Current concepts in medicine

Isolated diastolic heart failure – what is it?

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Summary

Epidemiological evidence suggests that 20 to 40% of all patients with heart failure have normal systolic function. Isolated diastolic dysfunction may be the principle pathophysiological mechanism in these patients. The diagnosis of isolated diastolic heart failure is problematic and not merely based on demonstrating normal systolic function. The prognosis in isolated diastolic heart failure is more favourable than in systolic heart failure. At the present time, there is no licensed treatment for isolated diastolic heart failure and treatment is largely empirical.

Keywords: diastolic heart failure

Figure 1 Relationship between diastolic pressure and volume

Hospital admission with congestive heart failure is usually associated with impairment of left ventricular systolic function or, in some cases, valvular heart disease. Less commonly symptoms of heart failure arise when systolic contraction is normal or even enhanced. In this situation, isolated diastolic dysfunction is often implicated as the principle cause of pulmonary congestion.^{1–5} In this article we will try to clarify the role of isolated diastolic dysfunction as a cause for presentation with heart failure.

What is isolated diastolic heart failure?

Isolated diastolic heart failure is a clinical syndrome in which, in the presence of normal systolic function, pulmonary and venous congestion results directly from an inability of the left ventricle to fill normally at a normal diastolic pressure.

Isolated diastolic dysfunction can be due to either abnormalities of ventricular relaxation or alterations in the structure of the myocardium which result in reduced ventricular compliance or increased ventricular stiffness. Compliance is a passive function which is described by the relation of pressure to volume during diastole. The net result of impaired relaxation and/or reduced compliance is reflected haemodynamically in an inability of the ventricle to fill adequately without a compensatory rise in filling pressure. This can lead to pulmonary venous hypertension.⁶ The outcome for patients with isolated diastolic heart failure is a shifting upwards of the normal diastolic pressure–volume relationship (figure 1). Here, on the steep portion of the pressure–volume curve, relatively small changes in volume can lead to large changes in pressure.

Incidence and prevalence

The incidence and prevalence of isolated diastolic heart failure are unknown. Many studies have tried to assess this in the hospital setting but results have been variable and difficult to assess due to methodological differences. In the published literature, heart failure with normal systolic function is said to account for between 13 and 74% of all patients hospitalised with heart failure.⁵ A figure of 20% is more widely quoted and is in keeping with our own observations (unpublished). Importantly, only a small percentage of patients hospitalised with heart failure and normal systolic function have isolated diastolic heart failure (see under Diagnosis below). In the community the prevalence may be greater.⁷ Here, diastolic dysfunction may cause symptoms of breathlessness well before presentation to hospital with overt systolic heart failure.

Aetiology

Left ventricular diastolic dysfunction may arise from a variety of conditions, including long-standing hypertension, coronary artery disease, and normal ageing.

ISCHAEMIA

The dominant effect of ischaemia in the context of heart failure is impairment of systolic contractility. Before the onset of systolic impairment due to ischaemia or infarction, however, coronary artery disease can cause diastolic dysfunction.⁸ Relaxation is an active process and therefore sensitive to oxygen supply and ATP concentrations.⁹ In ischaemia, alterations in calcium homeostasis have been documented which can prolong the rate of myocyte cross-bridge detachment at the end of systole and delay relaxation, resulting in impaired ventricular filling.¹⁰

HYPERTROPHY

Echocardiographic left ventricular hypertrophy is present in about 15% of the general population and it is a strong independent risk factor for future cardiovascular mortality.¹¹ It is associated with conditions associated with chronic pressure or volume overload. Common causes include systemic

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Accepted 23 April 1998

Abbreviations used in figures 2, 3 and 4

AC=aortic valve closure; MC = mitral valve closure; LV = left ventricle; LA = left auricle; IVRT= isovolumic relaxation time, ie, the time between aortic valve closure and mitral valve opening; peak E = the maximal velocity peak of early trans-mitral filling; peak A = the maximal velocity peak of late trans-mitral filling with atrial contraction; EDT = the deceleration time of early filling or mitral deceleration time, ie, the time elapsed between the peak maximal early velocity and reduction of the trans-mitral gradient to zero; diastasis = the stage of diastole between early and late filling when pressure between the left atrium and left ventricle equalise and little filling occurs

