

The past, present and future of heart failure therapies

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ABSTRACT The publication of a large number of randomised controlled trials in heart failure patients over the last 25 years has allowed the development of several excellent evidence-based guidelines.^{1–3} Revised SIGN guidelines for heart failure are due for publication this year.³ The major challenge facing us now is the implementation of these evidence-based therapies and the allocation of resources to allow the development and assessment of emerging technologies to ensure that patients receive the treatments they need.

KEYWORDS Please provide up to six keywords (list alphabetically)

LIST OF ABBREVIATIONS British Heart Foundation (BHF), B-type natriuretic peptide (BNP), chronic heart failure (CHF), cardiac resynchronisation therapy (+ defibrillator) (CRT(D)), electrocardiogram (ECG), general practitioner with a special interest (GPSI), left ventricular systolic dysfunction (LVSD), magnetic resonance imaging (MRI), National Institute for Health and Clinical Excellence (NICE), relative risk reduction (RRR)

DECLARATION OF INTERESTS No conflict of interests declared.

INTRODUCTION

At the recent College symposium on heart failure (www.rcpe.ac.uk/publications/online_abstracts.php), Dr T McDonagh from London set the scene with an overview of epidemiology and the diagnostic difficulties facing practitioners. Definitions have changed over the years and heart failure is now considered a syndrome characterised by the symptoms of shortness of breath, fatigue and oedema caused by cardiac dysfunction. Heart failure should no longer be thought of as a definitive diagnosis and a cause should be sought in most patients.

Diagnosis and medical treatment of heart failure

Unfortunately, clinical examination alone will correctly diagnose heart failure in only 50% of cases. While LVSD is unlikely in the presence of a normal ECG, Dr A Fuat, a GPSI, reminded us that the confident exclusion of ECG abnormalities by non-specialists is difficult.⁴ Furthermore, the chest radiograph is normal in at least 50% of people with significant LVSD but remains an important investigation in the breathless patient to exclude significant lung pathology. More recently, BNP can be routinely measured. B-type natriuretic peptide is elevated in patients with heart failure and importantly has a strong negative predictive value, i.e. if it is not raised, the patient is very unlikely to have heart failure.⁵ However, despite the inclusion of BNP in several guidelines, there appears to be a lack of consensus as to whether this test, when used in primary care, is cost-effective or reduces referrals to secondary care for further tests such as echocardiography.

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Clearly more work is required in this area to define the exact plasma concentrations of BNP that will guide clinical decision-making. Although echocardiography remains the most widely used test to confirm LVSD the use of MRI is likely to increase in the future.

Several evidence-based therapies exist for the treatment of heart failure (see Table 1). However, the use of these treatments remains poor and patients are often undertreated.⁶ Dr Fuat described some of the barriers to the implementation of heart failure therapies and discussed mechanisms for improving the uptake of heart failure therapy by addressing specific issues across primary and secondary care (see Figure 1).^{7,8}

Despite good heart failure treatments, many patients with heart failure will have other significant co-morbidities which impact on morbidity and mortality. There is an increasing awareness that anaemia may worsen symptoms and outcome in patients with heart failure. Dr R Gardner from Glasgow reported the results of preliminary studies using erythropoietin. The results of on-going larger randomised trials are awaited with interest.

Multidisciplinary heart failure teams

Dr C Cline from Sweden described the evidence for a 'multidisciplinary' team approach to the delivery of heart failure services.⁹ Whilst the individual needs of different heart failure populations will require local variations, dedicated heart failure nurses appear to be central to these multidisciplinary teams. Later in the symposium, Ms H Pryse-

TABLE 1 Pharmacological therapies for heart failure showing RRR for mortality and expected clinical effects.

	NYHA	RRR (mortality)	Symptomatic improvement
ACE-I	all	>30%	Yes
ARBs	all	~30%	Yes
Beta-blockers	II-IV	34-40%	No
Aldosterone inhibitors	III-IV	30%	Yes
Loop Diuretics	II-IV	No	Reduced oedema
Digoxin	III-IV	No	Reduced breathlessness

Hawkins, a heart failure nurse from London, described the function of heart failure nurses within multidisciplinary teams, calling for nurses to be more proactive in developing their roles. Currently the BHF provides short-term funding for many heart failure nurses although ongoing funding needs support from individual hospitals.

