁶ After the neurohormonal dysfunction in HF was recognized, Professor Philip A. Poole-Wilson defined HF as “a clinical syndrome caused by an abnormality



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of the heart and recognized by a characteristic pattern of hemodynamic, renal, neural, and hormonal responses.⁷ And, in 1988, Professor Jay Cohn suggested that HF should be defined as “a syndrome in which cardiac dysfunction is associated with reduced exercise tolerance, a high incidence of ventricular arrhythmias, and shortened life expectancy.”⁸ The Task Force of the European Society of Cardiology defined HF “as a condition when symptoms of HF, objective evidence of cardiac dysfunction, and response to treatment directed towards HF exist.”⁹

The definitions above were proposed to recognize systolic HF, since diastolic HF was only appreciated rather recently. The contemporary clinical definition of systolic HF is “a clinical syndrome associated with congestive symptoms and/or symptoms of low cardiac output due to impaired ventricular pump function (reduced EF).”

Distinguishing between diastolic and systolic heart failure

For the diagnosis of either systolic or diastolic HF, it is necessary to establish the presence of HF. HF is a clinical diagnosis, based on an analysis of the symptoms and signs of HF. **In clinical practice, Framingham or Boston criteria can be applied.^{10,11} The signs and symptoms are remarkably similar in systolic and diastolic HF.** Findings of systemic and pulmonary venous hypertension, pulmonary arterial hypertension, and secondary tricuspid regurgitation can be present in both types, particularly with overt and severe HF. Interestingly, in a considerable proportion of patients with diastolic HF, S3 gallop can be recognized.⁴ Radiologic findings of chamber enlargement and pulmonary venous hypertension cannot be used to distinguish between systolic and diastolic HF and there are no specific electrocardiographic findings that are characteristic of systolic or diastolic HF. The presence of HF, however, can be established by clinical evaluation in the vast majority of patients.

Various criteria have been proposed to distinguish between systolic and diastolic HF. For systolic HF, it is necessary to document that the LV ejection fraction (LVEF) is less than normal. Although decreased contractile function is the predominant cause of reduced LVEF, it is not necessary to assess contractile function for the diagnosis of systolic HF. Furthermore, in experimental post-infarction systolic HF with remodeling, myocyte contractile function may remain normal, even when the LVEF is reduced.¹² Diastolic dysfunction, as assessed by changes in the transmitral Doppler flow profile, is frequent in patients with advanced systolic HF.¹³

If “heart failure with preserved ejection fraction” is interchangeably used with “diastolic heart failure,” it is obvious that it is necessary only to establish that the LVEF is normal or near normal. The presence of diastolic dysfunction should not necessarily be a mandatory criterion for the diagnosis of the etiology of HF. On the other hand, for the diagnosis of primary diastolic HF, it is necessary not only to confirm that LVEF is preserved, but also that significant diastolic dysfunction is present.

It should be emphasized that clinical HF with preserved LVEF and without significant diastolic dysfunction is uncommon. Some patients with “high output failure” (chronic severe

anemia, hyperthyroidism, congenital arterio-venous communications) may have this functional profile. However, the vast majority of patients with clinical HF and preserved LVEF have intrinsic LV diastolic dysfunction, such as impaired active relaxation and increased passive stiffness.¹⁴ Thus, the term “diastolic heart failure” is appropriate to define this clinical subset of HF.

Vasan and Levy¹⁵ proposed the diagnostic criteria for “definite” diastolic HF. It requires definitive evidence of HF, normal or mildly abnormal LVEF, and evidence of abnormal LV relaxation, filling, diastolic distensibility, or diastolic stiffness. The European criteria¹⁶ are very similar to those of Vasan and Levy, but appear to be more specific. The requirements are:

- signs or symptoms of congestive HF
- normal or mildly reduced LV systolic function and normal chamber size
- abnormal LV relaxation, filling, and diastolic stiffness.

Vasan and Levy¹⁵ recommend cardiac catheterization to assess diastolic dysfunction, whereas the European recommendations¹⁶ allow echocardiographic and Doppler studies to document abnormalities in diastolic function. Obviously, cardiac catheterization is invasive, expensive and, therefore, impractical. But echocardiography is inexpensive and noninvasive, and therefore, very practical for clinical use. However, there has been controversy about whether or not an assessment of diastolic function is mandatory for the diagnosis of primary diastolic HF.¹⁷ Documentation of clinical HF, normal LVEF, and chamber size are sufficient, and demonstration of LV hypertrophy, concentric remodeling, and diastolic dysfunction are only confirmatory evidence.¹⁸ To confirm that LVEF and chamber size are normal, a noninvasive test and echocardiography are the most practical methods of diagnosis. Echocardiographic studies not only include the assessment of EF and LV volumes, but also diastolic function and even LV mass and types of ventricular remodeling.

