Therapy for Diastolic Heart Failure

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There is little objective data to guide the therapy of patients with diastolic heart failure. Because of the similarities of pathophysiologic abnormalities in diastolic and systolic heart failure, it is a reasonable inference to suggest that the proven therapy for systolic heart failure may also be of benefit in patients with diastolic heart failure. Treatment of underlying or exacerbating conditions in diastolic heart failure, such as hypertension, left ventricular hypertrophy, ischemia, diabetes, anemia, obesity and pulmonary disease is an important means of managing diastloic heart failure. Control of systolic blood pressure is effective in improving and preventing the development of diastolic heart failure. Treatment of diastolic heart failure is most effective when it is associated with hypertension. Production of systolic arterial pressure acutely reduces pulmonary congestion, ischemia, and chronically may lead to regression of left ventricular hypertrophy. Patients with diastolic heart failure in the absence of hypertension are very difficult to treat.

More than 40% of patients with congestive heart failure (HF) have a preserved left ventricular (LV) ejection fraction (>0.50%).[1-3] Although many of these patients have subtle abnormalities of contractile function, the HF is presumed to predominately result from diastolic dysfunction. Diastolic HF usually occurs in patients with hypertension in combination with the normal aging process as well as varying degrees of LV hypertrophy, coronary artery disease, and diabetes. Many patients with hypertrophic obstructive cardiomyopathy and restrictive cardiomyopathies also have diastolic dysfunction.

There is much less objective information available concerning the treatment of patients with primary diastolic dysfunction than about the therapy for systolic dysfunction.[4,5] This relative paucity of objective information is reflected in the American College of Cardiology/American Heart Association[6] and the European Society of Cardiology guidelines for the treatment of HF.[7] To paraphrase the recommendations of these guidelines concerning treatment of HF, (a) the goal of therapy for diastolic HF is to control symptoms by reducing ventricular filling pressure without reducing cardiac output, (b) diuretics and nitrates are indicated for symptomatic patients, (c) it is important to control arterial hypertension, (d) calcium-channel blockers, β-blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin II receptor blockers (ARB) may be of benefit beyond the treatment of hypertension, and (e) other possible but unproven therapeutic strategies include myocardial revascularization, avoiding tachycardia, and restoring sinus rhythm.

Treatment Based on Studies of Heart Failure and Reduced Ejection Fraction

There is a substantial body of evidence to guide therapy of patients with HF and a reduced (<0.40) ejection fraction. These studies clearly demonstrate an improvement in survival and symptomatic status in patients who are treated with ACE inhibitors and in patients who are treated with the β-adrenergic blocking agents, metoprolol, bisoprolol, and carvedilol.[6,8]

Because the pathophysiological abnormalities in patients with diastolic and systolic HF are similar,[9,10] it is a reasonable inference to suggest that these proven therapies for systolic HF may be of benefit in patients with diastolic HF

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as well. It is important to recognize that this is an inference and not a proven conclusion.

The use of ACE inhibitors and β-blockers has several potential advantages in diastolic HF. First, they are both effective therapies for arterial hypertension, which is an important cause of diastolic HF (see below). They may also result in regression of LV hypertrophy, which also is an important contributor to diastolic HF. Finally, β-adrenergic receptors may help limit tachycardia providing additional time for diastolic filling, especially during exercise (see below).

There is a difference in how β-blockers are used in diastolic HF versus systolic HF.[3,11] In patients with systolic HF, the initiation of β-blockers must be started at low doses and slowly titrated to be tolerated. This is usually not necessary in patients with diastolic HF, especially in association with marked hypertension.

Treatment Strategies

Based on the pathophysiology and causes of diastolic dysfunction, there are several potential treatment strategies that may be effective in treating patients with HF caused by diastolic dysfunction.[4]

Treat Underlying Causes of Diastolic HF

The major contributing causes of diastolic HF are shown in Table 1. It is important to recognize that many of these causes, including hypertension, LV hypertrophy, ischemia, and diabetes, are potentially treatable.[4,12] In addition, other reversible conditions including anemia, obesity, and pulmonary disease may contribute to the symptoms of diastolic HF.[13] Treatment of these underlying or exacerbating conditions is an important means of managing diastolic HF.[11]

Table 1. Causes of Diastolic HF

Hypertension*
LV hypertrophy*
Aging
Myocardial ischemia*
Diabetes*
Restrictive and infiltrative cardiomyopathies
Transplant rejection*

*Treatable.

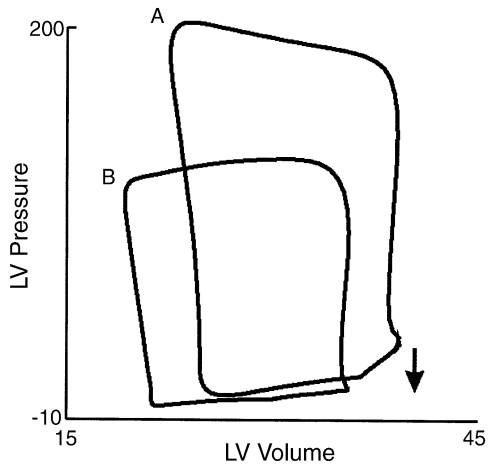

Fig 1. LV pressure-volume loops recorded in a conscious animal. A decrease in systolic pressure (movement from loops A to B) allows the ventricle to eject farther and operate at lower volumes. This results in a decrease in LV end-diastolic pressure (arrow). Data redrawn from Little et al.[17]

Hypertension

There is a strong association of diastolic HF with arterial hypertension, most markedly with systolic hypertension.[1,14] The most important strategy to prevent diastolic HF and to acutely improve LV diastolic performance is the lowering of systolic arterial pressure.[4] Stiffening of the aorta and the left ventricle, as occurs in many elderly patients with diastolic HF, increases the tightness of the coupling of arterial systolic and left atrial measures.[15,16] Increases in systolic arterial pressure result in an elevation of left atrial pressure.[17] Conversely, lowering of elevated arterial pressure decreases left atrial pressure.

Thus, controlling systolic hypertension allows the left ventricle to eject to a smaller end-systolic volume, allowing the left ventricle to operate with a smaller diastolic volume and reduced left atrial pressure. Lowering systolic pressure allows the ventricle to relax more rapidly, enhancing early filling. In addition, lowering systolic pressure may reduce or relieve ischemia. Thus, lowering elevated systolic arterial pressure provides a powerful method of acutely improving the diastolic performance of the left ventricle (Fig 1).

Long-term therapy for hypertension can result in regression of LV hypertrophy. This enhances LV distensibility and improves LV diastolic performance.[18-20] Control of isolated systolic hy-