DEVICE THERAPY

Cardiac resynchronisation therapy and implantable cardiac defibrillators

Many patients with heart failure have mechanical ventricular dys-synchrony, often associated with a wide QRS complex on the ECG. Cardiac resynchronisation therapy attempts to correct this using pacemaker technology (see Figure 2). Professor S Cobbe from Glasgow presented the evidence from randomised controlled trials showing mortality and morbidity benefits for patients who receive CRT.^{10,11} However, patient selection and funding remain significant hurdles to widespread implementation of this new therapy. In

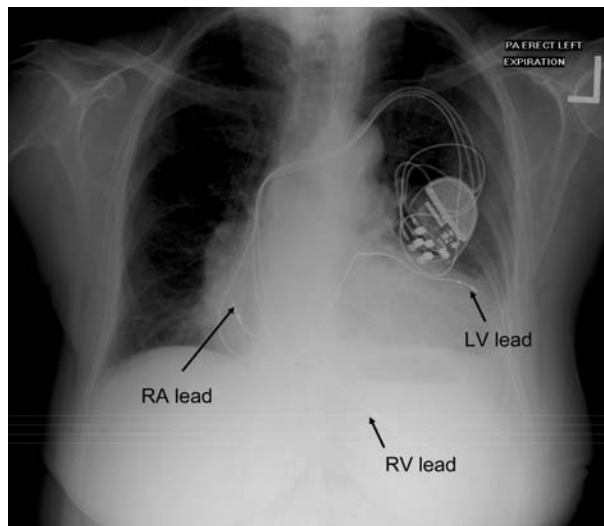


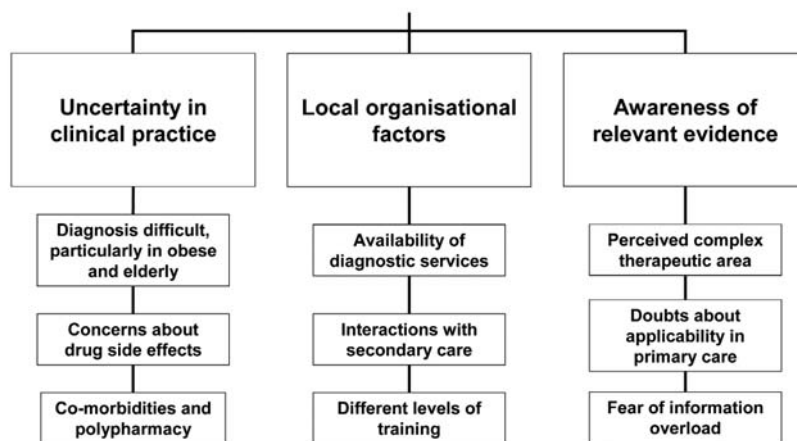
FIGURE 1 Cardiac resynchronisation therapy demonstrating pacemaker lead in right atrium (RA), right ventricle (RV) and left lateral vein pacing the left ventricle (LV).

England and Wales, CRT has been approved by NICE since 2003; the funding of CRT for appropriate patients is long overdue in Scotland. In addition, patients with heart failure commonly die from ventricular arrhythmias and the addition of a defibrillator to CRT (CRT-D) may give added benefit.¹⁰

Left ventricular assist devices

Despite optimal medical therapy, some patients will continue to have severe heart failure with organ hypoperfusion and pulmonary oedema. For the vast majority of patients this is terminal. However, in some (usually younger) patients there is the option of cardiac transplantation or the possibility of recovery from some reversible cause of LVSD, e.g. viral cardiomyopathy. Professor J Pepper described the surgical implantation of

Barriers to Accurate Diagnosis and Effective Management of CHF



Fuat A, Hungin APS, Murphy JJ. *BMJ* 2003;326:196-200

FIGURE 2 Barriers to accurate diagnosis and effective management of CHF.

LVADs which may allow time for definitive treatment or for recovery. It is proposed by some that mechanical heart pumps may in some patients provide 'destination' therapy. This is an area of medicine which is devoid of randomised controlled trials, however, several small series and anecdote suggest that it may be a suitable treatment option in certain, highly selected patients. Clinical trials are planned in the UK although lack of funding is hampering progress.

