Diastolic heart failure in the elderly

Diastolic dysfunction can coexist with systolic dysfunction, but a significant proportion of patients with clinical features of heart failure have isolated diastolic dysfunction. Differences in management mean that it is necessary to distinguish between the two types of ventricular failure.

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Between 20 and 40% of patients with typical clinical features of heart failure have a normal or near-normal left ventricular ejection fraction, which indicates that the failure is predominantly diastolic. This type of ventricular dysfunction is classically observed in hypertrophic and restrictive cardiomyopathy, but is far more common in hypertensive and ischaemic heart disease. Diastolic heart disease is particularly prominent in the elderly, among whom women are disproportionately affected.

Systolic and diastolic heart failure often coexist, especially when aetiological factors common to both are present, but differences in treatment mean that a distinction must be made between the two conditions (see the box on page 46). This article reviews current knowledge of the pathology and management of diastolic heart failure, with particular emphasis on elderly patients.

Causes of diastolic dysfunction

The causes of diastolic dysfunction are listed in Table 1; of these, systemic hypertension and coronary heart disease are the most common in the elderly.[2,3] In addition to having a greater predisposition to aetiological factors, elderly patients have 'physiological' changes that impair ventricular

IN SUMMARY

- **Diastolic dysfunction is common, especially in elderly patients, and can coexist with systolic dysfunction.**
- **Systemic hypertension and coronary heart disease are the most common causes of diastolic dysfunction in elderly patients, occurring against a background of age-related changes in myocardial compliance.**
- **The gold standard for diagnosis of diastolic function is direct assessment via cardiac catheterisation and haemodynamic studies. However, several noninvasive techniques are available – the most convenient and commonly used of these is Doppler echocardiography.**
- **At present, data from large randomised trials are not available for the pharmacological treatment of diastolic heart failure.**
- **Control of aetiological factors, particularly hypertension, coronary heart disease and arrhythmias, constitutes the mainstay of management of diastolic heart failure.**
- **Diuretics are effective in reducing pulmonary congestion and provide symptomatic relief, but must be used judiciously.**
- **Beta blockers, rate-limiting calcium channel antagonists and ACE inhibitors (or angiotensin II antagonists if there is true intolerance to ACE inhibitors) may be used to improve ventricular filling and/or retard ventricular remodelling. The choice of agent (or agents) should also be determined by comorbid conditions.**

filling.[1,4] Ageing is associated with decreased elasticity of the heart and great vessels, which leads to myocardial stiffness and increased afterload, respectively; both phenomena contribute to a decline in the rate of ventricular filling. The higher prevalence of diastolic dysfunction among elderly women may be explained by their greater susceptibility to these changes.[5]

The ongoing pathophysiological process in heart failure involves neurohormonal activation in response to decreased cardiac output, leading to increased vascular resistance as well as fluid and salt retention. Long term activation of the renin–angiotensin–aldosterone system and the sympathetic nervous system also causes myocardial remodelling,[6,7] which is characterised by apoptosis, cellular reproliferation, hypertrophy and fibrosis. Remodelling leads to myocardial stiffness and further impairment of myocardial contractility and elasticity.

Diagnosis

The three diagnostic criteria for isolated diastolic heart failure are:

- typical symptoms and signs of heart failure
- normal or only slightly reduced left ventricular systolic function
- impaired ventricular relaxation with elevated end-diastolic pressure.

The chest x-ray may reveal pulmonary venous congestion (see Figure 1), but this finding is not specific to diastolic heart failure. The differential diagnoses for a patient with clinical heart failure and normal systolic function are listed in Table 2.

Symptoms and signs

The typical symptoms of left ventricular failure are dyspnoea (especially on exertion), orthopnoea, paroxysmal nocturnal dyspnoea and lethargy. Peripheral venous congestion occurs with right sided failure. It must be borne in mind, however, that the clinical presentation of heart failure is often atypical – and therefore less obvious – in elderly patients, and that the symptoms may be masked by many other conditions, such as chronic airways disease and pneumonia.

