

Heart failure:

the ignored cardiovascular epidemic

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Introduction

There have been several remarkable advances in the management of cardiovascular diseases over the last 20 years. In particular, notable developments have occurred in the care of acute coronary syndromes, complex arrhythmias and in revascularisation techniques. However, amidst these developments two major and related cardiovascular syndromes have been to a certain degree left behind; hypertension and congestive heart failure today represent the major cardiovascular public health concerns.

Data from Western populations suggest that as many as one-fourth to one-fifth of the adult population have systemic hypertension and that control is inadequate in as many as three-quarters of this group. Heart failure, the focus of this article, continues to affect more and more people, as a result of many factors including the aforementioned neglect of hypertension.

Epidemiology

We don't at present have accurate data regarding the incidence and prevalence of heart failure in Ireland. However, some estimates can be made using data from other European or American epidemiology studies which have similar population demographics. From these sources it would appear that the prevalence of heart failure is approximately 1% of the

total population. This may increase to 4-5% in those over 70 years. Based on these data, it is possible to estimate that 40,000 people have heart failure in Ireland.

Recent information indicates that the prevalence of this condition is increasing, likely reflecting the ageing population, improved survival of patients with heart failure, continuing under treatment of hypertension and improved acute prognosis in conditions such as myocardial infarction, thereby increasing the number of people surviving this event with damaged hearts potentially at risk for the later development of this syndrome.

Despite advances in the medical management of heart failure outlook in this condition remains very poor. Annual mortality from heart failure may be as high as 15-20%, dependent on the severity of the syndrome. Again, extrapolating to Ireland, this would suggest 6,000-8,000 deaths per annum from this condition. Furthermore, there is significant morbidity for patients with heart failure. Indeed, data from the US suggest that heart failure represents the most common discharge diagnosis from hospitals in patients over 65 years.

Moreover, in those discharged from hospital with heart failure there is a strikingly high readmission rate of approximately 30% within the first three months. All in all, these data underline the significant medical and economic impact of this condition and the very real likelihood that, in both aspects, the cost of this disease will increase.

Causes of heart failure

- Coronary artery disease
acute myocardial infarction, complications of infarction, chronic ischaemia.
- Valvular heart disease
- Heart muscle disease
dilated cardiomyopathy, hypertrophic cardiomyopathy, restrictive cardiomyopathy, amyloidosis/sarcoidosis etc
- Hypertension
- Pericardial disease
- Congenital heart disease
- Infection
systemic and infective endocarditis, myocarditis rheumatic fever
- Tachyarrhythmias
- Cardiac tumours
- Miscellaneous

Diagnosis

The diagnosis of heart failure rests on the presence of the symptoms and signs of heart failure, supported by the demonstration of abnormal cardiac function in conjunction with improved clinical status following the initiation of appropriate therapy. It is important to stress in an era of elaborate cardiovascular investigations that heart failure remains a clinical diagnosis, based on a group of symptoms and physical signs. Investigations such as echocardiography and chest x-ray provide supportive data but do not make the diagnosis on their own.

The symptoms of heart failure are relatively non-specific. Dyspnoea on exertion is one of the major complaints and is explained not solely by pulmonary venous congestion but also by factors such as respiratory muscle fatigue. Presence of dyspnoea when lying flat or waking the patient from their sleep are more specific presentations of this symptom in heart failure. Fatigue is also a common complaint, though clearly again very non-specific. This symptom, like dyspnoea, is probably explained by many different abnormalities, including reduced cardiac output, reduced muscle mass, abnormal skeletal mus-



*Figure 1.
Skeletal muscle
atrophy in heart
failure.*



*Figure 2 and 3.
Elevated venous
pressure and ankle
oedema reflecting
right heart failure.*



Figure 3.



*Figure 4.
Marked increase in cardiothoracic ratio likely reflecting
reduced LV systolic function.*

**Table 1.
Common causes of bilateral pitting ankle oedema**

1. Venous insufficiency
2. Postural i.e. dependent oedema
3. Drug-induced e.g. calcium channel blockers
4. Right heart failure (JVP should be elevated above 4cm above sternal angle at 45 degree examination position)

cle metabolism and deconditioning (Figure 1).

Palpitation, presyncope and syncope can also occur and generally reflect tachyarrhythmias, but can also be explained by bradyarrhythmias or treatment-induced hypotension. Other symptoms may be present but generally reflect the cause of the heart failure rather than the syndrome itself i.e. angina from coronary artery disease and ischaemic cardiomyopathy.

Examination of patients with heart failure may be quite unremarkable, especially if symptoms occur only with activity. The specific examination findings of heart failure either reflect right heart failure (increased jugular venous pressure with resultant development of peripheral oedema) and/or left heart failure (gallop rhythm, basal lung crackles) (Figure 2). Associated physical signs include a displaced apex beat reflecting cardiomegaly, right ventricular heave suggesting pulmonary hypertension, ankle oedema and hepatomegaly from high right-sided heart pressures. One of the major errors in the diagnosis of heart failure is the assumption that bilateral ankle oedema is a specific feature of heart failure. If this sign is due to heart failure, jugular venous pressure should be elevated. Indeed most bilateral ankle oedema is not due to heart failure (Table 1).

