Diastolic Heart Failure

The evaluation of both systolic and diastolic functions is of great importance among patients presenting with signs of CHF, as the treatment may be quite different depending on the underlying condition.

By Michel D'Astous, MD, FRCPC

Congestive heart failure (CHF) is a major public health problem in developed countries and an important cause of morbidity and mortality. Approximately 20% to 40% of patients with CHF have normal or near-normal (preserved) systolic function. The evaluation of both systolic and diastolic functions, therefore, is of great importance among patients presenting with signs of CHF, as the treatment may be quite different, depending on the underlying condition. It is also important to emphasize that the signs and symptoms of CHF correlate poorly with the left ventricular ejection fraction (LVEF).[1,2]

A diagnosis of diastolic heart failure is often made after a patient presents with signs and symptoms of CHF and the LVEF is found to be preserved. Another cause of heart failure, however, such as a transient left ventricular (LV) dysfunction or a primary valvular abnormality, may be the underlying problem.

Proper assessment of patients presenting with a clinical picture of CHF involves the definition of the underlying pathology and the appropriate treatment.

About the author...

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Case

Ms. P.L., 78, presented to the emergency room with shortness of breath and lower leg edema.

She has a 25-year history of hypertension, which has been "well-controlled" according to her. She also has a history of hypothyroidism for which she is taking l-thyroxine. She has had a previous cholecystectomy and two caesarean sections. She has no history of ischemic heart disease, diabetes or dyslipidemia. She stopped smoking 12 years ago. Family history is significant for hypertension in a few members and one brother died at the age of 50 from a "weak heart."

Other than l-thyroxine, Ms. P.L. takes some natural remedies for her blood pressure (BP). When she feels it is high, she will take her prescribed medication (captopril) for a few days. She rarely sees her family physician, aside from her yearly visit. She is usually pretty active.

Over the last six months, she has been experiencing shortness of breath on exertion, which has increased progressively. She has noted lower leg edema for the last three weeks and recently (two nights ago) woke up, gasping for air and had to sit up to get relief. She denies any chest pains.

Physical examination reveals a woman looking younger than she is, who is mildly overweight and easily short of breath. Her BP is 195/100 mmHg, her pulse is at 96 beats per minute (BPM) and her respiratory rate is 22/min. The jugular veins are distended at 12 cm above the angle of Louis and carotid upstroke is normal. The apical impulse seems of normal size, but sustained, and the heart sounds show a normal S1, an increased S2 and an S4. There is also a faint apical murmur, but no S3 is heard. The pulmonary auscultation shows crackles in the lower half of both lungs. There is mild lower leg edema with essentially normal pulses.

Her electrocardiogram (ECG) shows sinus rhythm at 92 BPM, with signs of left ventricular hypertrophy (LVH) and repolarization abnormalities. There is no evidence of a prior infarction. Her chest X-ray shows a normal cardiac silhouette with interstitial edema and small bilateral pleural effusions.

Question: What condition is Ms. P.L. suffering from? How would you investigate this patient?
Discussion on page 36

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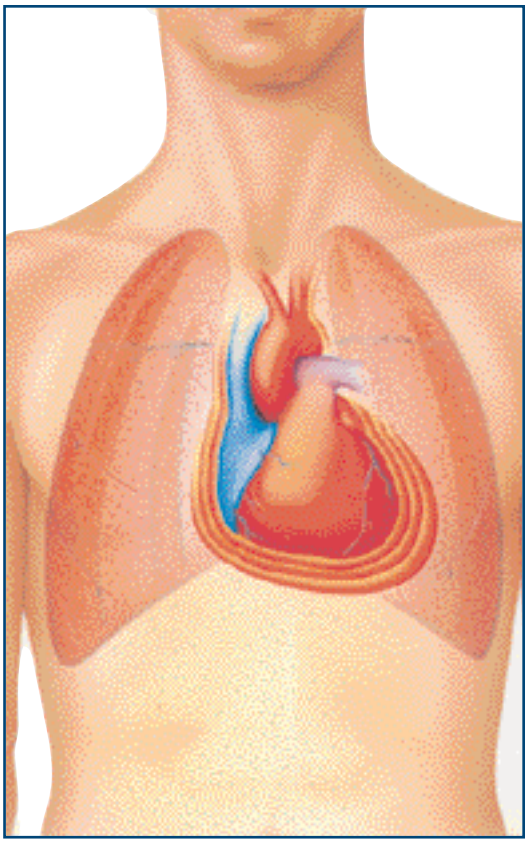


