Electrical Device-Based Therapies for Heart Failure

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Despite advances in pharmacological treatment for heart failure, there are still a growing number of patients with advanced symptoms who suffer from significant morbidity and mortality. This has given rise to the development of device-based therapies which have favourably impacted on the outcomes in patients with heart failure.

Cardiac Resynchronisation Therapy (CRT)

Approximately one third of patients with systolic heart failure have a QRS duration greater than 120 ms, which is most commonly seen as left bundle-branch block. Widened QRS complex represents both inter- and intraventricular conduction delays or electromechanical dyssynchrony. Such asynchronous contraction pattern contributes to mitral regurgitation, reduction in stroke volume and subsequently leading to deleterious left ventricular remodelling. CRT delivers electrical stimuli to the left and right ventricles simultaneously with the goal of synchronising the activation of both ventricles. This is achieved by introducing a specially designed pacing lead into the left ventricle -- usually implanted through an intravenous approach via the coronary sinus and into a lateral cardiac vein -- in addition to placement of standard right-sided leads. The proposed mechanism of benefit by CRT is to correct the dyssynchrony between the right and left ventricles and the intraventricular dyssynchrony within the left ventricle by pacing the right ventricular apex and lateral or posterolateral wall of the left ventricle. Minimising intraventricular dyssynchrony has been shown to increase left ventricular filling time, decrease septal dyskinesis, reduce mitral regurgitation and improve global left ventricular function. These acute mechanical effects are accompanied by more chronic adaptations that lead to long-term benefits including improvements in neurohormonal status and left ventricular ejection fraction (LVEF) and reversing the adverse left ventricular remodelling.

CRT alone or combined with implantable cardioverter defibrillator (CRTD) are now standard of care for moderate to severe heart failure patients with cardiac dyssynchrony. Results from randomised, controlled trials have consistently demonstrated significant improvements in quality of life, functional status, and exercise capacity in patients with New York Heart Association (NYHA) Class III and IV heart failure who are assigned to CRT. In these patients, cardiac resynchronisation has also been shown to improve cardiac structure and function while significantly reducing the risk of worsening heart failure. Survival benefit by CRT has also been demonstrated in COMPANION (Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure) and CARE-HF (Cardiac Resynchronization-Heart Failure) trials. In COMPANION, CRT pacing with or without ICD capability was associated with a significant one-year relative-risk reduction of about 20% for all-cause death or hospitalisation when added to optimal medical therapy in over 1600 patients with ischaemic or nonischaemic NYHA class III to IV heart failure, an LVEF <35%, and a QRS interval of >120 ms. CARE-HF randomised 813 patients with NYHA class III to IV heart failure despite standard drug therapy, an LVEF <35%, and QRS duration of at least 120 ms. Those with a QRS duration of less than 150 ms were required to have echocardiographic confirmation of ventricular dyssynchrony. Over a mean follow-up of nearly 30 months, CRT was associated with significant 37% reductions in the risk of the primary end point (all-cause mortality or an unplanned cardiovascular hospitalisation). There was a 36% relative reduction in all cause mortality and a 10% reduction in absolute risk in addition to standard pharmacologic therapy. Based on the results from these large-scale randomised trials, the heart failure management guidelines of the American Heart Association (AHA) and American College of Cardiology (ACC) have incorporated CRT as a Class I indication for patients with ejection fraction less than or equal to 35%, NYHA Class III or ambulatory Class IV, sinus rhythm and QRS duration greater than or equal to 120ms despite optimal heart failure medication. Recently, the indication of CRT has been extended to patients with chronic atrial fibrillation or continuous right ventricular pacing. For Class III or ambulatory Class IV patients with cardiac dyssynchrony who have atrial fibrillation or who have frequent dependence on ventricular pacing, CRT is also a reasonable treatment option (Class IIa indication) according to the 2008 ACC/AHA Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities. Preliminary data have suggested that CRT may also be beneficial in patients with less symptomatic heart failure and in patients with normal QRS complex but with evidence of other parameters of cardiac dyssynchrony. Further data are required before extending the device indications beyond those currently authorised by the guidelines.