Left ventricular systolic function

A left ventricular ejection fraction of 40% is the cutoff figure generally used to define isolated

Table 1. Causes of diastolic heart failure

Structural

- Systemic hypertension, causing concentric left ventricular hypertrophy
- Coronary heart disease, causing myocardial remodelling
- Aortic stenosis, causing concentric left ventricular hypertrophy
- Hypertrophic obstructive cardiomyopathy
- Restrictive cardiomyopathies (e.g. amyloidosis, sarcoidosis, haemochromatosis)
- Pericardial constriction (e.g. chronic pericarditis)
- Age-related changes: increased myocardial stiffness, decreased elasticity of great vessels and increased afterload

Functional*

- Atrial fibrillation

* Inadequate ventricular filling.

Table 2. Differential diagnoses*

- Isolated diastolic heart failure
- Primary valvular disease
- Heart failure associated with high metabolic demand (e.g. anaemia, thyrotoxicosis)
- Pulmonary vascular diseases causing pulmonary hypertension
- Atrial myxoma

* In a patient with clinical heart failure and preserved systolic function (assuming accurate assessment of left ventricular ejection fraction).

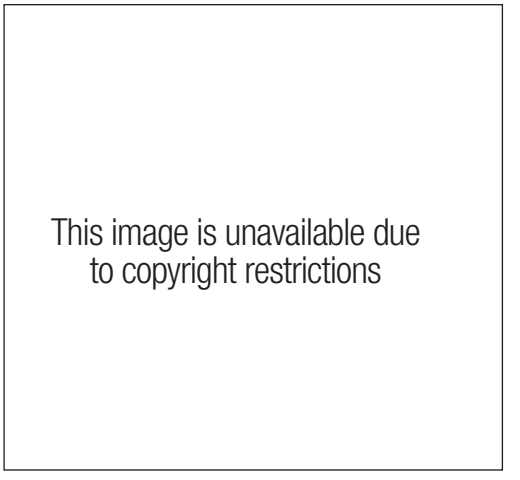

Figure 1. Chest x-ray of a patient with left ventricular failure secondary to hypertension, showing pulmonary venous congestion.

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diastolic dysfunction. The fraction is measured directly by gated cardiac blood pool scanning or estimated by echocardiography.

Ventricular relaxation and end-diastolic pressure

Cardiac catheterisation and haemodynamic studies constitute the gold standard for direct assessment of diastolic function. Several noninvasive techniques are used, but all of these are limited by heart rate, nonspecific transient changes in cardiac filling patterns, and mitral regurgitation. The most convenient and commonly used noninvasive technique for assessing diastolic function is Doppler echocardiography (see the box on page 49). Other noninvasive tests include magnetic resonance imaging and radionuclide angiography.

The pathophysiology of systolic and diastolic heart failure

The pathological hallmark of heart failure is ventricular dysfunction, which describes the inability of the heart to pump blood to meet the requirements of the metabolising tissues or the ability to do so only in the presence of elevated end-diastolic volumes and/or pressures. There are two types of ventricular dysfunction: systolic and diastolic (see Figure A below).

Systolic dysfunction

Systolic dysfunction is characterised by impairment of myocardial contractility, leading to decreased stroke volume for any level of end-diastolic volume and depressed maximal stroke volume. There is inadequate ventricular emptying and eventual ventricular dilatation.

Diastolic dysfunction

The principal abnormality of diastolic dysfunction is impaired relaxation of the ventricle and increased resistance to ventricular filling. The relationship between end-diastolic ventricular volume and stroke work is preserved, but there is a leftward shift in the diastolic pressure–volume curve such that end-diastolic ventricular pressure is increased for any level of end-diastolic volume. Augmentation of left atrial and pulmonary venous pressures is a prominent and early feature.