Definition

CHF is defined as "a pathophysiological state in which an abnormality of cardiac function is responsible for failure of the heart to pump blood at a rate commensurate with the metabolic requirements of the body or to do so only with elevated filling pressures."[1]

Not every patient presenting with signs of CHF and normal LVEF should be regarded as suffering from diastolic heart failure. In general, however, diastolic heart failure is associated with the following:

- Signs and symptoms of CHF;
- Normal or near-normal systolic function; and
- Invasive or non-invasive assessment, showing signs of abnormal diastolic function.[1]

Practical Point

Systolic dysfunction is associated with a poorly contracting heart that has difficulty ejecting its volume of blood. This increases its filling pressures, causing dyspnea and pulmonary congestion. Diastolic dysfunction is associated with a preserved contractility, ejecting its volume adequately, but having difficulty relaxing during diastole, therefore filling more slowly than usual and increasing its filling pressures rapidly with the arrival of blood from the left atria (LA), also causing dyspnea and pulmonary congestion.

Diastole

Like systole, diastole is an active process related to calcium dependant mechanisms.[3] The diastolic phase of the heart cycle is divided into four phases:

Isovolumetric relaxation time: The period between the closure of the aortic valve and the opening of the mitral valve. During this period, there is no blood flow from the LA to the LV.

Early filling period: The opening of the mitral valve with rapid blood flow from the LA to the LV. This represents approximately 80% of the normal diastolic flow.

Diastasis: The equilibration of pressures between the LA and LV with little or no blood flow (< 5%).

Atrial contraction: The pre-systolic flow of blood from the LA to the LV represents about 15% of the blood flow. There may be an increase of up to 25% to 30% in patients with relaxation abnormalities (*i.e.*, left ventricular hypertrophy [LVH]),

that depend more on the atrial contraction to "fill" the LV.[4]

In the presence of diastolic dysfunction, the contribution of each phase may vary. During exercise and tachycardia, the diastolic component of the cardiac cycle shortens more, as compared to the systolic phase. This may contribute to elevation of the filling pressures, with resulting shortness of breath.

Practical Point

The loss of the atrial "kick" during atrial fibrillation (AF), associated with a rapid heart rate, may be linked with more marked clinical deterioration in patients with diastolic dysfunction. This is due to the fact that the contribution of the atria is more important in these patients. Furthermore, the high heart rate shortens the period of diastolic filling, resulting in elevation of the end-diastolic filling pressures.

Clinical Presentation

Patients with diastolic heart failure present with very similar symptoms as patients with systolic dysfunction. Shortness of breath (or fatigue) on exertion are the usual symptoms, but this may progress to increasing dyspnea, orthopnea, paroxysmal nocturnal dyspnea, and lower leg edema. Physical examination may reveal elevated blood pressure (BP) and cardiac auscultation may show an S4, a sustained apical impulse (evidence of LVH) and sometimes an S3. If the patient is in overt heart failure, there may be associated jugular venous distension, pulmonary crackles or lower leg edema.

The presence of a normal cardiac silhouette on a chest X-ray, with signs of interstitial or alveolar edema, should raise the possibility of diastolic heart failure. LVH on the 12- lead-ECG might give us an indication to the often associated diastolic dysfunction.

The following factors should be considered clues to the presence of diastolic heart failure:

- If the patient is hypertensive and elderly (especially among women);
- Diabetes;
- LVH;
- Enlarged LA with normal systolic function; or
- Mild regional wall motion abnormalities.

Etiology of Diastolic Dysfunction

Numerous conditions are associated with abnormal diastolic function and may produce clinical signs of heart failure. The presence of these conditions should be looked for when faced with abnormalities of diastolic function.