It is clear therefore that the diagnosis of heart failure can be difficult and, in many cases, heart failure may be part of a differential diagnosis including other cardiac and respiratory disorders, if not other possibilities including deconditioning, increasing age etc. To help make the diagnosis of heart failure, two other important features can be taken into account: the response to empiric therapy for heart failure and the presence of abnormalities of cardiac function most commonly defined by echocardiography.

Investigation

The first step is to ensure the diagnosis. As mentioned above this can be difficult and may require investigations to provide supportive data or empiric data on the response to therapy. It is of interest that there is approximately a 15% false positive diagnosis on admission through A&E at our hospital, underlining the initial difficulty in confirming the diagnosis at presentation.

It is particularly important to distinguish heart failure with abnormal systolic function of the left ventricle from that associated with normal systolic function (Table 2). Heart failure is generally thought to be associated with reduced systolic function and, whereas this is true in the majority of cases, it is important to recognise that approximately 30-40% of cases of community heart failure are associated with well-preserved

left ventricular systolic function. This distinction is of therapeutic importance as certain therapies are only of proven benefit in situations of reduced systolic function. The most effective means of assessing ventricular function is with echocardiography, with left ventricular ejection fraction being the most commonly quoted parameter. A value of >45-50% is usually accepted as normal.

Unfortunately this investigation is not widely or promptly available. Whereas it is hoped that the development of open access echocardiography will improve this situation this facility is not as yet available. Chest x-ray can provide some indirect information of ventricular function as an enlarged cardiac silhouette in most cases reflects reduced systolic function (Figure 4).

Once systolic dysfunction has been defined then a search should be initiated for the cause. Ischaemic cardiomyopathy accounts for the majority of cases, with the remainder secondary to valvular heart disease, long-standing hypertension or unexplained processes (idiopathic dilated cardiomyopathy) probably related to viral infections, toxins (including alcohol) and systemic diseases. Isolated right heart failure can occur from pulmonary processes, most notably chronic obstructive lung disease. The most important cause to define is ischaemia as this can significantly influence management, with revascularisation being a real therapeutic option in certain circumstances. Otherwise, aside from valve surgery, cause-specific therapy is very limited and treatment should focus on standard therapy for heart failure.

Less is known about heart failure associated with preserved systolic function of the left ventricle. Some cases are secondary to severe mitral regurgitation or aortic stenosis and therefore effective treatment requires valve replacement or repair. However, the majority in our experience appear to be due to impaired diastolic function i.e. impaired filling of the left or right ventricle. This is generally the result of a disease process that results in either reduced compliance of the ventricular myocardium, (hypertension, infiltrative cardiomyopathies, diabetes mellitus) or constriction of the myocardium from pericardial processes. Little is known about the effective management of diastolic heart failure.

Management

Part I. Systolic dysfunction

Diuretic therapy

Most patients present with symptoms and signs of congestion, and therefore usually get prompt relief with diuretics. The loop diuretics (frusemide or bumetanide) are the most effective. Combined diuretic therapy, referred to as sequential nephron blockade, can be of immense benefit especially in refractory cases. This is best achieved with the administration of metolazone 30 minutes before the administration of the loop diuretic. Cautious monitoring of potassium and renal function should be applied when using this approach. If an effective diuresis is still not forthcoming then intravenous diuretic therapy should be considered. This is especially pertinent where an elevated jugular pressure indicates the possibility of bowel congestion, therefore probably reducing absorption and subsequent bioavailability of orally administered diuretic.

ACE inhibitor therapy

In most cases, fairly prompt improvement in symptoms will be seen with diuretic therapy. Indeed many patients may report that they are back to normal. Nonetheless, it is important to clarify whether the patient will derive further benefit from additional therapy. For those with impaired systolic function, ACE inhibitor therapy is of unequivocal benefit, both in terms of reducing morbidity and improving prognosis. There does not appear to be a difference among ACE inhibitors with respect to these end-points. If possible, therapy should be titrated to high doses based on data from the Atlas study.

Concerns with ACE inhibitors have been overstated and the tendency to cease therapy or reduce dose because of low blood pressure should be avoided unless symptoms of poor perfusion are present i.e. significant postural symptoms, intermittent confusion or worsening angina or renal function. Many patients with this condition do well with systolic blood pressures around 90mmHg. In our experience, 90-95% of patients can be effectively treated with ACE inhibitor therapy, with the well-advertised cough rarely a problem. If cough is an issue one should consider the alternative explanation of persistent pulmonary congestion and temporarily increase diuretic to differentiate between these entities.

Digoxin therapy

Patients with heart failure, systolic dysfunction and preserved sinus rhythm also derive symptomatic but not prognostic benefit from digoxin.

The combination of digoxin, diuretic and ACE inhibitor therapy in patients with heart failure and systolic dysfunction has been referred to as standard triple therapy for this condition and, up until recently, represented the limit of proven effective therapy for this condition (some benefit to be derived from hydralazine/nitrate combination but tolerance of this regimen has been unpredictable). Recently, three further approaches have been shown to be of benefit in the medical management of systolic dysfunction and heart failure.