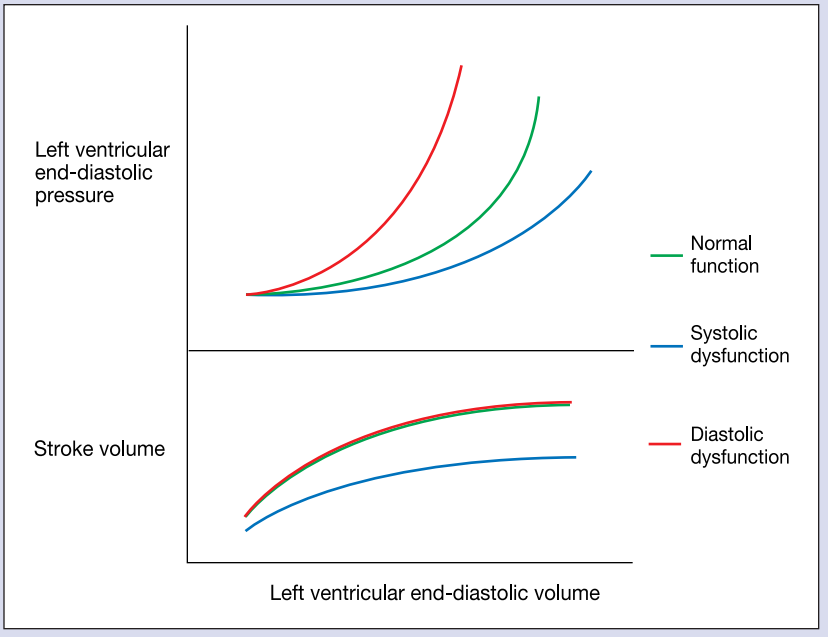

Figure A. The relation between left ventricular end-diastolic volume and pressure (top) and stroke volume (bottom), shown for normal ventricular function (green) and for systolic (blue) and diastolic dysfunction (red).

Management

Data from large randomised clinical trials are lacking for the pharmacological treatment of diastolic heart failure. Current strategies aim to optimise physiological factors and are influenced by the presence of comorbid conditions.

Treating aetiological factors

Specific attention to the underlying cause (or causes) of diastolic heart failure constitutes the cornerstone of management. In particular, treatment of hypertension, coronary heart disease and arrhythmias is crucial.

Systolic and diastolic hypertension both need to be controlled. Consideration should be given to target levels below those recommended for patients with uncomplicated hypertension[1] – that is, less than 130/80 mmHg.

Patients with coronary artery disease in whom ischaemia is contributing to diastolic dysfunction should be considered for coronary revascularisation. At the least, medical management should be optimised.

In patients who have atrial fibrillation, reversion to sinus rhythm should be attempted electrically. Beta blockers and amiodarone are alternatives to electrical cardioversion, and are agents of choice for prevention of recurrence. Digoxin (Lanoxin), with its positive inotropic effects, should be used with caution because it reduces diastolic filling time and can exacerbate diastolic heart failure.

Reducing central blood volume

Constriction of circulating blood volume is important because it is a major determinant of ventricular pressures. Fluid intake should be restricted to 1.5 L/day or, in severe cases of heart failure, to 1 L/day. Daily weighing is desirable, and medical consultation should be sought if weight increases by more than 1.5 kg in a 24-hour period or if there is other evidence of excessive fluid retention. Dietary sodium should not exceed 2000 mg/day.

Diuretics are effective in reducing pulmonary congestion and provide symptomatic relief. However, they must be used judiciously because patients with diastolic dysfunction are particularly susceptible to the consequences of excessive diuresis – namely, underfilling and further reduction in stroke volume. This volume sensitivity is explained by the steep end-diastolic volume–pressure curve observed with diastolic dysfunction (see the box on page 46).

Extra precautions apply specifically to elderly patients. Diuresis may be problematic if there is poor mobility and incontinence. As with other blood pressure-lowering medications, postural hypotension is common with diuretics and may predispose to falls.

Improving left ventricular relaxation and filling

Beta blockers and rate-limiting calcium-channel antagonists (i.e. verapamil and diltiazem) are most commonly used to improve ventricular filling. These negatively inotropic and chronotropic agents act by prolonging diastolic filling time. Conversely, inotropic drugs may worsen diastolic failure.