1. **Hypertension**: Often associated with diastolic dysfunction, with or without LVH. In fact, this may precede LVH and is found in approximately 75% to 85% of patients with mild to moderate hypertension.
2. **Ischemic heart disease** (IHD), with or without prior myocardial infarction (MI).
3. **Older age**: Fibrosis of the myocardium and loss of its elastic properties are associated with the aging process and may cause an abnormal diastolic function.

4. **Obesity**.
5. **Diabetes**.

Some specific cardiac conditions may be associated with abnormal diastolic function. These include the following:

- Restrictive cardiomyopathies (*i.e.*, amyloidosis, hemochromatosis, sarcoidosis);
- Pericardial constriction; and
- Hypertrophic cardiomyopathies.

In general, diastolic dysfunction is found in the older population, especially among women, most of whom have hypertension.

Differential Diagnosis

The differential diagnoses in a patient with heart failure and preserved systolic function are numerous. However, incorrect diagnosis of heart failure and inaccurate measurement of LVEF must always be considered. Additionally, primary valvular abnormalities (aortic and mitral valve disease) and atrial myxoma should be ruled out. Episodic or reversible causes of LV systolic dysfunction may be attributed to diastolic dysfunction, if the ejection fraction is measured when the systolic function is back to normal.

High output states with associated heart failure should be considered (anemia, thyrotoxicosis, arteriovenous [AV] fistulae). Lung conditions (*i.e.*, chronic obstructive pulmonary disease with right heart failure, pulmonary hypertension with vascular disorders) may mimic heart failure.

Investigation

Before considering diastolic dysfunction as the cause of heart failure, it is imperative to appropriately assess the systolic function of the LV, as the treatment of both conditions is very different.

Cardiac ultrasonography remains the most widely used non-invasive method of assessing the diastolic function. It also evaluates the systolic function, the underlying valvular structures and the size of the different chambers. It often provides important hemodynamic information.

Doppler evaluation of the mitral valve inflow is the most commonly used technique.[5-7] It measures the ratio of the E wave velocity (velocity of flow during the early filling period) to A wave velocity (atrial contraction velocity), sometimes with preload reduction maneuvers such as Valsalva's maneuver. The deceleration time of the E wave, the Doppler assessment of the pulmonary veins (systolic, diastolic and atrial contraction velocities) are also used. Tissue Doppler interrogation of the mitral valve annulus is sometimes used as it is not influenced by the preload.

Diastolic function can also be quantitated by echocardiography:

1. Mild diastolic dysfunction or "impaired relaxation" (Grade 1)

- Could also be subdivided with likely normal resting LV filling pressures (mild) and likely elevated left ventricular end-diastolic pressure (LVEDP) — mild to moderate; and

- Usually no symptoms at rest with mild exercise limitation.

2. Moderate diastolic dysfunction or "pseudonormal" (Grade 2)

- Associated with elevated LVEDP; and
- Associated with exertional dyspnea and moderate functional impairment.

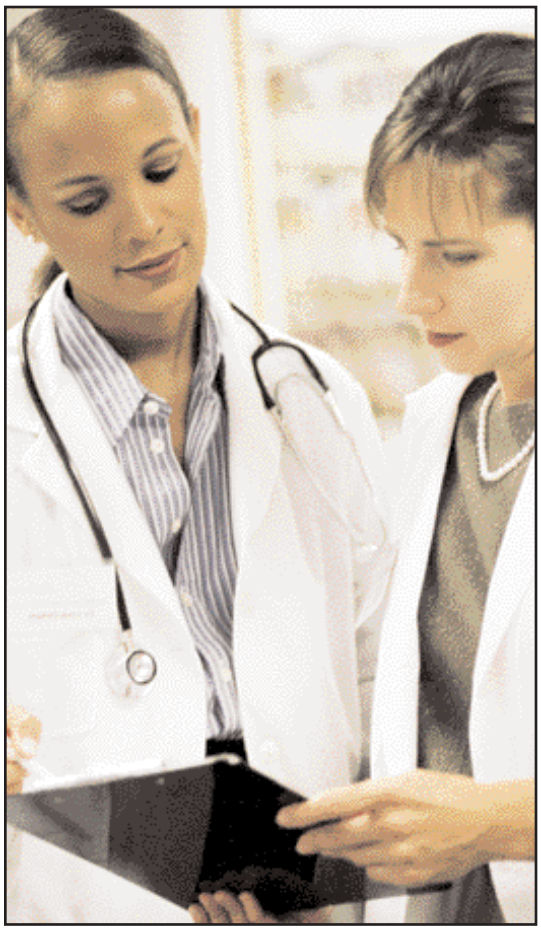
3. Severe diastolic dysfunction or "restrictive physiology" (Grade 3)

