Cardiac resynchronisation therapy for the treatment of heart failure

Guidance

1. Cardiac resynchronisation therapy with a pacing device (CRT-P) is recommended as a treatment option for people with heart failure who fulfil all the following criteria.

    - They are currently experiencing or have recently experienced New York Heart Association (NYHA) class III–IV symptoms.
    - They are in sinus rhythm:
        i. **either** with a QRS duration of 150 ms or longer estimated by standard electrocardiogram (ECG)
        ii. **or** with a QRS duration of 120–149 ms estimated by ECG **and** mechanical dyssynchrony that is confirmed by echocardiography.
    - They have a left ventricular ejection fraction of 35% or less.
    - They are receiving optimal pharmacological therapy.

2. Cardiac resynchronisation therapy with a defibrillator device (CRT-D) may be considered for people who fulfil the criteria for implantation of a CRT-P device in section 1.1 and who also separately fulfil the criteria for the use of an implantable cardioverter defibrillator (ICD) device as recommended in NICE technology appraisal guidance 95.

Development of the Guidance

The Appraisal Committee understood that the benefits of implantation of a CRT device are related to improvements in the symptoms of heart failure and the extension of life of patients with heart failure, as well as a reduction in the incidence of sudden cardiac death in this patient group. It also appreciated that the risk of sudden cardiac death in patients with heart failure is related to the presence of both

ventricular dyssynchrony and other underlying cardiac conditions that could add to the risk of sudden cardiac death.

The Appraisals Committee considered the evidence base for the clinical effectiveness of CRT-P and CRT-D in patients with heart failure. Four RCTs were assessed but particular attention was paid to the larger studies – COMPANION and CARE-HF. These two RCTs reported different results on the rate of death from heart failure. The CARE-HF study reported a statistically significant reduction in the incidence of death from heart failure for CRT-P compared with optimal pharmacological therapy alone, whereas the COMPANION study reported no difference in treatment effect. Pooled analysis, however, demonstrated a statistically significant reduction in death from heart failure for CRT-P compared with optimal pharmacological therapy alone. In addition, the studies indicated a statistically significant reduction in the risk of worsening heart failure, improvements in NYHA class and quality of life and overall a reduction in hospitalisations for heart failure. Similar results were reported for CRT-D compared with optimal pharmacological therapy.

The COMPANION study was the only RCT that provided a basis for direct comparison between the effectiveness of CRT-P and CRT-D but it was not powered to detect differences for this comparison. However, in this trial the use of CRT-D was associated with a statistically significant reduction in incidence of both death from all cardiac causes and specifically sudden cardiac death.

The cost effectiveness analysis compared:

- CRT-P with optimal pharmacological therapy
- CRT-D with optimal pharmacological therapy
- CRT-P with CRT-D.

CRT-P and CRT-D were both considered to be a cost effective use of NHS resources when compared with OPT alone on the basis of cost per quality-adjusted life year (QALY –NICE's preferred measure) at about £16,000 and £23,000, respectively.

The Appraisals Committee took into consideration all of the evidence available to it, including the testimony of both specialist clinicians and patients with experience of

these technologies, and concluded that the case for the cost effective use of CRT-P had been made. This was specifically for the group of patients with low left ventricular ejection fraction (less than 35%) who have (or have recently experienced) symptoms of heart failure rated as NHYA class III/IV despite optimal pharmacological therapy, and who additionally have evidence of cardiac dyssynchrony on the basis of the criteria defined in the principal RCTs.

Although CRT-D was cost effective when compared with optimal pharmacological therapy alone, the Appraisals Committee was not persuaded that this was the appropriate comparison. The comparison of CRT-D with CRT-P was more complex. In the absence of head-to-head trial evidence of these two technologies, the cost effectiveness analysis indicated that implanting a CRT-D rather than a CRT-P device would have a cost per QALY of about £40,000, making it not a cost effective use of NHS resources.

However, the Committee accepted that the cost effectiveness of CRT-D is likely to be considerably improved in people with additional risk factors for sudden cardiac death over and above those associated with cardiac dyssynchrony. Thus the Committee concluded that adding a defibrillator in the form of a CRT-D device should be considered for people with heart failure due to left ventricular systolic dysfunction who fulfil the criteria in section 1 of the guidance for the implantation of a CRT-P device, and also have additional risk factors for sudden cardiac death that separately fulfil the criteria for the use of an ICD device (as detailed NICE technology appraisal guidance 95) .

The decision on whether a CRT-P, CRT-D or ICD device is most appropriate should be made for each patient individually. It will depend on the relative importance of the risks associated with the underlying left ventricular dysfunction, ventricular dyssynchrony and symptomatic heart failure, as well as other factors that might contribute to the risk of sudden cardiac death.

The guidance on CRT should therefore be seen as complementing the earlier NICE guidance on ‘Implantable cardioverter defibrillators for arrhythmias’ (NICE technology appraisal guidance 95), because it provides additional treatment options for some of the groups of people covered in that guidance.