abstract

The incidence of heart failure is rising rapidly, and it is currently the most common cardiovascular disease. Approximately 20–40% of patients with heart failure have preserved left ventricular systolic function, and an impairment of ventricular relaxation is considered the primary cause. There is controversy surrounding the definition of diastolic dysfunction and the diagnostic criteria for diastolic heart failure. Moreover, there are few studies on therapy for diastolic heart failure, which makes the management of these patients a real challenge.

Key words: *heart failure, treatment, diagnosis, diastolic dysfunction*

Diagnosis and Management of Diastolic Heart Failure

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Introduction

The incidence of heart failure is rising rapidly, and it is currently the most common cardiovascular disease. More than 400,000 Canadians are afflicted with this condition, and more than 50,000 new cases are diagnosed per year.[1] Moreover, the average period of hospitalization due to heart failure is eight days, and more than one billion Canadian dollars are spent each year on inpatients. However, approximately 20–40% of patients with heart failure have preserved left ventricular systolic function, and an impairment of ventricular relaxation is thought to be the primary mechanism leading to symptoms. The prevalence of diastolic heart failure increases with age, approaching 50% in patients over 70 years.[2] The annual mortality rate for patients with diastolic heart failure is 5–8% versus 10–15% for patients with systolic heart failure.

There is controversy surrounding the definition of diastolic dysfunction and the diagnostic criteria for diastolic heart failure. In addition, there are few studies on therapy for diastolic heart failure, which makes the management of these patients a real challenge.

This review examines the current evidence for the diagnosis and treatment of this unique clinical entity and emphasizes particular features of this condition in older patients.

Definitions

It is important to differentiate diastolic heart failure from diastolic dysfunction.

Diastolic heart failure is a clinical syndrome characterized by symptoms and signs of heart failure, a preserved ejection fraction, and abnormal diastolic function.[3] Diastolic heart failure is the consequence of a decrease in ventricular relaxation and / or an increase in ventricular stiffness. Patients may present with clinical signs and symptoms of congestive heart failure, such as dyspnea, orthopnea, and pulmonary rales.

Diastolic dysfunction refers to a condition in which abnormalities in mechanical function are present during diastole. Diastolic dysfunction can occur in the presence or absence of a clinical syndrome of heart failure and with or without normal systolic function. Therefore, whereas diastolic dysfunction describes an abnormal mechanical property, diastolic heart failure describes a clinical syndrome.

Pathophysiology

The underlying pathophysiology of diastolic dysfunction is impaired relaxation of the left ventricle (LV), resulting in reduced left ventricular compliance and therefore inadequate filling of the LV at normal diastolic pressures.[4]

Diastolic dysfunction is primarily a disease of older people. This observation may be related to the fact that aging has a greater impact on diastolic than systolic function. There is a progressive loss of myocytes and hypertrophy of the remaining myocytes with aging.[5] Other physiologic changes occur with aging: systemic vascular resistance is increased, LV stiffness is increased, LV compliance is decreased, systolic blood pressure is increased, early LV diastolic filling is decreased, and LV relaxation is impaired.[6] Increased LV stiffness occurs with aging because of increased

interstitial fibrosis and cross-linking of collagen in the heart. Older patients are also more likely to have hypertension, myocardial ischemia due to coronary disease, and LV hypertrophy caused by hypertension or aortic stenosis. These deleterious effects on diastolic function are exacerbated by a decrease in beta-adrenergic receptor density and a decline in peripheral vasodilator capacity, both of which are characteristic of older patients. In addition, the incidence of chronic atrial fibrillation increases with age. The development of atrial fibrillation may adversely affect the diastolic properties of the heart or decrease the time available for ventricular filling.

Diagnosis

Diagnosis of diastolic heart failure cannot be made on the basis of patient's history, physical examination, or chest radiograph alone because patients with either systolic or diastolic heart failure may share similar history and examinations.[3]

The diagnosis of heart failure is currently based on three criteria[7] (see Table 1): the presence of signs (pulmonary rales, jugular venous distension and a cardiac gallop, peripheral edema, etc.) or symptoms of congestive heart failure (dyspnea, fatigue); documentation of normal or only minimally reduced LV systolic function by a cardiac imaging technique; and evidence of abnormalities of LV diastolic function.

The diagnosis of diastolic dysfunction may be performed by cardiac catheterization, which may demonstrate increased ventricular diastolic pressure with preserved systolic function and normal ventricular volumes.

