

Diastolic Dysfunction and Its Management in Elderly Patients

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Congestive heart failure (CHF) is a common cause of morbidity and mortality in elderly persons. With aging, major changes occur in heart function, specifically in left ventricular diastolic function. Given the aging of the US population, CHF has thus become a major public health concern. Although persons age 65 years and older comprise the fastest growing segment of the US population (a trend that promises to continue), this population group has not been studied extensively in clinical trials. As a result, physicians may not be adequately prepared to deal with some aspects of cardiovascular disease in elderly persons.

This article provides a brief review of diastolic dysfunction, particularly as it concerns elderly patients. The epidemiology, prognosis, pathophysiology, major characteristics, diagnosis, and management of diastolic CHF are discussed.

EPIDEMIOLOGY

The exact prevalence of mild diastolic dysfunction without clinical symptoms and of moderate diastolic CHF limited to exercise-induced symptoms is unknown. However, it is known that the prevalence of diastolic CHF increases with age. CHF is the most common hospital discharge diagnosis in patients age 65 years or older.

Approximately 50% of elderly patients presenting with CHF have evidence of diastolic dysfunction.¹ Yet, as many as one third of patients with CHF have a normal left ventricular ejection fraction, as estimated by echocardiography.²

PROGNOSIS

The prognosis of patients with diastolic CHF is less



ominous than that of patients with systolic CHF, but it is still poorer than that of age-matched control patients.³ In the Framingham study, the annual mortality from diastolic CHF was approximately half that of patients with systolic CHF.⁴ In addition, morbidity from diastolic CHF is quite high, requiring frequent outpatient visits, hospital admissions, and significant health care expenditure.

PATHOPHYSIOLOGY

The pathophysiology of diastolic CHF is incompletely understood, and a universally accepted definition is lacking.⁵ Except for persons with evidence of significant systolic dysfunction, ischemic or valvular heart disease, and pulmonary diseases, CHF patients can be expected to have diastolic dysfunction as the origin of their symptoms. These patients tend to have a history of significant systemic hypertension; considerable left ventricular hypertrophy and distention are evident on echocardiography.⁶ The pathologic disease processes that cause diastolic CHF include pressure overload hypertrophy, genetic hypertrophy, and infiltrative cardiomyopathies.

The basic mechanisms by which pressure overload hypertrophy and genetic hypertrophy cause diastolic CHF include extramyocardial factors and factors intrinsic to the myocardium, including changes in both

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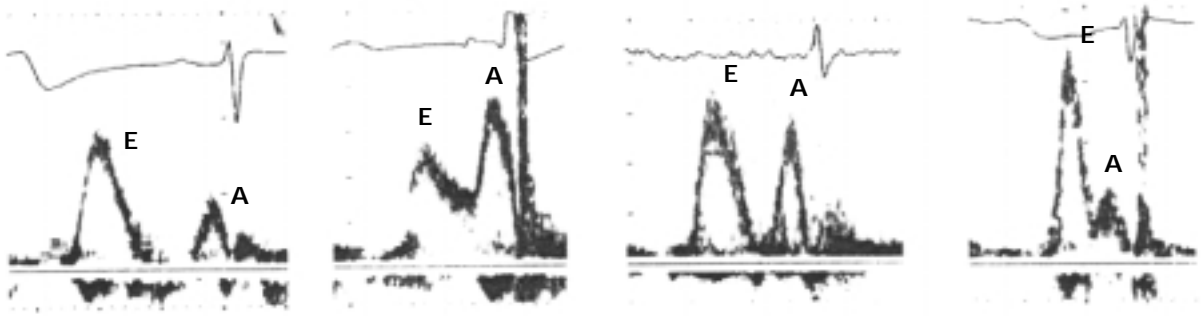


Figure 1. Echocardiographic tracing showing patterns of mitral valve inflow, from normal to restrictive physiology. (Reprinted with permission from Oh JK, Seward JB, Tajik AJ. *The echo manual*. 2nd ed. Philadelphia: Lippincott-Raven; 1999:55.)

cardiac muscle cells and the extracellular matrix that surrounds cardiomyocytes.⁷ In addition, local myocardial neuroendocrine activation can impair relaxation and increase stiffness. Activation of neurohormones (eg, the renin-angiotensin-aldosterone system) can act directly to alter diastolic properties or can act indirectly by disturbing calcium hemostasis.

It has been shown that patients with CHF have an inability to increase stroke volume by way of the Frank-Starling mechanism, despite severely increased left ventricular filling pressure (indicative of diastolic dysfunction⁸), resulting in severe exercise intolerance. Exercise intolerance manifested as exertional dyspnea and fatigue is the primary symptom of CHF.

MAJOR CHARACTERISTICS

Major distinguishing features of diastolic CHF include older age, female preponderance, history of hypertension, normal or small left ventricular cavity size with significant hypertrophy, normal or supernormal contractility, increased left ventricular filling pressure, and increased neurohormonal activation.

