Cardiac Resynchronisation Therapy

by Dr Reginald Liew

Updates on use in heart failure

Many patients with congestive heart failure (CHF) have ventricular dyssynchrony which manifests as a prolonged QRS duration (>120ms) on the surface ECG (commonly left bundle branch block, LBBB) and delayed left ventricular (LV) depolarisation and abnormal septal wall motion on the echocardiogram. Over time, this leads to LV dilatation, reduced ejection fraction and worsening symptoms of heart failure. The development of cardiac resynchronisation therapy (CRT) for patients with symptomatic heart failure has revolutionized treatment of such patients, especially those who continue to experience symptoms despite being on optimal medical therapy. The techniques and equipment for CRT have evolved over the past few decades along with an improved understanding of the pathophysiology of heart failure and which patients are likely to benefit the most from CRT. This article summarises the recent advances in the field of CRT, including the latest guidelines on which patients should be considered for the technology and current methods for patient selection and follow-up.

How is cardiac resynchronisation achieved?

CRT involves the delivery of a specially designed pacing lead to the LV wall (either endocardially via the coronary sinus or epicardially through a mini-thoracotomy). The majority of CRT procedures nowadays are performed in a similar way to standard pacemaker insertions with the placement of three leads – one to the right atrium (unless the patient has chronic atrial fibrillation, in which case an atrial lead is not used), one to

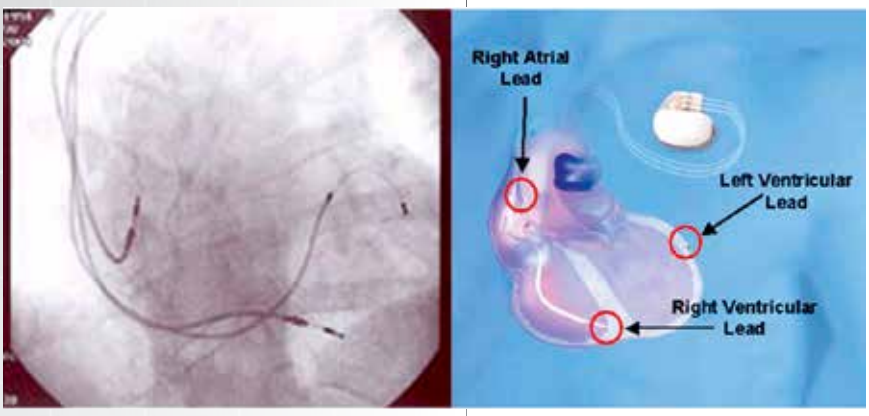

Figure 1. ***A) Fluoroscopic image of CRT leads; B) Diagram showing position of CRT leads within the heart chambers***

the right ventricle and one to the left ventricle (targeting the most posterolateral aspect possible) **[Figure 1].** The right ventricular lead may be a standard pacing lead in the case of CRT-P devices or a defibrillator lead if the CRT device also has an implantable cardioverter defibrillator (ICD) component (so called CRT-D devices) if the objective is to shock the rhythm out of life-threatening ventricular arrhythmias as well as delivering CRT pacing. The procedure can take two to four hours to perform and is usually done using moderate sedation in the cardiovascular lab or operating theatre. Risks of the procedure are low and include the risks associated with pacemaker insertion, such as bleeding, infection, pneumothorax, as well as additional risks associated with placement of the LV lead, including coronary sinus dissection and need to use contrast which can worsen renal function in patients with pre-existing renal disease.