Thus, for practical and clinical purposes, all patients with suspected HF should have echocardiographic studies, not only to assess systolic and diastolic functions, but also to distinguish between systolic and diastolic HF. However, it should be appreciated that neither systolic nor diastolic dysfunction is always associated with clinical HF. It is also necessary to recognize that, although the measurements of brain natriuretic peptide or N-terminal brain natriuretic peptide are helpful for the diagnosis of cardiac or noncardiac dyspnea, they are not useful to distinguish between systolic and diastolic HF.¹⁹

Another practical clinical problem in distinguishing between systolic and diastolic HF is ascertaining what level of EF and which imaging technique should be used to determine EF. In various studies, an EF as high as 50% and as low as 40% has been used to distinguish between systolic and diastolic HF.^{20,21} Furthermore, there are variable methods to assess EF and determinations by echocardiography, radionuclide ventriculography, and angiography can be different. EF is not load-independent and, therefore, acute changes in “loads” can substantially change EF value. In clinical practice, it is unusual to consider changes in loading conditions when determining EF.

Incidence, prevalence, and prognosis

There is ongoing controversy regarding the incidence, prevalence, and prognosis of patients with systolic or diastolic HF. This is due to differences in the definition and diagnostic criteria, as well as variations in the severity of HF used in the various studies. The majority of the studies were retrospective, uncontrolled, and lacked objective criteria to distinguish between systolic and diastolic HF. In many, EF was assessed qualitatively; however, even when a quantitative assessment of EF was performed, various levels of EF were used to separate patients with preserved EF from those with reduced EF. When an EF of 40% is used instead of 50%, the incidence and prevalence of HF with preserved EF and, therefore, of primary diastolic HF, will be considerably higher. Furthermore, the lower the level of EF, the higher the likelihood of remodeling, which is characteristic of systolic HF, to occur.

Nevertheless, irrespective of the level of EF used, the incidence and prevalence of both systolic and diastolic HF is considerable and increasing.²² Recently, Hogg et al reviewed the epidemiology, clinical characteristics, and prognosis of HF with preserved LV systolic function.²³ The incidence of systolic and diastolic HF appears to be 61%-68% and 16%-39%, respectively. Cross-sectional population echocardiographic studies have reported that 40% to 71% of patients with HF have preserved systolic function.

Asymptomatic LV systolic dysfunction is regarded as Stage B systolic HF.²⁴ Its prevalence in the community is high, between 3% to 6%.²⁵ In prospective, randomized, controlled trials, the average annual rate of development of congestive HF in the placebo groups ranged from 20% to 49%, and the average annual mortality rates ranged from 5.1% to 10.5%.²⁵⁻³⁰ Recognition of Stage B systolic HF has important therapeutic implications because appropriate interventions with angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) and beta-adrenergic antagonists can reduce the risk of development of overt HF and mortality.^{26,27,31}

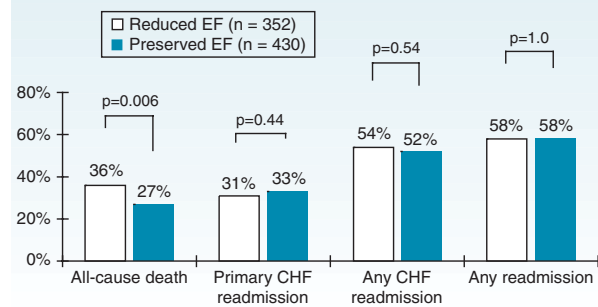
Natural history

The natural history of patients with asymptomatic LV diastolic dysfunction and preserved EF has not been adequately studied and the prevalence and prognosis of such patients remains unclear. This paucity of information is due to the lack of an accepted definition of diastolic dysfunction and HF in prospective controlled studies.^{4,32,33,34} Nevertheless, echocardiographic and Doppler studies have reported that patients with asymptomatic LV diastolic dysfunction have a higher incidence of all-cause mortality adjusted for age, sex, and EF.²¹ Compared to asymptomatic subjects with normal diastolic function, those with mild diastolic dysfunction and moderate-to-severe diastolic dysfunction were associated with an 8.3- and 10.2-fold increased risk of mortality, respectively.²¹

Whether or not there are substantial differences in mortality and morbidity between symptomatic patients with systolic and diastolic HF also remains controversial and unclear. In the Helsinki Aging Study,³⁵ in the patients with overt HF, the 4-year mortality was 43% in patients with preserved systolic function and 54% in those with reduced EF. In the Cardiovascular Health Study,³⁶ the mortality rate was higher in symp-

Figure 1: One-year, all-cause mortality in severe systolic (open bar) and diastolic (closed bar) heart failure.