Beta blockade

This appears counter-intuitive, to use a negative inotropic agent in patients with impaired systolic function. However, the accepted concept that the progression of heart failure due to systolic dysfunction of the left ventricle is the result of an intense neuroendocrine imbalance with heightened levels and activity of vasoconstrictors and pro-growth substances (catecholamines, angiotensin II, endothelin etc) over vasodilator, anti-growth substances (bradykinin, natriuretic peptides, nitric oxide etc) has led to great efforts to modify this neuroendocrine imbalance.

The success of ACE inhibitor therapy is a very good example of the effectiveness of this approach. Sympathetic nervous system blockade with beta blockade has also recently been shown to improve symptoms and prognosis. For this particular indication, beta blockers are initially prescribed in low dose and gradually titrated over a period of weeks to months. They should only be used in patients with stable heart failure and patients should be made aware that they may not see the symptomatic benefits of this therapy in the initial few months. Indeed some patients experience a modest deterioration in their symptoms before noticing benefit.

Table 2.
Systolic and diastolic heart failure

	SYSTOLIC	DIASTOLIC
Prevalence;	60-70%	30-40%
Presentation	No distinction	
Causes	Hypertension Diabetes mellitus Old age (stiff heart)	Ischaemic heart disease Valvular heart disease Idiopathic cardiomyopathy
	Valvular disease Ischaemic heart disease	Hypertension
Function	Ejection fraction < 45%	Normal ejection fraction
Treatment	Treat cause if possible	
Symptom relief	Diuretics Digoxin	Diuretics
Improve prognosis	ACE inhibition Beta blockade Hydralazine and nitrates Angiotensin receptor blockade Spironolactone	None known

Angiotensin receptor blockade

Angiotensin receptor blockade (ARB) therapy represents a novel way of modulating the renin-angiotensin-aldosterone system. They have been incorrectly referred to as new ACE inhibitors when, in fact, their mechanism of action appears to be significantly different from ACE inhibitors. The receptor blockers are in routine use for the management of hypertension. These agents specifically block the effect of angiotensin II at receptor level and provide another means of reducing the effect of this peptide which is thought to stimulate many processes believed to be deleterious in heart failure (aldosterone secretion, sodium and water retention, cardiac myocyte hypertrophy etc).

Indeed, these agents may be more effective than ACE inhibitor therapy in blocking the effects of angiotensin II. At present, their role in the management of ventricular dysfunction and heart failure remains unclear. One of this class, losartan (Cozaar), has been approved in Ireland and several other European countries for use in heart failure associated with systolic dysfunction of the left ventricle. Several studies are under way to further define their role in heart failure, the majority of which are focusing on the potential benefit of adding this therapy to ACE inhibitor therapy to provide a more complete blockade of the renin-angiotensin-aldosterone system.

Spironolactone

The recent demonstration that spironolactone therapy, added to standard triple therapy, can improve prognosis has provid-

ed further evidence of the importance of reducing the activity of the renin-angiotensin-aldosterone system. Aldosterone levels tend to be elevated in heart failure, and this hormone has been shown to stimulate many deleterious processes, including myocardial fibrosis, sodium and water retention, potentiation of the sympathetic system and abnormalities of the baroreflexes. Standard triple therapy does not tend to reduce aldosterone levels, which probably explains why addition of spironolactone may be of benefit. However, ARB therapy may be as effective as spironolactone in reducing the effects of aldosterone (although this has not as yet been adequately studied).

Other therapies

No other agents have been consistently shown to improve prognosis in heart failure associated with systolic dysfunction. Anticoagulation is of benefit in those with atrial fibrillation. Its role in other situations awaits clarification from an ongoing study designed to address this issue. Data on amiodarone has been inconsistent, possibly dependent on whether the aetiology is ischaemic or otherwise.

Part II. Diastolic dysfunction

Diuretics

The major symptoms seen in diastolic dysfunction are those of congestion, and therefore, as in systolic dysfunction, diuretics are the mainstay of therapy. However, beyond diuretics there are no therapies that have been shown to be effective. This is partly explained by the lack of studies in this area, coupled by the fact that this form of heart failure represents a heterogenous population with many diverse aetiologies.

However, as hypertension contributes to many cases of diastolic heart failure, it is clear that control of blood pressure and prevention of the development of increased left ventricular mass are of importance. It is likely that we will learn more about the appropriate management of this form of heart failure in the next few years as there is increasing focus on this area.

Prognosis

Despite the increasing array of effective pharmacological strategies available in this condition prognosis remains poor. For those with stable heart failure managed in the community the three year mortality is approximately 30%. As these figures come from multicentre studies reflecting a select group of patients, it is likely that prognosis may indeed be worse than that quoted above. These figures apply to systolic dysfunction of the left ventricle; prognosis in diastolic dysfunction is unclear, again due to the lack of formal study of this group. From the Veterans study in the US, it appears that prognosis is not as bad as in systolic dysfunction

In the next edition of *HeartWise* there will be a follow-up article on heart failure focusing on problems with today's approach to this syndrome and the likely developments over the next few years.

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