DIAGNOSIS

In rare cases, diastolic CHF can be distinguished from systolic CHF on the basis of history, physical examination, chest radiography, and electrocardiography alone.⁹ More commonly, however, echocardiography, radionuclide ventriculography, or contrast ventriculography will be needed to determine whether CHF is caused by systolic or diastolic dysfunction, because these tests can estimate left ventricular size and function.

When a patient has dyspnea or pulmonary edema, conditions such as mitral stenosis and noncardiogenic pulmonary edema must first be ruled out. If these conditions are excluded, the finding of normal left ventricular end-diastolic volume and normal ejection fraction

support the diagnosis of isolated diastolic CHF. There are 3 additional factors measured by echocardiography that can help in distinguishing abnormal from normal diastolic function: (1) filling patterns, (2) early deceleration time, and (3) pulmonary venous flow.¹⁰

Filling dynamics can be assessed using Doppler echocardiography techniques that record mitral valve inflow.¹¹ The “E” wave observed represents early rapid filling, and the “A” wave represents late ventricular filling¹² produced by atrial contraction (**Figure 1**). Diastolic filling can be quantitated by measuring the peak velocity, the area within the velocity-versus-time integral, and the rate of deceleration, as well as the E:A velocity ratio. When diastolic dysfunction is present, E-wave velocity is decreased, A-wave velocity is increased (ie, reversed E:A ratio), velocity-versus-time integral is decreased, and deceleration time is prolonged. These data, however, need to be interpreted cautiously, because diastolic filling and Doppler parameters can be altered by many factors, including a wide variety of cardiovascular disorders, use of cardiovascular medication, and changes in heart rate, preload, afterload, and contractility that accompany normal aging.¹³

Diastolic dysfunction can be graded according to the diastolic filling pattern, with grade I indicating impaired relaxation, grade II a pseudonormalized pattern, grade III a reversible restrictive pattern, and grade IV an irreversible restrictive pattern.¹² In grade I, a delayed relaxation pattern is normally seen in healthy older persons who appear free of cardiovascular disease.

Early deceleration time is particularly useful in evaluating left ventricular filling in elderly persons, because it does not appear to shorten with aging. Doppler-derived pulmonary venous flow velocity and Doppler studies performed during a Valsalva maneuver may provide helpful information in order to better interpret the indices of filling derived from Doppler studies.¹⁴

Pulmonary venous flow is divided into 3 periods: (1) forward flow during ventricular systole (S wave), (2) forward flow during early diastole (D wave), and (3) reverse flow during atrial contraction (reverse A wave). An increase in left atrial pressure resulting from diastolic dysfunction causes a decrease in the S wave or an increase in the reverse A wave.

TREATMENT

Heterogeneity of subjects, poor understanding of pathophysiology, absence of reliable tests, and lack of a clear definition of diastolic dysfunction render randomized prospective trials of therapies for diastolic dysfunction very difficult to conduct. Consequently, in the absence of randomized trials, treatment of this disorder remains largely empiric. The use of diuretics and nitrates have been discussed in American College of Cardiology/American Heart Association guidelines published in 1995.¹⁵

Diuretics

Although administration of diuretics is appropriate therapy for the relief of the congestion and edema associated with diastolic CHF, caution has been advised, because stroke volume may be dependent on preload. When such a dependency exists, volume depletion may result in underfilling of the left ventricle, reduction of cardiac output, and hypotension. As a result, the doses of diuretics used to treat diastolic CHF are generally smaller than doses used to treat systolic CHF.

Nitrates

Use of nitrates lowers pulmonary and systemic venous pressure and relieves congestive symptoms.¹⁵ However, as with diuretics, nitrates need to be used cautiously in cases of diastolic CHF, especially in elderly patients, because they may reduce stroke volume and cardiac output.

Digoxin

Positive inotropic agents (such as digoxin) are generally not recommended in the treatment of patients with isolated diastolic CHF, because left ventricular ejection fraction is preserved in these patients. However, results of the Digitalis Investigation Group trial¹⁶ suggest that even patients with a normal ejection fraction may have fewer symptoms and fewer hospitalizations if they are treated with digoxin. This effect may result from its ability to blunt neuroendocrine activation.

β -Blockers

In patients with diastolic CHF, β -blockers are used

to decrease heart rate, increase left ventricular filling time, and modify the hemodynamic response to exercise by increasing the ischemic threshold. All of these actions have hypothetical benefits in the treatment of diastolic CHF.¹⁷

Calcium Channel Blockers

Calcium channel blockers, such as diltiazem, nifedipine, and verapamil, have been proposed as potentially useful agents in the treatment of diastolic CHF, although supportive data are limited.¹⁸ In patients with hypertrophic cardiomyopathy, a disorder in which diastolic dysfunction is common, verapamil does appear to improve symptoms.¹⁹

Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Blockers

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II blockers have documented efficacy in patients with systolic CHF by reducing mortality and hospital admissions and by improving exercise tolerance and symptoms.²⁰ These effects are thought to be primarily caused by interference with the increased neurohormonal activation of the CHF state. Intuitively, one would expect neurohormonal activation to be present in diastolic CHF, because it shares the same hemodynamic consequences of increased left ventricular filling pressure and decreased stroke volume with systolic CHF. There is growing evidence that ACE inhibitors and angiotensin II blockers can be beneficial in cases of diastolic CHF.

