Cardiac Resynchronization Therapy
Helpful Now in Selected Patients With CHF
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Drs. Leclercq and Hare\(^1\) and Auricchio and Abraham\(^2\) have comprehensively reviewed the state of cardiac resynchronization therapy (CRT). As they emphasize, this novel pacing approach to treat heart failure shortens or optimizes the atrioventricular interval necessary to resynchronize lateral-septal contractions and improves atrioventricular mechanical synchrony by abolishing late diastolic ventriculoatrial gradient and the "presystolic mitral regurgitation" that is often seen with ventricular dysynchrony. Pacing from the left lateral wall produces early activation of the papillary muscle region and may decrease systolic mitral regurgitation. Relative optimization of ventricular loading conditions as provided by CRT improves myocardial efficiency at no increased oxygen cost and increases systolic function with little effect on diastolic function. In addition to the positive hemodynamic effects mentioned above, CRT reduces sympathetic activity and may induce "reverse remodeling" of the failing left ventricle. With CRT, optimal responders develop smaller left ventricles and contractility is improved in the subsequent days to weeks.

The CRT device has more sophisticated software and hardware than standard pacemakers and requires more extensive follow-up visits and, thus, a higher cost. The software allows storage of intracardiac electrograms and monitoring of a patient's physical activity and heart rates and heart rate variability. It is anticipated in the future that selected respiratory characteristics, body temperature, and body water content might also be possible to obtain with advanced software currently under development.

CRT is indicated for selected patients with symptomatic heart failure. These patients should be in a functional New York Heart Association class III, they should have a QRS duration of 130 ms or greater, left ventricular ejection fractions of 35% or less, and left ventricular end-diastolic diameters \(>55\) mm for one to see improvement in symptoms, functional status, and exercise capacity. Evidence from several clinical trials suggests that CRT markedly reduces combined measures of morbidity and probably of mortality when used alone or with a defibrillator.

Current recommendations call for the use of optimized pharmacological therapy, including angiotensin-converting enzyme inhibitors, selected \(\beta\)-adrenergic blockers, and an aldosterone inhibitor before initiating CRT therapy.

There are a number of issues that remain unresolved as regards CRT therapy. First, it is not clear whether dyssynchrony represents a cause or a consequence of heart failure. It seems possible that it may be a marker of progressive cardiac dysfunction. Secondly, there is a paucity of evidence as regards potential long-term clinical benefit from CRT; clinical trials that have been done to date are relatively short, months to 1 year. The ongoing COMPANION and CARE-HF trials will provide longer follow-up evaluations, and the COMPANION trial will also provide information about long-term clinical benefits both of CRT and of CRT with a defibrillator. Thirdly, the efficacy of CRT for the treatment of patients with narrow QRS duration has only recently been explored as more definitive measures of detecting asynchrony evolve.\(^3\),\(^4\) Can earlier application of CRT before ventricular dilatation alter the natural progression of dilated congestive cardiomyopathy? Can left ventricle-only pacing achieve long-term effects similar to those of biventricular...
stimulation? Lastly, CRT is expensive. In the United States, the cost of the device ranges from $25 000.00 to $40 000.00, and total per-patient charges, including hospital and professional fees, may reach $100 000.00 in some patients. It is estimated that \( \approx 10\% \) of patients meet current guidelines for the use of CRT; this represents \( \approx 500 \text{,}000 \) patients in the United States and \( 50 \text{,}000 \) in Western Europe. As pointed out by Drs Leclercq and Hare,\(^1\) the estimated annual cost for treating patients with heart failure is \( \approx 20 \text{ billion dollars, and CRT costs alone have the potential to exceed the entire heart failure budget. Therefore, there is a need to be very mindful of these costs when recommending CRT for individual patients. As the technology improves and clinical criteria for selecting patients with this form of therapy become more focused, one hopes that the cost of the procedure may be reduced. It is also important to consider that in the patient with a very substantial reduction in morbidity and mortality from CRT therapy, long-term costs might actually become more favorable as compared with the best pharmacological therapy with fewer admissions to the hospital and more productive time for patients. Finally, some patients who appear to be ideal candidates for CRT do not show the expected clinical and hemodynamic benefit. Whether this is the result of less than optimal selection of pacing sites or other factors is unclear presently.

As pointed out by Leclercq, Hare, Auricchio, and Abraham,\(^1,2\) there are other potential uses for CRT, and these should be evaluated in appropriate clinical trials in the future. Specifically, selected patients with atrial fibrillation and heart failure might benefit from this form of therapy. Patients with heart failure with standard right ventricular pacemakers and ventricular dyssynchrony that follows might also benefit from CRT.

It will be useful if additional methods can be developed that identify dyssynchrony in the human heart in a more sensitive and specific way, and potentially helpful if they are utilized to help place CRT leads in the future. Ensuring that dyssynchrony has been eliminated by careful selection of the ventricular locations for CRT therapy may reduce the number of nonresponders to this form of therapy. One hopes that the short-term benefits established for CRT therapy will be maintained in the longer term and one will be able to show additive benefit in reducing morbidity and mortality to what otherwise occurs with today’s pharmacological therapy. Despite these issues, CRT therapy has clearly helped a subset of patients with severe heart failure who were very symptomatic despite optimal medical therapy. The burden is on the congestive heart failure physician and scientific community to improve this form of therapy and to find ways for its beneficial effects to be sustained in the long term.

**References**

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