Box 1

Figure 2 Mitral flow velocities are measured by pulse wave Doppler with the sample volume placed between the leaflet tips and are determined by the relative pressure across the mitral valve from left atrium to left ventricle. This illustrates a normal trans-mitral profile of a young adult. Following aortic valve closure there is a brief time period until the onset of filling. There is an initial rapid flow of blood as pressure in the LV drops below that in the left atrium (measured as peak E wave velocity). With simultaneous phonocardiography the isovolumic relaxation time, or time between the first component of aortic valve closure and start of ventricular filling can be measured. As the ventricle fills in early diastole there is a rise in pressure that exceeds left atrial pressure causing a deceleration of flow. The rate of deceleration is measured as the mitral deceleration time. During mid-diastole there is equilibrium of LV and LA pressures with low levels of forward flow due to inertia. Finally with atrial contraction there is a re-acceleration of trans-mitral flow as LA pressure rises above that in the LV (Peak A wave velocity). Quantitative measures derived from this flow velocity curve include, (a) maximal E and A velocities and their ratio, (b) velocity time integrals of early late and total diastolic flow, (c) time intervals such as the IVRT, the length of diastole and atrial filling period, and (d) measures of acceleration and deceleration of E and A waves. For expansion of abbreviations, see box 1

hypertension and valvular disease. The development of hypertrophy serves to maintain normal systolic function, at least for a time, but it consistently results in impaired diastolic function. This effect can be related both to a change in the rate of active relaxation and reduced diastolic distensibility.¹²

NORMAL AGEING

Early ventricular filling is normally reduced with age, an effect related to 'normal' age-induced changes in compliance due to alterations in collagen deposition and content.¹⁴ In addition, ventricular mass increases with age and this can further impair diastolic function.

Other causes of diastolic heart failure include the infiltrative and restrictive cardiomyopathies due to sarcoid, amyloid, and haemochromatosis. Similarly, pericardial disease and pulmonary veno-occlusive disease can cause heart failure with preserved systolic function. Here, variations in right ventricular pressure and filling result in abnormal left ventricular filling and pulmonary congestion due to ventricular interaction.¹⁵

Diagnosis

A large number of parameters have been used to measure diastolic function and this is a reflection of the absence of a single index of diastolic function that is universally acceptable. Fundamental to the diagnosis of isolated diastolic dysfunction is the demonstration of elevated left ventricular filling pressures with normal systolic function.

CLINICAL DIAGNOSIS

Clinical diagnosis is not easily achieved, as signs and symptoms of pulmonary congestion are common to both systolic and diastolic dysfunction. Some studies have suggested that features such as elevated blood pressure on admission, and a history of hypertension together with no history of myocardial infarction, were more common in patients with diastolic rather than systolic heart failure, although these features have consistently failed to identify patients with preserved systolic function in other studies.⁵ At the bedside, however, certain clues may indicate possible diastolic mechanisms. Suspicion of diastolic dysfunction should be aroused in long-standing hypertensive patients who present with pulmonary oedema, especially if elderly, and there is clinical and electrocardiographic evidence of left ventricular hypertrophy.¹⁶ Furthermore, elderly patients with ventricular hypertrophy may develop pulmonary oedema with the onset of atrial fibrillation. Here, diastolic heart failure results from the combination of reduced atrial filling and reduced ventricular compliance which can result in pulmonary congestion even in the presence of normal systolic contractility. Similarly, history and clinical examination may suggest valvular, pericardial or infiltrative disease such as amyloid.

In terms of diagnosing isolated diastolic heart failure, one consistent error is the assumption that clinical signs and symptoms of heart failure in the presence of normal systolic cardiac function implies diastolic heart failure. This notion is flawed. Firstly, pulmonary disease and oedema of other causes must be ruled out. In addition, valvular disease, such as mitral regurgitation which can be associated with a normal ejection fraction despite significantly reduced systolic contraction, needs to be ruled out. Thirdly, and perhaps most importantly, intermittent ischaemia resulting in global or regional systolic dysfunction or mitral incompetence and paroxysmal arrhythmia should be excluded. Finally, before diagnosing diastolic heart failure, there should be some evidence of raised ventricular filling pressure.

CARDIAC CATHETERISATION

The definitive method of defining diastolic function remains cardiac catheterisation and direct pressure and volume measurements. Here the rate of pressure decay at the end of systole can be accurately measured and pressure volume loops throughout the cardiac cycle can be constructed.¹⁷ Invasive studies can be related accurately to changes in relaxation and compliance, although they clearly remain impractical for widespread use.

ECHOCARDIOGRAPHY

In terms of noninvasive assessment of diastolic function, the advent and widespread use of echocardiography and Doppler echocardiography represent major advances. Systolic and valvular function can be assessed and trans-mitral and pulmonary venous Doppler analysis can provide indirect information about diastolic function. The application of the trans-mitral Doppler profile to the assessment of diastolic function was first described by Kitabakate *et al.*¹⁸ In the

Figure 3 When abnormal relaxation is the predominant abnormality the isovolumic relaxation time is long and initial decline in LV pressure is slow. Hence early filling is reduced and there is a large compensatory filling at atrial contraction. The ventricle continues to relax after opening of the mitral valve and it takes longer to equalise ventricular pressure with atrial pressure resulting in a longer deceleration time. For expansion of abbreviations, see box 1

