Cardiac Resynchronization Therapy for Treatment of Congestive Heart Failure

Adegboyega Q. Adigun, MD
Kevin E. Rist, MD, PhD

Congestive heart failure (CHF) remains an important public health concern. Despite the treatment options for CHF, 5-year mortality remains unacceptably high at 50%.[1,2] Alternatives to pharmacotherapy for CHF include mechanical assist devices and cardiac transplantation; however, these approaches are limited by cost, potential for infection, and the need for chronic anticoagulation for mechanical assist devices, and by organ availability and cost for cardiac transplantation.[3,4]

Cardiac resynchronization therapy (CRT), also called atrial synchronized biventricular pacing, is a new treatment modality for CHF that may relieve symptoms, improve patient quality of life, and prevent rehospitalization.[5] In August 2001, the US Food and Drug Administration (FDA) approved the use of CRT in heart failure treatment. It is estimated that the number of heart failure patients in the United States receiving this therapy will increase exponentially in the coming years. The aim of this brief review article is to provide an overview of the current role of CRT in the management of CHF for primary care providers, who collectively exclusively manage up to 60% of patients with CHF.

CARDIAC DYSSYNCHRONY AND THE RATIONALE FOR RESYNCHRONIZATION

The heart relies on a coordinated sequence of electrical impulse generation and conduction that allows repeated filling and emptying of the atria and ventricles. Cardiac electrical activity depends on the integrity of the sinoatrial node, the atrioventricular node, and the specialized conducting tissue of the His-Purkinje system. In approximately 30% of patients who have CHF, aberrant electrical conduction is noted on surface electrocardiogram as QRS prolongation of 120 ms or greater.[6] This finding may result from abnormal conduction in the left and/or right His bundle. The delay in ventricular electrical activation causes abnormal ventricular contraction, termed *dyssynchrony.*[7] In the setting of CHF, the consequences of this electromechanical abnormality are abnormal ventricular filling, reduction in the left ventricular systolic output, and worsening of mitral regurgitation.[6] Several studies have shown that intraventricular conduction delay is an independent risk factor for mortality in heart failure.[6,8]

The aim of CRT is to improve electromechanical coupling in the heart by generating a more efficient sequence of impulse generation and conduction. The immediate hemodynamic benefits of the procedure include improved diastolic filling and more efficient systolic contractility. Mortality from CHF is a result of either progressive pump failure or sudden death caused by arrhythmia. CRT can slow the progression of pump failure and, when combined with an implantable cardioverter defibrillator (ICD), prevent sudden cardiac death.

TECHNIQUE

Dual-chamber pacing is accomplished by placing pacing wires in the right atrium and right ventricle using subclavian or cephalic vein access. In CRT, an additional wire is inserted via the right atrium through the coronary sinus into a cardiac vein on the lateral wall of the left ventricle (**Figure**).[9] The left ventricular lead can also be placed surgically via thoracotomy or laparoscopic thoracostomy. Left ventricular lead placement is technically difficult; however, the complication rate has dramatically decreased as experience with this procedure has increased.[10] The presence of a pacemaker lead in the left ventricular free wall allows for simultaneous pacing of both ventricles and more physiologic atrioventricular timing. The result is more effective left ventricular contraction and improvement in stroke output.

Dr. Adigun is a resident in internal medicine, Reading Hospital and Medical Center, West Reading, PA. Dr. Rist is a cardiologist/electrophysiologist, Reading Hospital and Medical Center, and an investigator for Medtronic, Inc., Minneapolis, MN, and for Guidant Corporation, Indianapolis, IN.

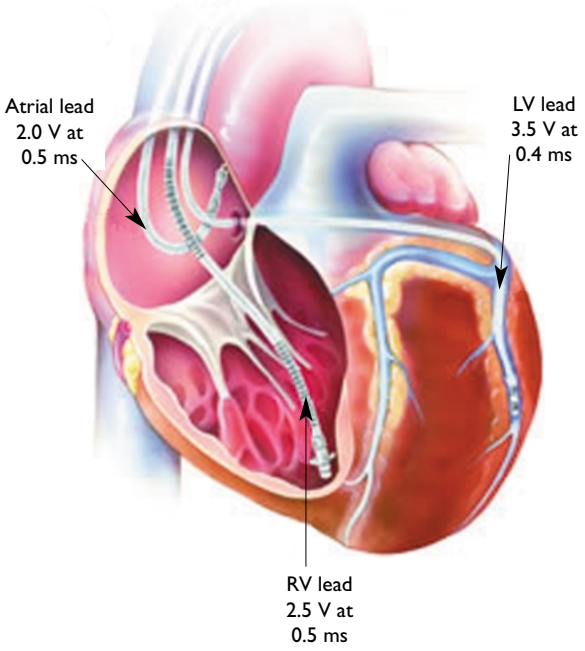

Figure. Schematic illustration of lead placement and sample programming parameters. (Adapted with permission from Guidant Corporation, Indianapolis, IN.)