With advances in technology, the delivery of left ventricular lead is much easier than those of early generation though the procedure is still not risk-free.
Complications, though uncommon, related to positioning of the left ventricular lead include coronary sinus dissection or perforation, lead dislodgement, diaphragmatic pacing and contrast nephropathy. The overall success rate for CRT implantation ranges between 85 to 95%. However, a significant proportion of eligible patients after successful implant do not respond to CRT, the so-called non-responders. The non-response rate is up to around 30% in terms of clinical improvement. Potential causes for poor response to CRT include inappropriate patient selection, suboptimal left ventricular lead implantation site, left ventricular scarring and inappropriate programming of the atrioventricular and interventricular intervals after the procedure.

Implantable Cardioverter Defibrillator (ICD)

The implantable cardioverter defibrillator (ICD) is the single most effective treatment for the prevention of sudden cardiac death in patients at risk or who have had resuscitated sudden cardiac death. There is no argument that ICD should be used for secondary prevention once heart failure patients have resuscitated cardiac arrest or documented haemodynamically significant ventricular tachycardia. The role of ICD has now been extended for primary prevention of sudden cardiac death in heart failure patients who have poor left ventricular function. Patients with heart failure are at risk of sudden cardiac death. Heart failure is a major cause of sudden cardiac death and more than half of the deaths of patients with heart failure are due to sudden cardiac death. The Sudden Cardiac Death in Heart Failure (SCD-HeFT) study addressed the prophylactic effectiveness of ICD devices in decreasing mortality in patients with heart failure of either ischaemic or nonischaemic aetiology and an LVEF <35% and without ventricular arrhythmias. In SCD-HeFT, ICD therapy was more effective than pharmacological therapy in preventing mortality among patients with mild to moderate heart failure. The study showed that ICD therapy was associated with a decreased risk of death of 23% after five years of therapy. This mortality benefit was observed in patients who were already optimally managed on drug therapy. In the latest ACC/AHA/HRS 2008 Guidelines for Device Based Therapy of Cardiac Rhythm Abnormalities, ICD therapy is indicated (Class I, Level of evidence: A) in all symptomatic heart failure patients in NYHA functional Class II or III when the LVEF is < 35% due to previous myocardial infarction who are at least 40 days post infarct. Similarly, ICD therapy is also indicated in patients with nonischaemic dilated cardiomyopathy who have an LVEF less than or equal to 35% and who are in NYHA functional Class II or III. (Class I, Level of Evidence: B). Since ICD is an expansive device, these recommendations should be applied only to patients who are receiving optimal medical therapy and have a reasonable expectation of survival with good functional status for more than 1 year.

Cardiac Contractility Modulation (CCM)

Only a proportion of heart failure patients can benefit from CRT, because it is only applicable to patients with evidence of cardiac dyssynchrony and as many as 30% of implanted patients are considered non-responders. A new form of electrical therapy, called cardiac contractility modulation (CCM), has been proposed for enhancing ventricular contractile strength independent of the synchrony of myocardial contraction. This technique involves implanting a pacing-type device, with a sensing lead in the right atrium and two right ventricular leads that deliver relatively large amplitude electrical stimuli during the absolute refractory period of the myocardium. The mechanism of effect is thought to be due to improved cardiac myocyte calcium handling without increasing myocardial oxygen demand. Preliminary studies have shown that CCM therapy can enhance contractile performance acutely, reverse remodelling as evidenced by reduction of left ventricular systolic volume and reverse the cardiac mal-adaptive myocardial foetal gene expression. A randomised, double blind, cross-over study showed that after three months of CCM therapy in 164 patients with LVEF of less than 35% and in NYHA Class II to III, exercise tolerance in terms of peak oxygen consumption and quality of life score significantly improved. CCM is a potential device therapy for heart failure patients who are not CRT candidates. Larger scale studies of CCM therapy are underway to confirm its benefit. CCM therapy is now available for commercial use in Hong Kong.

Conclusion

With the advances of device-based therapies and optimal pharmacological treatments, the outcomes of patients with heart failure have much improved. However, many heart failure patients are not receiving the appropriate therapies recommended by treatment guidelines. Recent studies showed that only around 40% of patients eligible for CRT or ICD received them. There are deficiencies in heart failure care, particularly when it comes to device-based therapies, which are more complicated for physicians to deal with than are drug therapies. Understanding the effectiveness and latest indications of these device-based therapies can help us to select patients who will benefit from these treatments.

References