Figure 4 With more severe diastolic dysfunction a Doppler pattern known as restriction occurs. Here with high left atrial pressure the IVRT shortens and E velocity becomes higher, ventricular compliance is reduced and the rise in ventricular diastolic pressure is very rapid during the early filling phase (short E deceleration time). An elevated left ventricular diastolic pressure reduces filling due to atrial contraction (reduced A velocity). For expansion of abbreviations, see box 1

To establish a diagnosis of isolated diastolic heart failure the clinician must

- establish the diagnosis of pulmonary congestion
- demonstrate normal systolic function
- exclude mitral incompetence and intermittent ischaemia
- demonstrate abnormal trans-mitral and pulmonary venous flow profiles on comprehensive Doppler examination
- ideally, document elevated left ventricular end diastolic pressure

Box 2

General guidelines of treatment of isolated diastolic heart failure

- maintain atrial-ventricular synchrony
- control blood pressure
- treat myocardial ischaemia
- slow the heart rate
- treat congestive symptoms by cautious use of diuretics and nitrates

Box 3

last two decades numerous other investigators have explored and expanded the role of noninvasive Doppler assessment of diastolic filling.¹⁸⁻²⁵ Three Doppler flow profiles have been recognised and these are illustrated and explained in detail in figures 2, 3 and 4 (see box 1 for explanation of the abbreviations used). In addition to characterising diastolic filling, analysis of the trans-mitral Doppler flow profile can provide prognostic information. In dilated cardiomyopathy prognosis correlates with the mitral deceleration time, irrespective of systolic function.²⁴

While undoubtedly useful, there are problems with the interpretation of Doppler profiles. One important and often under-appreciated limitation is that these measurements reflect filling and not function and are dependent on patient characteristics such as heart rate, age, and physiological variables such as preload and rate of left ventricular relaxation, elastic recoil, left atrial pressure, and left atrial and ventricular compliance.¹⁸⁻²⁵ These complexities limit the usefulness of Doppler echocardiography. This is particularly evident where measurements are limited to isolated Doppler measurements. These should be interpreted with caution, especially if not corrected for heart rate and age.

Another difficulty with the interpretation of Doppler indices of diastolic filling is the vexing problem of pseudonormalisation. This pattern represents a transition phase between abnormal relaxation and restriction where rising left atrial pressure in the setting of abnormal relaxation can produce a profile identical to that seen in normal subjects despite grossly abnormal diastolic function. These problems have been recognised by experts in the field of diastolic pathophysiology who suggest that for clinical usefulness the Doppler examination should be as comprehensive as possible and ideally include supplementary information obtained from an analysis of pulmonary venous flow.²⁵ On a positive note, newer techniques such as flow propagation velocity, exercise Doppler studies, and tissue Doppler echocardiography may prove of more clinical use in the future.²⁶⁻²⁷

RADIONUCLEOTIDE SCINTIGRAPHY

Radionuclide techniques can similarly be employed to provide indices of diastolic filling. By analysing time-activity curves, parameters such as the peak filling rate, and atrial filling fraction can be derived.²⁸ Once again, these are measures of the atrioventricular pressure gradient and reflect filling rather than function. The diagnosis of isolated diastolic heart failure is summarised in box 2.

Treatment

As yet, there are no large-scale, placebo-controlled trials evaluating the efficacy of therapy in isolated diastolic heart failure, and limited data on agents that selectively enhance myocardial relaxation. In spite of this, several treatment guidelines are recommended. One general principle for patients with decompensated diastolic heart failure is the restoration of atria-ventricular synchrony in atrial fibrillation. In this respect, cardioversion to sinus rhythm should be attempted, if possible. In terms of symptomatic treatment, diuretics which may lower the operating point on the diastolic pressure volume relationship are recommended but only with caution so as not to excessively reduce preload.²⁹ The treatment of hypertension and regression of left ventricular hypertrophy is an obvious goal, although it is not yet clear whether regression of left ventricular hypertrophy is associated with sustained improvement in diastolic function. Slowing of the heart rate (and therefore increasing diastolic filling time) and treating ischaemia with beta-blockers or calcium channel antagonists is indicated where appropriate.³⁰

Prognosis

There is little information in the literature regarding the prognosis of isolated diastolic heart failure. In the V-HeFT study, subgroups of patients with preserved systolic function had lower mortality and this, together with the results of other studies, tends to suggest a more favourable outlook in heart failure associated with normal systolic cardiac function.⁵⁻³¹

Conclusions

Diastolic dysfunction is the principle pathophysiological process in a significant minority of cases of heart failure. The diagnosis of isolated diastolic heart failure is difficult and is not merely a diagnosis of exclusion. It is based on the demonstration of raised ventricular filling pressure, normal ventricular volume and systolic function, and the absence of mitral incompetence, and intermittent

ischaemia. As yet there is no specific treatment that improves diastolic function directly. Treatment guidelines include the restoration of sinus rhythm, control of tachycardia, and the cautious use of diuretics and nitrates to relieve pulmonary congestion.

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