

# Economic implications of cardiac resynchronisation therapy

Many patients with heart failure remain symptomatic despite optimal drug therapy. Resynchronisation using a biventricular pacemaker has been proven in clinical trials to improve symptoms and life expectancy. Although these devices are relatively expensive, this treatment is cost effective, and should be employed more often than is currently the case in the UK, explains **Professor Martin Cowie**.

One to two per cent of the population in the UK have heart failure. Both the incidence and prevalence increase steeply with age, with the median age at diagnosis being 76 years<sup>1</sup>. Heart failure has significant economic implications for the health care system. It accounts for one to two per cent of the total NHS budget. This is driven by hospitalisation costs, with inpatient care accounting for 60 per cent of the total cost of heart failure<sup>2</sup>. Repeated hospitalisation for management of decompensation is common in patients with chronic heart failure. Considerable efforts are being made to improve the management of heart failure and to reduce unplanned hospitalisations. Multidisciplinary chronic disease management programmes, together with improved uptake of evidence-based drug therapies, such as angiotensin converting enzyme inhibitors and beta-blockers, have led to a recent decline in rates of heart failure hospitalisation. However, the total number of hospitalisations is increasing, in large part because of the ageing population. It has been predicted that hospital admissions for heart failure could rise by 50 per cent over the next 25 years<sup>2</sup>.

Despite improvements in the pharmacological management of heart failure, many patients remain symptomatic and have a poor quality of life, and the prognosis of patients with heart failure remains poor. Death is most commonly due to progressive pump failure or sudden cardiac death due to ventricular arrhythmia.

## What is cardiac resynchronisation therapy (CRT)?

CRT, or biventricular pacing, is a new technology for selected heart failure patients whose symptoms are moderate-to-severe and are inadequately controlled on medical treatment. The rationale for CRT is that a high proportion of patients — up to 30 per cent — with chronic heart failure and left ventricular systolic dysfunction have ventricular dyssynchrony, identified most easily on the electrocardiogram (ECG) as left bundle branch block. Ventricular dyssynchrony exists when the smooth and co-ordinated sequence of contraction between the atria, and within and between the ventricles, is lost.

CRT is designed to restore synchronous ventricular (and atrioventricular) contraction and thereby to improve cardiac function. It involves insertion of pacing leads via the cephalic or subclavian veins into the right atrium and right ventricle (as in conventional dual chamber pacing), with a third lead inserted via the coronary sinus to pace the left ventricle<sup>3</sup>. CRT treatment can also be given in combination with an implantable defibrillator (CRT-D).

## CRT clinical trials

Early studies showed CRT can improve cardiac performance and quality of life, and reduce

**PROFESSOR MARTIN COWIE** is professor of cardiology, National Heart & Lung Institute, Royal Brompton Hospital, Imperial College, London

hospitalisations in heart failure patients with left bundle branch block, but they gave no clear indication of its effects on mortality. Two recent large randomised controlled trials, COMPANION<sup>4</sup> and, particularly, CARE-HF<sup>5</sup>, have now demonstrated mortality benefits. Both studies involved patients with NYHA class III or IV heart failure due to left ventricular systolic dysfunction (ejection fraction  $\leq 35$  per cent) and evidence of ventricular dyssynchrony.

COMPANION (Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure) was a multicentre US study with 1,520 patients (median age 67 years). Patients were randomised to three groups: optimal medical therapy alone, optimal medical therapy plus CRT, or optimal medical therapy plus CRT-D. Both types of CRT reduced the combined risk of death or first hospitalisation from any cause (the primary trial end point) by approximately 20 per cent. Death from any cause (a secondary end point) was also reduced in both groups, but this survival benefit was statistically significant only in the CRT-D group.

CARE-HF (Cardiac Resynchronisation – Heart Failure) was a simpler study. It was a multicentre randomised trial to compare medical therapy alone with medical therapy plus CRT. The trial was carried out in 82 centres in 12 European countries and involved 813 patients who were followed for a mean of 29.4 months. Median age of patients in the CRT group was 67, with 25 per cent of patients being aged over 73 years. There was a 37 per cent reduction in death from any cause or unplanned hospitalisation for a major cardiovascular event (the primary trial end point). Unplanned hospitalisations for worsening heart failure were reduced by 52 per cent. In addition, the risk of death from any cause (the principal secondary end point) was reduced by 36 per cent in the CRT group. This is therefore the first trial to provide definite evidence of mortality benefits from CRT alone. CARE-HF also showed evidence of benefit from CRT in major sub-groups, including patients with diabetes<sup>6</sup>.