Although the mortality 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.



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tomatic patients with reduced systolic function than in those with preserved systolic function. In the Framingham Heart Study, congestive HF patients with reduced EF had an annual mortality rate of 18.9% as compared to 8.7% in those with preserved systolic function and clinical HF.³⁷ In patients with severe clinical HF, mortality appears to be higher in patients with reduced EF than in those with preserved systolic function.^{23,38}

Dauterman et al³⁸ reported that in patients with congestive HF requiring hospital admission for treatment, the one-year all-cause death rate was 27% in patients with preserved EF and 36% in those with reduced EF (Figure 1). The prognosis for patients with overt HF remains unfavorable after being discharged from the hospital. The In-CHF Registry reported a one-year mortality rate of 18.8% in patients with an EF of <35%, and 8.9% in patients with an EF >45%.³⁹ In the Acute Decompensated Heart Failure National Registry (ADHERE), hospital mortality rate was also higher in patients with systolic HF (4% vs 3% P ≤ .0001).⁴⁰ It appears that the overall prognosis for patients with systolic HF is somewhat worse than for those with diastolic HF, and the mortality rate increases with increasing severity of clinical HF in both types.

It should be appreciated that considerable advances have been made in the treatment of systolic HF over the last 3 decades that have led to substantial improvements in prognosis. However, no such therapeutic advances have been made in the management of diastolic HF. An analysis of earlier placebo-controlled studies in systolic HF and a recent study in diastolic HF may provide some insight (Table 1).

- In the CONSENSUS 1 trial, patients with severe HF (New York Heart Association [NYHA] Class IV) were enrolled. The estimated first-year mortality in the placebo group in this trial was 52%.⁴¹

- In the SOLVD-Treatment Trial, patients with mild-to-moderately severe (NYHA Class II, III) systolic HF were enrolled. The estimated first-year mortality in the placebo group was 15.7%.⁴²

- In the CHARM-Preserved Trial, mild-to-moderately severe (NYHA II, III) diastolic HF (average EF, 54%) patients were enrolled.⁴³ During the 36.6 months of follow-up, 11.3%

Table 1: Mortality differences in systolic and diastolic heart failure

Trial	Systolic or Diastolic	NYHA Class	Placebo group: First year mortality
CONSENSUS 1 (1987)	Systolic	IV	52%
SOLVD Treatment (1991)	Systolic	II, III	15.7%
CHARM-Preserved (2003)	Diastolic	II, III	Approximately 3.8%

of patients in the placebo group had cardiovascular death (an approximate annual mortality rate of 3.8%).⁴³

These findings confirm that, in general, the prognosis for patients with diastolic HF is better than that for patients with systolic HF.

Mode of death

There is insufficient information regarding the mode of death in diastolic HF. In patients with systolic HF, up to 50% of deaths are sudden and unexpected; while in those with HF, the rate of sudden cardiac death is 6 to 9 times higher than in the general population.⁴⁴ With increasing severity of clinical HF, the incidence of sudden cardiac death decreases and the incidence of pump failure death increases.⁴⁵ Lower EF and increasing cardiotoracic ratio are associated with an increased risk of sudden cardiac death.⁴⁶

Although the incidence of late sudden death in post-myocardial infarction patients with normal LVEF has been reported to be as high as 50%, it is not apparent if these patients had clinical diastolic HF. Ventricular hypertrophy, regardless of etiology (hypertension, valvular or hypertrophic cardiomyopathy) is associated with a higher incidence of ventricular arrhythmia. As a result, sudden cardiac death is expected to be considerable in patients with diastolic HF, in whom LV hypertrophy is common. However, clinical experience in patients with primary overt diastolic HF (who are usually older) demonstrates that pump failure death is more common and that sudden cardiac death is very infrequent. It should be appreciated that, frequently, a heterogeneous group of disorders are included in diastolic HF that influences prognosis.⁴⁷ The presence of significant coronary artery disease (CAD) is associated with a worse prognosis.

Morbidity

In general, there appears to be little difference in morbidity between patients with systolic and diastolic HF.²³ The changes in the quality of life and comorbidity index are very similar in the 2 groups. In hospitalized patients, length of hospital stay is also very similar.