Echocardiography is the most commonly used tool to evaluate LV diastolic function. Doppler techniques can measure intracardiac blood flow and thereby infer pressures. The most familiar of these are the mitral inflow velocities. Other echocardiographic parameters of diastolic dysfunction are isovolumetric relaxation time and pulmonary wave flow.[8]

Many other techniques available for diagnosis of diastolic dysfunction are not used routinely in the clinical setting, including pressure / volume loops using invasive hemodynamic monitoring, nuclear medicine radionuclide techniques, magnetic resonance imaging, and ultrafast CT scan.

Table 1: Diagnosis of Diastolic Heart Failure

Presence of signs or symptoms of congestive heart failure
Documentation of normal or only minimally reduced LV systolic function by a cardiac imaging technique
Evidence of abnormalities of LV diastolic function

B-type natriuretic peptide (BNP) has also been proposed as a useful tool for the diagnosis of heart failure. Currently, the most established clinical application of BNP is for the detection of cardiac etiologies in patients who present to an urgent care setting with dyspnea, and in whom the diagnosis is not readily apparent after clinical evaluation.[9] Also, BNP is useful in distinguishing diastolic heart failure from chronic obstructive lung disease.[10] Several studies have demonstrated elevated BNP levels in patients with heart failure and documented diastolic dysfunction.[11,12] However, at this point, BNP level by itself cannot differentiate between systolic and diastolic dysfunction. It should be noted that BNP level can increase in conditions other than heart failure. Plasma BNP levels increase with aging, are generally higher in females, and increase in renal disease, advanced pulmonary disease, and other cardiac conditions. In a patient who presents to an urgent care setting with a low BNP level, i.e., less than 50–80pg / ml, the probability of heart failure as an etiology for the dyspnea is likely to be low.

Treatment

There are few studies on therapy for diastolic heart failure. Guidelines for the management of diastolic heart failure are based on clinical research with small numbers of patients and concepts based on pathophysiological mechanisms. The management of these patients should be directed to the relief of symptoms and the control of underlying pathophysiologic factors that are known to exert important effects on ventricular relaxation (Table 2).[13]

The first step in treating patients with diastolic heart failure is to reduce fluid overload. Fluid and salt restriction in addition to diuretics should be considered the first-line treatment. It is important to consider that age-related decreases in renal function and circulating plasma

Table 2: Treatment of Diastolic Heart Failure

Goal	A. Relief of symptoms B. Control of underlying pathophysiologic factors
Approach	1. Reduce fluid overload a. Fluid and salt restriction b. Diuretics
	2. Prevent and treat tachycardia
	3. Maintain normal sinus rhythm a. Control of ventricular rate in patients with atrial fibrillation b. Restoration of sinus rhythm in patients with atrial fibrillation
	4. Control of hypertension
	5. Treat myocardial ischemia a. Medical therapy b. Coronary revascularization

volume may reduce the efficacy of diuretics in older patients with diastolic heart failure. On the other hand, overdiuresis should be avoided because older patients with diastolic heart failure require high left ventricular filling pressures to maintain an adequate stroke volume and cardiac output, and cannot tolerate intravascular depletion. Some patients with refractory heart failure should be treated with intravenous diuretics and hospitalization. Refractory cases may require ultrafiltration or dialysis.

Tachycardia is not well tolerated by patients with diastolic heart failure. Tachycardia may promote ischemia due to an increase in oxygen demand and decrease in coronary perfusion time, which may in turn be aggravated by the presence of ventricular hypertrophy. Also, tachycardia impairs ventricular diastolic relaxation. For patients on atrial fibrillation, restoration of normal sinus rhythm is essential and may improve symptoms.

Hypertension treatment is a priority in patients with diastolic heart failure. Hypertension produces a deleterious effect on diastolic function, while an increase in systolic blood pressure results in impaired myocardial relaxation.

Because myocardial ischemia can impair ventricular relaxation, coronary revascularization should be considered in patients in whom symptomatic or demonstrable myocardial ischemia is judged to have an adverse effect on diastolic function.

Despite the absence of evidence-based data, it is recommended that clinicians consider some pharmacologic approaches for the management of patients with diastolic heart failure.[8, 14]

Pharmacologic Treatments

Diuretics are the cornerstone of management of these patients. Beta-blockers and calcium channel blockers have an important role in slowing the heart rate and therefore prolonging left ventricular filling time. Also, their anti-ischemic and antihypertensive properties may confer extra benefit in these patients.

Angiotensin-converting enzyme (ACE) inhibitors and Angiotensin Receptor Blockers (ARB) may prevent the deleterious effect of angiotensin II on myocardial relaxation.