Both COMPANION and CARE-HF reported improved symptoms and quality of life in CRT patients. An important point to emphasise is that the benefits of CRT seen in these two trials are additional to the benefits of optimal pharmacological therapy. In CARE-HF there was a reduced incidence of sudden death in the CRT

group as well as a reduced incidence of death from worsening heart failure. It is, of course, possible that additional use of a defibrillator – CRT-D – will have further mortality benefits over CRT alone, but the only data so far has come from the COMPANION study which was not set up to compare the two types of CRT.

### Cost effectiveness of CRT

Although these key trials have demonstrated the potential clinical benefits of CRT in selected patients, the treatment is relatively expensive: as well as the cost of the device, implantation requires high technical expertise, the implant needs to be fine-tuned to optimise its benefit, and patients will require regular follow-up. Policy makers will want to know how cost effective CRT is in today's health care environment. This has been assessed using both the CARE-HF and COMPANION data.

The CARE-HF investigators calculated incremental cost effectiveness based on their study data with mean follow-up of 29.4 months. This assessment, calculated from a UK health systems perspective, took account of all resource costs, quality of life measured during the trial, and survival data<sup>7</sup>. It showed CRT was associated with a cost per quality adjusted life year (QALY) gained of €19,319 (around £13,000) – well below the (notional) threshold set by the National Institute for Health and Clinical Excellence (NICE) of £30,000. A further CARE-HF analysis<sup>8</sup> used an economic model to assess long-term cost effectiveness of CRT. A further CARE-HF analysis<sup>8</sup> modelled likely costs and benefits over a patient's lifetime, rather than only the relatively short duration of the study, and also showed treatment to be cost effective.

The COMPANION investigators used their study data in a model assessing cost effectiveness over a seven-year period, based on the US health system. Analysis of incremental cost effectiveness relative to optimal pharmacological therapy showed both types of CRT (with or without a defibrillator) to be cost-effective<sup>9</sup>. The researchers note their model did not take account of the fact effective treatment might reduce carer burden, an aspect that could increase overall cost effectiveness. Compared with some other cardiovascular health care interventions, including bypass surgery and angioplasty for chronic angina, CRT therefore certainly appears to be cost

## Key points

- Cardiac resynchronisation therapy (CRT) has been shown to improve mortality and morbidity in heart failure patients with a low ejection fraction and a broad QRS complex who are still symptomatic despite optimal drug therapy.
- Although the devices are expensive, CRT is cost effective with an estimated cost per quality-adjusted life year of £13,000.
- Use of CRT is limited in the UK by the number of centres able to implant such devices.
- Patients failing to respond to standard medical therapy for heart failure and who have a low ejection fraction and bundle branch block should be referred for assessment for CRT.

effective and cost should not be a reason to limit capacity.

The treatment is not currently widely used in the UK. In 2005, around 1,200 CRT devices were implanted, but numbers are growing at about 40 per cent a year<sup>10</sup>. Limitations to increased use include a lack of awareness of this treatment among healthcare professionals as well as a shortage of skilled staff to carry out the implantation procedure. An interesting possibility for the future, currently under investigation, is whether implanting a CRT device in patients with mild (NYHA stage II) heart failure will delay progression. This is being examined in an ongoing clinical trial.

For now, it seems appropriate to select patients for CRT on the basis of the CARE-HF patient population, in order to try to replicate the positive outcomes seen in this trial. This means that the treatment should be considered for patients with a low ejection fraction and broad QRS, who are symptomatic despite best therapy. This represents a large number of heart failure patients, perhaps more than 25,000 people in the UK. NICE is currently assessing clinical and cost effectiveness of CRT (with and without an implantable cardioverter-defibrillator (ICD)) for treatment of heart failure, but its report is not expected until July 2007.

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## Conclusion

We now have clinical trial evidence that CRT offers great opportunities for improving cardiac function and reducing morbidity and mortality in selected patients with moderate-to-severe symptoms despite optimal drug therapy. Consequently, heart failure patients who have left bundle branch block and remain symptomatic despite optimum pharmacological therapy should be referred to a cardiologist for consideration of this new treatment. Cost should not be a limitation to the use of CRT, as long as the patient does not have a co-morbidity that markedly reduces their life expectancy.

**Conflict of interest:** Professor Cowie has received honoraria for advisory boards and lectures related to treatments mentioned in this article.