QUALITY OF LIFE AND DEATH ISSUES

Exercise

In 1711, J Addison stated that:

'Exercise ferments the humors, casts them into their proper channels, throws off redundancies, and helps nature in those secret distributions, without which the body cannot subsist in its vigor, nor the soul act with cheerfulness.'

However, as recently as 1988, expert opinion was that 'rest was good for the failing heart'. Dr A Clark from Hull presented data, supporting the benefit of exercise therapy in patients with heart failure. Whilst many of the studies involved highly specific supervised training programs, there is evidence to suggest that even simple exercise advice, such as using stairs rather than lifts, may be of benefit. The advice to stable heart failure patients, even with grade III symptoms (see Table 2) should be to undertake regular exercise three times per week.

Palliative care

The quality of death for patients with heart failure is poor.¹² Dr M Johnson from Scarborough reviewed some of the issues facing the patient dying of heart failure and reported the positive findings of their study into the use of morphine in heart failure patients with breathlessness. There are, as yet, few evidence-based studies of use of palliative care methods in patients with heart failure, although it is likely that strategies for patients with cancer could be used for patients with heart failure. It may be difficult for some cardiologists to decide when palliative care services are needed for their patients and Dr Johnson called for earlier discussion of patients and better communication between cardiologists and palliative care physicians.

The future

Two speakers addressed topics that may be of clinical interest in the future. The Davidson Lecture was given by Professor E Alton, who delivered an excellent overview of the challenges facing gene therapy and stem cell research. Professor Alton discussed the limited evidence and lack of well-conducted clinical

TABLE 2 New York Heart Association classification of Heart Failure.

Grade I	No limitation: Ordinary activity does not cause undue fatigue, dyspnoea or palpitation.
Grade II	Slight limitation of physical activity: Such patients are comfortable at rest. Ordinary activity results in fatigue, dyspnoea or angina
Grade III	Marked limitation of physical activity: Although comfortable at rest, less than ordinary activity will lead to symptoms.
Grade IV	Inability to carry on any physical activity without discomfort: Symptoms of congestive failure are present even at rest. With any physical activity increased discomfort is experienced.

trials in this area. He suggested that stem cells may have a therapeutic future, but there were many difficulties in this area of research, not least the major issue of stem cell or gene delivery to the myocardium. Indeed, even with an effective delivery system, detection of stem cells in the myocardium may be difficult. The two approaches most likely to be successful are direct injection via an endocardial catheter or by retrograde coronary vein injection. A randomised, double-blind controlled study is currently ongoing to assess delivery of stem cells by retrograde coronary vein injection. He concluded his talk optimistically with a quote from Sir Stanley Davidson:

'Let us freely admit our ignorance and the difficulties of the subject. Carefully controlled researches will unravel the problems, and when a solution is forthcoming, the whole therapeutic field of medicine will be revolutionised.'

Later in the day, Dr T Gershlick described percutaneous coronary intervention, proposing that early intervention would reduce the number of people who eventually develop chronic heart failure. Whether evidence of silent ischaemia should be sought in all patients with chronic heart failure, and how intensively should these patients undergo revascularisation, is uncertain, but clinical trials are ongoing to answer some of these questions.

CONCLUSIONS

This was an interesting symposium, reviewing the vast literature and evidence behind current heart failure therapies and outlining the work still to be done. The challenge for the future, however, is not only to continue to develop and adequately assess novel therapies, but also to effectively implement the therapies that we already have. This task, while considerably less attractive than the development of new therapies, may be more useful to the patients who currently suffer from heart failure.

Symposium learning points

- The diagnosis of heart failure is difficult.
- Less than half of patients with suspected heart failure will have evidence of LVSD
- Despite guidelines for evidence-based therapies, patients with heart failure remain under-treated.
- Implantable defibrillators can reduce mortality.

- New pacing modalities (CRT) can reduce mortality and improve symptoms.
- Funding of new proven therapies is difficult.
- Funding of research into new developments is difficult.
- Palliation of patients with advanced heart failure could be improved.

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