Clinical studies on CRT

The early landmark randomized clinical trials published in the early/ mid 2000s demonstrated that the use of CRT in patients with moderate to severe CHF (New York Heart Association, NYHA, class III and ambulatory IV heart failure symptoms) improves the quality of life, NYHA functional class, exercise capacity and peak VO2 max as well as significantly improving the LV ejection fraction. Furthermore, there was a reduction in heart failure hospitalisations in patients who received a CRT device.[1-3] More recent CRT trials have shown that the benefits of CRT pacing extend to patients with milder forms of heart failure (NYHA class I/ II symptoms) thereby increasing the pool of patients who could be offered this treatment. The Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT)[4] and Resynchronization/Defibrillation for Ambulatory Heart Failure (RAFT) study[5] validated the benefits of CRT in patients with milder forms of CHF. MADIT-CRT was the largest trial with patients with mild heart failure-1820 patients had NYHA class I/II heart failure, with QRS duration ≥130 ms and LV ejection fraction ≤30% were enrolled. The study demonstrated the benefits of CRT-D over ICD therapy alone with a significant reduction in non-fatal heart failure events in the CRT-D group. The Resynchronisation/Defibrillation for Ambulatory Heart Failure (RAFT) study also had a large NYHA class II cohort. Patients with NYHA class II/III heart failure symptoms with QRS ≥120 ms and LVEF ≤30% who were randomised to CRT-D instead of ICD had an improvement in overall mortality and decrease in heart failure events. Subsequent analysis of the CRT trials suggests the greatest benefit is seen in patients with LBBB versus right bundle branch block (RBBB) or other non-LBBB conduction abnormalities, although non-LBBB patients still gain significant benefits with CRT therapy.

Current guidelines

The latest international guidelines on which patients with heart failure should be considered for a CRT device are summarized in **Table 1.** It should be noted that both the European and American guidelines advocate the use of CRT as a class 1 indication (i.e. the treatment is recommended based on the evidence that it is beneficial and effective) in patients who have LV ejection fraction ≤35%, are in sinus rhythm, have broad LBBB with a QRS duration ≥150 ms on their ECG and NYHA class II, III or ambulatory IV symptoms on medical therapy. Thus, CRT can be recommended on the basis of symptoms, echocardiographic and ECG criteria alone. Patients

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Table 1. ***Current international guidelines for CRT***

	ESC 2013 Guidelines	2012 ACCF/AHA/HRS guidelines
Class I	1. CRT is recommended for patients who have LVEF ≤35%, sinus rhythm, LBBB with a QRS duration ≥150 ms and NYHA class II, III or ambulatory IV symptoms on medical therapy 2. CRT is recommended for patients who have LVEF ≤35%, sinus rhythm, LBBB with a QRS duration 120–149 ms and NYHA class II, III or ambulatory IV symptoms on medical therapy	1. CRT is indicated for patients who have LVEF ≤35%, sinus rhythm, LBBB with a QRS duration ≥150 ms and NYHA class II, III or ambulatory IV symptoms on medical therapy
Class IIa	1. CRT should be considered for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with a QRS duration ≥150 ms and NYHA class II, III or ambulatory IV on medical therapy	1. CRT can be useful for patients who have LVEF ≤35%, sinus rhythm, LBBB with a QRS duration 120–149 ms and NYHA class II, III or ambulatory IV symptoms on medical therapy 2. CRT can be useful for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with a QRS duration ≥150 ms and NYHA class III/ambulatory IV symptoms on medical therapy 3. CRT can be useful in patients with AF and LVEF ≤35% on medical therapy if (a) the patient requires ventricular pacing or otherwise meets CRT criteria and (b) AV nodal ablation or pharmacological rate control will allow near 100% ventricular pacing 4. CRT can be useful for patients on medical therapy who have LVEF ≤35% and are undergoing new or replacement device placement with anticipated requirements for significant (>40%) ventricular pacing
Class IIb	1. CRT may be considered for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB with a QRS duration 120–149 ms and NYHA class II, III or ambulatory class IV symptoms on medical therapy	1. CRT may be considered for patients who have LVEF ≤30%, ischaemic heart failure, sinus rhythm, LBBB with a QRS duration ≥150 ms and NYHA class I symptoms on medical therapy 2. CRT may be considered for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB with a QRS duration 120–149 ms and NYHA class III/ambulatory class IV symptoms on medical therapy 3. CRT may be considered for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB with a QRS duration ≥150 ms and NYHA class II symptoms on medical therapy

ACCF, American College of Cardiology Foundation; AF, atrial fibrillation; AHA, American Heart Association; AV, atrioventricular; CRT, cardiac resynchronisation therapy; ESC, European Society of Cardiology; HF, heart failure; HRS, Heart Rhythm Society; LBBB, left bundle branch block; NYHA, New York Heart Association.

with less broad QRS duration and/ or non-LBBB pattern on the ECG can still be considered for CRT, although use of CRT in such groups is considered a class II recommendation. According to the American guidelines, CRT can also be considered in patients with AF and heart failure, especially if AV-nodal ablation is required (which will render the patient 100% pacing-dependent).