Table 1. Indications for Cardiac Resynchronization Therapy

New York Heart Association (NYHA) functional class III* or IV† heart failure despite optimal medical therapy‡
QRS duration greater than 120 ms
Systolic heart failure with ejection fraction less than 35%
Left ventricular end-diastolic dimension greater than 55 mm

NOTE: Essential criteria are functional status on optimal therapy and QRS prolongation.

*NYHA functional class III (moderate heart failure): Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.

†NYHA functional class IV (severe heart failure): Unable to carry out any physical activity without discomfort; symptoms of cardiac insufficiency at rest.

‡Optimal medical therapy defined as appropriate doses of angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers, β-blockers, diuretic agents, or aldosterone antagonists.

INDICATIONS

Eligibility criteria for treatment with CRT are adapted from published studies.[5] Briefly; the two most important criteria are severe symptomatic heart failure despite optimal medical therapy, and QRS prolongation (**Table 1**). Current criteria may not be optimal, however, because the nonresponder rate in clinical trials is as high as 30%.[5] Some clinicians have suggested that the addition of variables, such as paradoxical septal motion or Doppler echocardiography features of asynchrony, to the selection criteria for CRT may increase the response rate.[11]

BENEFITS

As shown in recent randomized controlled trials,[12–15] the benefits of CRT include the following:

- Improved cardiac contractility and increased ejection fraction
- Reduced mitral regurgitant fraction, which enhances cardiac output
- Improved exercise tolerance in the 6-minute walk test
- Improved New York Heart Association functional class
- Improved quality of life
- Reduced re-hospitalization for worsening heart failure

The role of CRT without an ICD in reducing mortality from heart failure is still unresolved. A recent meta-analysis by Bradley et al that pooled data from 4 randomized trials using CRT alone (2 trials) and CRT-ICD (2 trials) suggests that cardiac resynchronization reduces mortality from progressive heart failure by 51%.[16] Although CRT alone clearly improves symptoms of heart failure, the addition of a defibrillator appears to confer significant improvement in survival. The Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial enrolled patients to medical therapy, medical therapy plus CRT, and medical therapy plus CRT-ICD.[17] This study, the first to directly compare CRT and CRT-ICD in patients without established criteria for defibrillator therapy, confirmed that the addition of a defibrillator to CRT has a significant impact on reducing heart failure–related mortality.

CRT represents an important adjunct to existing medical therapies, and patients in reported trials were continued on angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers, β-blockers, diuretic agents, and aldosterone antagonists as appropriate.

LIMITATIONS

The most important limitation of CRT as a modality of treatment for CHF is a relatively high nonresponder rate. Lack of response to CRT is explained by suboptimal patient selection and technical questions relating

Table 2. Complications of Cardiac Resynchronization Therapy in Patients with Heart Failure

Complication	Incidence (%)
Lead placement failure	11
Coronary sinus dissection	3
Lead dislodgement	1.6
Ventricular tachycardia/fibrillation	1
Cardiac perforation	0.8
Heart block	0.7
Pericardial effusion	0.5

Data from Young JB, Abraham W T, Smith AL, et al. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD Trial. Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE ICD) Trial Investigators. JAMA 2003;289:2685–94.

to placement of the left ventricular lead as well as timing of the atrioventricular interval delay. Several studies have suggested that tissue Doppler and magnetic resonance imaging may be superior to QRS prolongation as a marker of cardiac dyssynchrony.[7] Further experience in patient selection, lead placement, and pacemaker programming will hopefully maximize patient benefit from CRT and reduce complications.

COMPLICATIONS

Complications of CRT are shown in **Table 2**. In a recent multicenter trial (the Multicenter InSync ICD Randomized Clinical Evaluation [MIRACLE ICD] trial) involving more than 400 patients, the overall complication rate was approximately 28%; however, most complications were minor and no mortality was reported.[18] Failure of lead placement was the most frequent complication, and cardiac perforation and coronary sinus dissection were the most serious adverse events.[18] Complication rates appear to be lowest in centers where the procedure is frequently performed and where the physicians have a large number of patients.[10]

CONCLUSION

Over the last 10 years, the rate of hospitalization for CHF has increased by more than 150%.[19] This trend will most likely continue because of an aging population and increased survival after acute myocardial infarction. Currently, an estimated 10% of patients with CHF are eligible for CRT: these patients have a low ejection fraction, evidence of dyssynchrony, and severe symptoms of CHF despite optimal medical therapy.[20] For a treatment modality that is free of compliance issues and appears to be well tolerated, CRT should be considered for all patients who have advanced CHF and meet existing criteria.

In patients with CHF, CRT has the potential to improve exercise capacity and patient well being, reduce rehospitalization, and, most likely, reduce mortality. When combined with an ICD, CRT also reduces the risk of sudden arrhythmic death. Several ongoing large randomized trials will shed more light on patient selection, technical issues of lead placement, role of CRT in atrial fibrillation, and the long-term tolerability of CRT. **HP**

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