- Associated with high LV filling pressures (LVEDP);
- Dyspnea with minimal exertion and marked functional impairment; and
- May be further classified as Grade 4, if the mitral Doppler inflow is not reversed with Valsalva's maneuver.

Radionuclide ventriculography is a useful tool to assess the systolic function.[8] It gives fairly reproducible results and is generally accessible. It must be stressed that the nuclear ventriculography measures the diastolic and systolic volumes and calculates the ejection fraction (EF) by dividing the difference between the diastolic and systolic volumes by the diastolic volume (DV-SV/DV=EF).

The radionuclide ventriculography does not take into consideration the direction of the blood flow during systole and relies uniquely on the volumes of the LV cavity. Regurgitant valvular disease (*i.e.*, severe mitral regurgitation) may, therefore, overestimate the true systolic function of the heart by creating a smaller systolic volume and surreptiously giving us a higher EF. Caution must be used with heart failure patients who have a "normal EF" — especially when there is an audible murmur.

The ventriculography can also be used to assess the diastolic function by measuring the peak filling ratio (PFR) and the time to PFR, both of which are increased in patients with abnormal diastolic function.



In the absence of trials to guide therapy, physicians must base their management of diastolic dysfunction on the control of physiological factors adversely affecting the relaxation of the ventricle.

Finally, left heart cardiac catheterization and evaluation of pressure-volume curves at rest and during exercise is often considered the gold standard for the assessment of diastolic function. It is an invasive technique, however,

Case Discussion

Ms. P.L. clearly presented with signs and symptoms of CHF. She was treated with oxygen and IV furosemide. She has improved with diuresis. Captopril was re-introduced for her hypertension and furosemide was added for control of circulating volume.

Systolic dysfunction is the more common cause of CHF, but 20% to 40% of patients have normal or near-normal systolic function. Ms. P.L. has a few elements that may suggest diastolic dysfunction: long-standing hypertension in an elderly woman, a sustained apical impulse of normal size, an S4, LVH on the ECG and an X-ray showing signs of heart failure with a normal cardiac silhouette.

An echocardiogram was performed and showed a normal size LV cavity with significant concentric LVH, an ejection fraction of 65% and signs of grade 3 (severe or "restrictive physiology") diastolic dysfunction. There is also mild mitral regurgitation.

An exercise test with radionuclide imaging was performed to look for underlying ischemia and was negative. Of note, due to the associated repolarization abnormalities on the ECG, radionuclide imaging is indicated as the ST-segment analysis on the exercise ECG is often unreliable in that context.

The patient then was treated with verapamil for control of her hypertension and to control her heart rate at rest and during exercise (my bias is to control BP with a chronotropic negative drug [i.e., a beta blocker, verapamil, diltiazem] although the current recommendation is to control BP in accordance to published guidelines). Furosemide was also added and titrated carefully to control her volume status.

At follow-up three months later, Ms. P.L. had lost weight, and her BP was 135/80 mmHg with a resting heart rate of 62 BPM. She feels much better than she has over the last few years.

and mostly used when patients are being referred for another diagnosis (*i.e.*, IHD).

Treatment

There are a number of clinical trials to refer to when treating heart failure due to systolic dysfunction. Very few are available to assist in the management of patients with heart failure due to diastolic dysfunction.[2,9-11] Small trials, with inconclusive results, have been performed with angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta blockers, digitalis and calcium channel blockers (CCBs). Currently, the optimal treatment of diastolic heart failure has not been defined.

In the absence of trials to guide therapy, physicians must base their management of diastolic dysfunction on the control of physiological factors adversely affecting the relaxation of the ventricle.