Optimisation and monitoring of CRT

Despite the strong clinical trial data showing the benefits of CRT in patients with heart failure, about 20% of patients may not derive benefit from CRT (so called non-responders). This is because there are a number of critical factors that influence how effective CRT may be, including the degree of mechanical and electrical dyssynchrony, presence of myocardial scar altering conduction pattern, patient co-morbidities and where the LV lead is actually placed (which is constrained by the coronary sinus anatomy). Consequently an individualised approach integrating strategies other than simply using LV ejection fraction and QRS duration and morphology may improve the selection of potential CRT candidates and thereby improve responder rates. Additional aids to improve responder rates may include using more sophisticated imaging (such as cardiac MRI scan and dyssynchrony echo) prior to CRT insertion. Furthermore, improvements in LV lead technology and pacing algorithms also have the potential to improve response to CRT. Larger trials are needed to better understand the role of targeted LV placement in patients with non-LBBB QRS morphologies.

An exciting development in the monitoring of CRT recipients (and other patients with intracardiac devices) is the use of remote monitoring (RM). The concept of RM is that patients are discharged with a home monitoring device which they keep at home and allows the transmission of data from

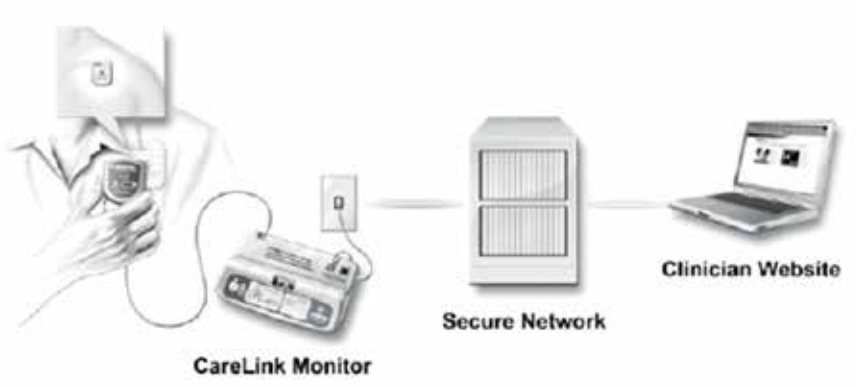

Figure 2. ***Remote monitoring system (Medtronic Carelink Network). Data from the pacemaker of ICD device is transmitted via the home monitor to a central secure network. Any abornormalities detected or problems with the device are relayed to the clinic, allowing them to be treated earlier.***

their pacemaker/ ICD to the RM device at regular intervals. The information is then sent to a central server which is managed by the device company and any important alerts or major abnormalities (with the lead or devices) are automatically sent to the specialists in charge of monitoring the patients' intracardiac device **[Figure 2].** The specialist can then act on this data much earlier compared with conventional follow-up visits (usually every 4 to 6 months). Such an improved workflow could allow for earlier detection of atrial fibrillation and the initiation of appropriate therapy and anticoagulation. In patients with specialised CRT devices that allow for monitoring of intrathoracic impedance (which is a surrogate marker of increasing fluid accumulation in the lungs), RM may allow the clinician to detect worsening signs of heart failure and initiate therapy earlier to improve symptoms and reduce hospitalization. Recent clinical studies have shown that RM of intracardiac devices reduce hospitalisation rates, improve patient satisfaction and may improve outcomes.[6]

Conclusions

CRT is an important additional therapeutic option in patients with moderate to severe heart failure (LV ejection fraction <30%) and LBBB on their ECG. It has been shown to be effective in improving symptoms, functional capacity and LV function and is recommended in international guidelines in appropriately selected patients. Advances in implant technique, tools and patient selection as well as more convenient and improved follow-up using remote monitoring have further increased the usefulness of CRT in heart failure patients. MG

Dr Reginald Liew is a Senior Consultant Cardiologist at Gleneagles Hospital, Singapore. He is an experienced cardiac electrophysiologist and widely recognized in the field of implantable cardiac devices and heart rhythm disorders. He studied medicine at Cambridge University and completed his cardiology and sub-speciality training in leading teaching hospitals in London, United Kingdom. Dr. Liew is passionate about teaching and continues to teach medical students and regularly proctors cases in the region on CRT implantation techniques and catheter ablation of cardiac arrhythmias.

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