Risk factors

The risk factors for primary systolic and primary diastolic HF are also very similar. Increasing age, hyper-

Table 2: Mass, volumes, and functional parameters determined by magnetic resonance imaging in patients with dilated cardiomyopathy compared to normals⁴⁸

	Normals	Dilated cardiomyopathy
LVEDV Index (ml/m ²)	62.3 ± 7.3	116.8 ± 28.4
LVESV Index (ml/m ²)	21.7 ± 3.9	71.6 ± 23.9
LVEF %	65.1 ± 3.6	35.1 ± 3.4
LV Mass Index (ml/m ²)	79.5 ± 7.6	152.5 ± 31.1
LV Wall Stress (dynes 10 ³ /cm ²)	43.0 ± 10.7	91.2 ± 20.2

LVEDV = Left ventricular end-diastolic volume

LVESV = Left ventricular end-systolic volume

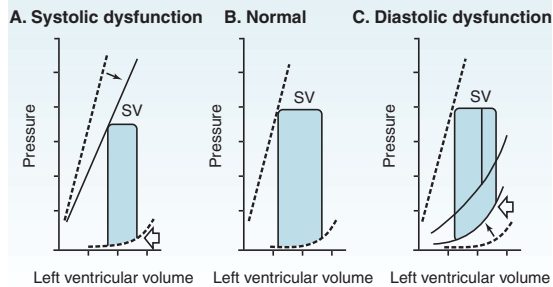
LVEF = Left ventricular ejection fraction

tension, diabetes, obesity, and CAD are risk factors common to both types of HF. Primary diastolic HF is more common in elderly females, but diastolic dysfunction is more common in elderly males.⁴⁸ Although hypertension has been reported to be more common in diastolic HF,²¹ a substantial proportion of patients with systolic HF have a history of hypertension. Similarly, although the incidence of CAD is higher in patients with systolic HF, many patients with diastolic HF have CAD. In the ADHERE Registry, 63% of patients with systolic and 54% of patients with diastolic HF have CAD.⁴⁰ For preventive therapy, modification of the same risk factors should be employed in both systolic and diastolic HF.

Changes in ventricular function, hemodynamics, and remodeling

Although there are considerable differences between primary systolic and primary diastolic HF regarding changes in ventricular function and remodeling, the changes in hemodynamics may be similar. In systolic HF, LV cavity size is increased with an increase in both end-systolic and end-diastolic volumes. As the magnitude of increase in end-systolic volume is relatively greater than that of end-diastolic volume, the EF is reduced. Although LV mass is increased, the cavity/mass ratio is increased due to the disproportionate increase in LV cavity size. As wall thickness may only increase slightly, or remain unchanged, wall stress is substantially increased (Table 2).⁴⁹ In systolic HF, there is alteration in the shape of the left ventricle, which becomes more spherical than ellipsoidal. This altered shape is an important contributing factor for secondary mitral regurgitation. In a substantial number of patients with systolic HF, mechanical dyssynchrony – with or without – electrical dyssynchrony is present, which can cause a further reduction in EF and mechanical inefficiency. The rationale of resynchronization therapy in systolic HF is to decrease the adverse effects of mechanical dyssynchrony on ventricular remodeling.

Figure 2: Schematic diagram of pressure volume loops in normals, systolic and diastolic heart failure (modified figure). In systolic heart failure, end-systolic pressure-volume line shifts downwards and to the right, indicating decreased contractile function, which is the principal cause of reduced stroke volume. In primary diastolic heart failure, diastolic pressure-volume relation (dashed line) shifts upwards and to the left, indicating a greater increase in diastolic pressure for increase in diastolic volumes, which is the principal cause of pulmonary congestion. If there is also a decrease in end-diastolic volume, there is also a decrease in stroke volume.



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In systolic HF, global contractile function is impaired as evident from the downward and rightward shift of the end-systolic pressure-volume line (Figure 2).⁵⁰ Depressed contractile function is the major mechanism for reduced EF in systolic HF. However, myocardial shortening may remain unchanged in the presence of reduced global EF.¹² The other mechanism for reduced EF in systolic HF is increased wall stress (ie, afterload). Diastolic function, as assessed by echocardiographic Doppler studies, is frequently abnormal in patients with overt systolic HF.⁵¹

Conclusion

Part 2 of this topic, in the next issue of *Cardiology Rounds*, will continue the discussion of the differences and similarities between diastolic and systolic HF with an examination of the principal functional derangements, changes in extracellular matrix and collagen synthesis, and ventricular remodeling, as well as therapeutic options, for both entities.

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Dr Chatterjee discloses that he has received speaker honoraria from Scios Inc., CV Therapeutics, Merck Sharp & Dohme, Pfizer, and Bristol-Myers Squibb.



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