Beta blockers and rate-limiting calcium-channel antagonists are also useful for treating hypertension, coronary heart disease and arrhythmias if these conditions are contributing to diastolic dysfunction; beta blockers also prevent myocardial remodelling. Verapamil and diltiazem are, however, contraindicated in patients who have coexistent systolic heart failure, and elderly patients with systolic dysfunction may have heightened sensitivity to beta blockade. This contraindication is a consequence of the negatively inotropic effects of these agents.

Retarding ventricular remodelling

Angiotensin converting enzyme (ACE) inhibitors counter neurohormonal activation in heart failure and lead to retardation of myocardial remodelling. Current evidence from clinical trials of the efficacy of these agents is limited to systolic dysfunction,[8-10] but results will soon be available from the Perindopril for Elderly People with Chronic Heart Failure (PEP–CHF) study, a trial involving approximately 1000 elderly subjects

Doppler echocardiography

Doppler echocardiography is a noninvasive technique used for assessing diastolic function based on the recording of transmitral velocity patterns (Figure B). Diastolic function is indicated by the ratio of early (E) to atrial (A), or late, filling velocity. In healthy young individuals, most diastolic filling occurs early (E/A >1). When ventricular relaxation is impaired, initial changes are a decrease in early filling and a compensatory increase in atrial contraction, resulting in a reversed E/A ratio – the 'delayed relaxation' pattern (E/A <1). With disease progression, the rise in end-diastolic pressure and left atrial pressure increases early filling, despite impaired relaxation, and a pseudonormal E/A pattern is observed (E/A >1). Further deterioration in ventricular compliance leads to markedly elevated left atrial pressures and vigorous compensatory early filling. This 'restrictive' pattern (E/A >>1) is associated with abrupt deceleration of flow during diastole, with little filling during mid-diastole and atrial contraction.

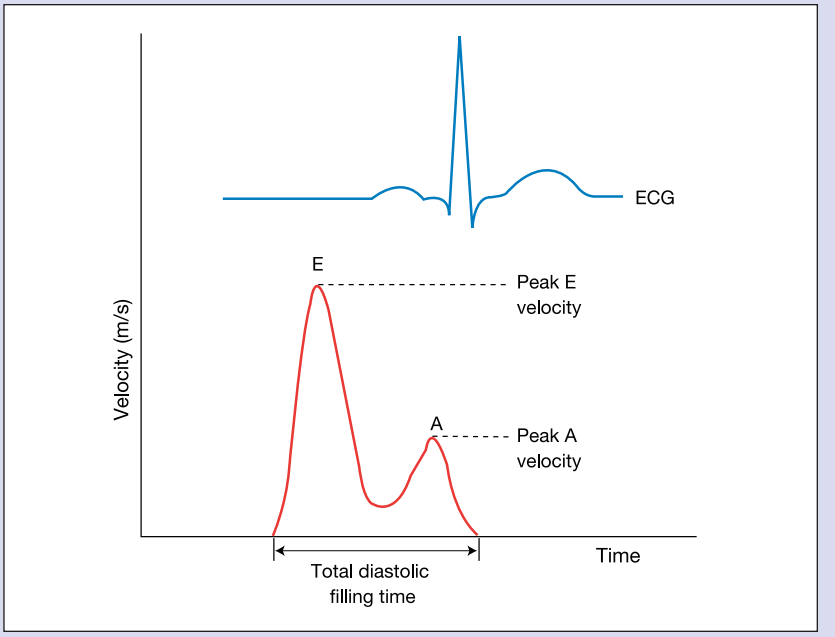

Figure B. Doppler echocardiograph for calculating the E/A ratio, shown for a normal mitral valve with the corresponding ECG trace. E = peak mitral flow velocity of early rapid ventricular filling. A = peak mitral flow velocity of late ventricular filling (atrial systolic).

with isolated diastolic dysfunction.[11] Until then, it will remain unclear if the clinical benefits of ACE inhibitors can be extrapolated to diastolic heart failure, but these agents can be considered for improving myocardial compliance. Their use is particularly supported in the presence of comorbid conditions such as coronary heart disease and diabetes mellitus, or situations where beta blockers and calcium channel antagonists are contraindicated.