CONCLUSION

Given the aging of the US population, CHF has become a major health concern of growing import. Approximately 50% of elderly patients with CHF have evidence of diastolic dysfunction. In the absence of randomized trials, treatment of diastolic dysfunction remains largely empiric. There is growing evidence that administration of ACE inhibitors and angiotensin II blockers can be beneficial in elderly patients with this disorder. HP

REFERENCES

1. Tresch DD, McGough MF. Heart failure with normal systolic function: a common disorder in older people. *J Am Geriatric Soc* 1995;43:1035–42.
2. Wong WF, Gold S, Fukuyama O, Blanchette PL. Diastolic dysfunction in elderly patients with congestive heart failure. *Am J Cardiol* 1989;63:1526–8.
3. Setaro JF, Soufer R, Remetz MS, et al. Long-term outcome in patients with congestive heart failure and intact systolic

- left ventricular performance. *Am J Cardiol* 1992;69:1212-6.
4. Vasan RS, Larson MG, Benjamin EJ, et al. Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction: prevalence and mortality in a population-based cohort. *J Am Coll Cardiol* 1999;33:1948-55.
 5. How to diagnose diastolic heart failure. European Study Group on Diastolic Heart Failure. *Eur Heart J* 1998;19:990-1003.
 6. Topol EJ, Traill TA, Fortuin NJ. Hypertensive hypertrophic cardiomyopathy of the elderly. *N Engl J Med* 1985;312:277-83.
 7. Gaasch WH, Shick EC, Zile MR. Management of left ventricular diastolic dysfunction. In: Smith TW, Antman EM, et al, editors. *Cardiovascular therapeutics: a companion to Braunwald's heart disease*. Philadelphia: WB Saunders; 1996:237-42.
 8. Kitzman DW, Higginbotham MB, Cobb FR, et al. Exercise intolerance in patients with heart failure and preserved left ventricular systolic function: failure of the Frank-Starling mechanism. *J Am Coll Cardiol* 1991;17:1065-72.
 9. Gaasch WH. Diagnosis and treatment of heart failure based on left ventricular systolic or diastolic dysfunction. *JAMA* 1994;271:1276-80.
 10. Little WC, Ohno M, Kitzman DW, et al. Determination of left ventricular chamber stiffness from the time for deceleration of early left ventricular filling. *Circulation* 1995;92:1933-9.
 11. Garcia MJ, Thomas JD, Klein AL. New Doppler echocardiographic applications for the study of diastolic dysfunction. *J Am Coll Cardiol* 1998;32:865-75.
 12. Oh JK, Seward JB, Tajik AJ. *Assessment of diastolic function. The echo manual*. 2nd ed. Philadelphia: Lippincott-Raven; 1999:45-57.
 13. Spirito P, Maron BJ. Doppler echocardiography for assessing left ventricular diastolic function. *Ann Intern Med* 1988;109:122-6.
 14. Rossvoll O, Hatle LK. Pulmonary venous flow velocities recorded by transthoracic Doppler ultrasound: relation to left ventricular diastolic pressures. *J Am Coll Cardiol* 1993;21:1687-96.
 15. Guidelines for the evaluation and management of heart failure. Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Evaluation and Management of Heart Failure). *J Am Coll Cardiol* 1995;26:1376-98.
 16. The effect of digoxin on mortality and morbidity in patients with heart failure. The Digitalis Investigation Group. *N Engl J Med* 1997;336:525-33.
 17. Colucci WS, Ribeiro JP, Rocco MB, et al. Impaired chronotropic response to exercise in patients with congestive heart failure. Role of postsynaptic beta-adrenergic desensitization. *Circulation* 1989;80:314-23.
 18. Millaire A. [Diastolic cardiac failure: therapeutic modalities.] [Article in French.] *Arch Mal Coeur Vaiss* 1998;91:1365-9.
 19. Dimitrow PP, Surdacki A, Dubiel JS. Verapamil normalizes the response of left ventricular early diastolic filling to cold pressor test in asymptomatic and mildly symptomatic patients with hypertrophic cardiomyopathy. *Cardiovasc Drugs Ther* 1997;11:741-6.
 20. Massie BM, Conway M. Survival of patients with congestive heart failure: past, present, and future prospects. *Circulation* 1987;75(5 Pt 2):IV11-9.

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