In patients with hypertension and LV hypertrophy, losartan (an angiotensin II receptor [type AT1] antagonist) reduced cardiovascular complications compared with atenolol (a beta-1-selective adrenoreceptor blocking agent).[15]

The ARB candesartan has a moderate impact in preventing admissions for CHF among patients who have heart failure and LVEF higher than 40%.[16] In this study, patients with New York Heart Association functional class II-IV CHF and a LV ejection fraction higher than 40% were randomized to receive either candesartan or placebo in addition to conventional medical therapy. Cardiovascular death did not differ between groups, but fewer patients in the candesartan group than the placebo group were admitted to hospital for CHF once or multiple times. There are several ongoing trials evaluating ACE inhibitors, ARB, and beta-blockers in patients with diastolic heart failure.

Digoxin has not been shown to be effective for the management of patients with diastolic heart failure unless it is used for arrhythmic management. The clinical benefit of digoxin is unclear. Although the Digitalis Investigation Group Trial suggested that patients with heart failure and preserved LV function may have fewer symptoms and hospitalizations, a detailed analysis of these data has not been published. Digitalis may produce an increase in systolic energy demands while adding to a relative calcium overload in diastole.

Summary

Diastolic heart failure is a unique clinical entity, which is diagnosed based on clinical features and the demonstration of normal or near-normal systolic function. The prevalence of diastolic heart failure increases with age. There is limited data regarding pharmacological treatment of this disease; at present, diuretics are the cornerstone of therapy. Control of predisposing conditions such as tachycardia, hypertension, and coronary disease is essential. Ongoing trials are evaluating the long-term benefits of ACE inhibitors, ARB, and beta-blockers in patients with diastolic heart failure.

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References

1. Liu P, Arnold M, Belenkie I, et al. The 2001 Canadian Cardiovascular Society consensus guideline update for the management and prevention of heart failure. Can J Cardiol 2001;17(Suppl. E):S5–25.
2. O'Conner CM, Gattis W, Shaw L, et al. Clinical characteristics and long-term outcomes of patients with heart failure and preserved systolic function. Am J Cardiol 2000; 86:863–7.
3. Zile MR, Brutsaert DL. New concepts in diastolic dysfunction and diastolic heart failure, Part 1: diagnosis, prognosis, and measurements of diastolic dysfunction. Circulation 2002;105:1387–93.
4. van Kraaij DJ, van Pol PE, Ruiters AW. Diagnosing diastolic heart failure. Eur J Heart Fail 2002;4:419–30.
5. Aronow WS. Epidemiology, pathophysiology, prognosis and treatment of systolic and diastolic heart failure in elderly patients. Heart Disease 2003;5:279–94.
6. Oxenham H, Sharpe N. Cardiovascular aging and heart failure. Eur J Heart Fail 2003;5:427–34.
7. European Study Group of Diastolic Heart Failure. How to diagnose diastolic heart failure. Eur Heart J 1998;19:990–1000.
8. Hunt S, Baker DW, Chin MH, et al. ACC / AHA Guidelines for the evaluation and management of chronic heart failure in the adult: executive summary. A report of the American College of Cardiology / American Heart Association task force on practice guidelines. Circulation 2001;104:2996–3007.
9. Maisel AS, McCord J, Nowak RM, et al. Bedside B-Type natriuretic peptide in the emergency diagnosis of heart failure with reduced or preserved ejection fraction. Results from the Breathing Not Properly Multinational Study. J Am Coll Cardiol 2003;41:2010–17.
10. Morrison LK, Harrison A, Krishnaswamy P, et al. Utility of a rapid B-natriuretic peptide assay in differentiating congestive heart failure from lung disease in patients presenting with dyspnea. J Am Coll Cardiol 2002;39:202–9.
11. Mottram PM, Leano R, Marwick TH. Usefulness of B-type natriuretic peptide in hypertensive patients with exertional dyspnea and normal left ventricular ejection fraction and correlation with new echocardiographic indexes of systolic and diastolic function. Am J Cardiol 2003;92:1434–8.

12. Lubien E, DeMaria A, Krishnaswamy P, et al. Utility of B-natriuretic peptide in detecting diastolic dysfunction: comparison with Doppler velocity recordings. Circulation 2002;105:595–601.
13. Zile MR, Brutsaert DL. New concepts in diastolic dysfunction and diastolic heart failure, Part 2: causal mechanisms and treatment. Circulation 2002;105:1503–8.
14. Angeja B, Grossman W. Evaluation and management of diastolic heart failure. Circulation 2003;107:659–63.
15. Dahlof B, Devereux RB, Kjeldsen SE, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE); a randomized trial against atenolol. Lancet 2002;359:995–1003.
16. Yusuf S, Pfeffer MA, Swedberg K, et al. Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: the CHARM-Preserved Trial. Lancet 2003;362:777–81.