The initial doses of an ACE inhibitor – especially the first dose – can be associated with marked hypotension. This effect is more likely in elderly patients and with concurrent use of other blood pressure lowering medications. Cough can be troublesome; hyperkalaemia and worsening of renal function are less common adverse effects. Elderly patients have a higher risk of renal impairment than younger patients, especially in the presence of existing renal parenchymal or renovascular disease, or coadministration of potentially nephrotoxic drugs like nonsteroidal anti-inflammatory drugs (NSAIDs).

The angiotensin II antagonists have similar effects on the renin–angiotensin–aldosterone system as ACE inhibitors but are not associated with increased levels of bradykinin and are therefore generally better tolerated. To date, however, the head-to-head comparisons of angiotensin II antagonists and ACE inhibitors in trials of systolic failure have been at best equivocal in terms of mortality benefit.[12,13] Studies using candesartan (Atacand) to treat both types of ventricular dysfunction are currently underway.[14] However, until these or other trial results suggest otherwise, angiotensin II antagonists should only be used as alternatives to ACE inhibitors when there is true intolerance to the latter (particularly cough). A history of angio-oedema secondary to ACE inhibitors generally contraindicates the use of angiotensin II antagonists.

As with ACE inhibitors, evidence of survival advantage conferred by beta blockade is confined to systolic heart failure,[15-18] but because beta blockers prevent myocardial remodelling (by reducing chronic adrenergic activity in the failing heart),[19] they may have further use in diastolic dysfunction. If systolic dysfunction is present, these agents should be introduced only when heart failure is stabilised, started at very low doses and up-titrated very gradually. There should be careful monitoring for adverse effects, including worsening of existing systolic function, to which elderly patients are particularly susceptible.

Using other treatments

As with systolic heart failure, anticoagulation for patients with diastolic heart failure is indicated in the presence of atrial fibrillation or proven thromboembolic disease. Elderly patients have an increased tendency to falls and bleeding that requires greater attention to warfarin administration and monitoring. In situations where anticoagulation is contraindicated or not feasible, antiplatelet agents should be considered.

Spironolactone is a nonselective antagonist to aldosterone. It is a weak diuretic, but its main action in heart failure is prevention of aldosterone-mediated ventricular remodelling. This drug has been shown to decrease mortality in patients with moderate to severe heart failure, when added to ACE inhibitors,[20] but effects on diastolic dysfunction have not been studied specifically. This lack of evidence and the availability of ACE inhibitors and angiotensin II antagonists means spironolactone is generally not recommended in this setting.

Other vasodilators are commonly used in chronic heart failure but, with the exception of the combination of hydralazine and high-dose nitrates, none has proven survival benefit.[21] ACE inhibitors (or angiotensin II antagonists if there is intolerance to ACE inhibitors) should be the vasodilators of choice.

Summary

Diastolic dysfunction is common, especially among elderly patients with heart failure. It can coexist with systolic dysfunction, but differences in management mean that it is necessary to distinguish between the two conditions. The most common causes of diastolic dysfunction in the elderly are hypertension and coronary heart disease, which occur against a background of age-related changes to myocardial compliance.

Diagnosis relies on demonstrating impaired ventricular relaxation with elevated end-diastolic pressure, either by invasive haemodynamic studies or, more conveniently, by Doppler echocardiography.

Control of aetiological factors, particularly hypertension, coronary heart disease and arrhythmias, constitutes the mainstay of management of diastolic heart failure. Restriction of intravascular volume by limiting fluid intake and administering diuretics provides symptomatic relief but must be undertaken carefully given the risk of ventricular underfilling. Digoxin and other inotropic agents should be avoided or used cautiously because these agents may also lead to reduced ventricular filling.

Drugs that are commonly used to improve ventricular filling and/or retard ventricular remodelling, although not mandated by randomised controlled trials, include beta blockers, rate-limiting calcium-channel antagonists, ACE inhibitors and angiotensin II antagonists. The choice of agents should also be determined by comorbid conditions. In the presence of coexisting systolic dysfunction, rate-limiting calcium-channel antagonists are contraindicated and beta blockers should be used with care. MT

A list of references is available on request to the editorial office.

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