1. Treat underlying cardiovascular disease:

- Control of systolic and diastolic hypertension in accordance with published guidelines. Consider aiming BP to < 130/80 mmHg.
- Reverse LVH, or minimize. Almost all classes of anti-hypertensives regress LV mass.
- Carry out appropriate screening and treatment of myocardial ischemia. Directed medical therapy or revascularization.
- Treatment of diabetes. Its impact is not well understood.

2. Facilitate diastolic filling time:

- Tachycardia shortens the time for ventricular filling and coronary perfusion. Control of ventricular rate in atrial fibrillation can provide symptomatic relief in patients with diastolic dysfunction.
- The benefits of restoring sinus rhythm are less clear.

3. Control of volume status:

- Use diuretics to control pulmonary congestion and peripheral edema. Diuretics may improve breathlessness by decreasing ventricular filling pressures.
- Volume depletion may cause orthostatic symptoms.

Considering the above, beta blockers and non-dihydropyridine CCBs (verapamil, diltiazem) seem like interesting drugs for controlling BP and heart rate, but there are no solid data showing their superiority to other drugs, such as ACE inhibitors or ARBs. Diuretics are often used in association to decrease circulating blood volume and filling pressures.

My personal approach is to control heart rate with beta blockers or non-dihydropyridines CCBs, then add a diuretic if symptoms persist or if I have evidence of excessive volume or high filling pressures.

Prognosis

In general, the prognosis of patients with diastolic heart failure is felt to be better than that of patients with systolic dysfunction. However, observational studies of patients discharged with a diagnosis of diastolic heart failure suggest their short-term mortality is lower, but the long-term mortality appears to be the same as patients with systolic heart failure, as are the rates of recurrent hospitalization.[12,13]

The assessment of the diastolic function in patients with systolic dysfunction may also guide our therapy. Recent studies suggest patients with reduced EF and Grade 4 diastolic dysfunction may not tolerate beta blockers. More data are needed, however, before this is generally accepted.

Finally, since diastolic heart failure is primarily a disease of the elderly, it may become a major health issue as our population ages.

References

1. Vasan RS, Levy D: Defining diastolic heart failure: A call for standardized diagnostic criteria. Circulation 2000; 101:2118-21.
2. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult. Executive Summary JACC, December 2001, p. 36-50.
3. Bonow R, Udelson JE: Left ventricular diastolic dysfunction as a cause of congestive heart failure: Mechanisms and management. Annals of Internal Medecine 1992; 117:502-10.
4. Honos G: Diastolic dysfunction: Clinical recognition and therapeutic approach. Contemporary Cardiology 1992; November/December:6-12.
5. Rakowski H: Canadian consensus recommendations for the measurement and reporting of diastolic dysfunction by echocardiography. Journal of the American Society of Echocardiography 1996; 9(5):736-60.
6. Lippincott W: *Assessment of Diastolic Function*, Chapter 5, The Echo Manual. Second Edition. J Ho, 1999, p. 45.
7. Balghith M: Assessment of diastolic dysfunction after myocardial infarction using Doppler echocardiography. Can J Cardiol 2002; 18(1):69-77.
8. La dysfonction diastolique: Perspectives cliniques. Travaux des symposiums sur le consensus canadien. Toronto, juillet 1992.
9. Cody R: Cardiology Clinics: Diastolic function and dysfunction. The Treatment of Diastolic Heart Failure 2000; 18(3):589-6.
10. Braunwald E, Libby P, D Zipes: *Heart Disease: A textbook of cardiovascular medicine*. Sixth Edition. W.B. Saunders Company, 2001, p. 302.
11. Appleton C, Firstenberg M, Garcia M, et al: Cardiology Clinics: Diastolic function and dysfunction. The Echo-Doppler Evaluation of Left Ventricular Diastolic Function 2000; 18(3):513-46.
12. Grossman W: Defining diastolic dysfunction (Editorial). Circulation 2000; 101:2020-1.
13. Banerjee P: Diastolic Heart Failure: Neglected or misdiagnosed? JACC 2002; 39(1),2002:138-41.