Generator Exchange in a Primary Prevention Cardiac Resynchronziation Responder

Do You Reimplant a Defibrillator?

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KEYWORDS

• Cardiac resynchronization therapy (CRT) • Biventricular pacing
• Implantable cardioverter-defibrillator (ICD) • Ventricular arrhythmias • Ejection fraction

KEY POINTS

- Cardiac resynchronization therapy (CRT) with biventricular pacing improves cardiac function and ejection fraction (EF) and decreases the risk of ventricular arrhythmias (VAs) and death.
- In cardiac resynchronization responders, there is an inverse relationship between improvements in EF and the risk of VAs.
- Despite a decreased risk of arrhythmias in cardiac resynchronization responders with mild to moderately reduced EF (0.35–0.5) compared with nonresponders with a severely reduced EF (<0.45), the former still have a relatively high risk of developing VAs.

Case History

A 51-year-old man with an ischemic cardiomyopathy has a cardiac resynchronization with a pacemaker-defibrillator (CRT-D) for primary prevention. At the time of implantation 6 years ago, the left ventricular ejection fraction was confirmed to be 20% to 25%, by echocardiogram and nuclear imaging. He presents for replacement of his implantable cardioverter-defibrillator due to normal battery depletion, and the left ventricular ejection fraction measures 45% to 50%. The patient has been on stable medical therapy for the past 4 years and has no symptoms of angina or heart failure. The unpaced rhythm is sinus with a left bundle branch block pattern of 155 ms. How do you evaluate this patient? What device would you use for replacement, cardiac resynchronization with a pacemaker or CRT-D?

INTRODUCTION

CRT is one of the most beneficial nonpharmacologic therapies for congestive heart failure. CRT has been proved to have morbidity and mortality benefits for patients with severe cardiomyopathies and a wide QRS morphology, as well as for patients with depressed EFs and need for frequent ventricular pacing.[1–6] Responders to CRT can at times have normalization or near normalization of their EF. At the time of CRT implantation, most of these patients meet an indication for an ICD implantation. As such, a large portion of the CRT devices implanted have defibrillation function.[7]

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The improvement in EF can be a clinical conundrum for the electrophysiologist at the time of generator exchange. Does a patient with a normalized or near-normalized EF still benefit from having an implanted device with defibrillating capabilities? The clinical scenario presented in the section Case History serves as a background to discuss the risks and benefits of CRT. Is there a decreased risk of VAs in patients with CRT? What are the logistic challenges that can arise as the CRT device is exchanged from one that has defibrillation function to one that is just a pacemaker?

BENEFITS OF CARDIAC RESYNCHRONIZATION THERAPY

Initial CRT studies were small trials that demonstrated the hemodynamic benefits of biventricular pacing. These studies demonstrated improved left ventricular systolic contractile function, reduced filling pressures, and improved myocardial efficiency.[8–11] In the 2003 MIRACLE-ICD trial, patients assigned to CRT had improvement in New York Heart Association (NYHA) class and quality of life scores.[12]

In 2004, the landmark Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial was presented that demonstrated significant morbidity and mortality benefit with CRT. This investigation enrolled 1520 patients with severely reduced left ventricular ejection fraction (LVEF) from either ischemic or nonischemic cardiomyopathies, a QRS greater than 120 ms in sinus rhythm, and NYHA class III or IV symptoms. The patients were randomized in a 1:2:2 manner to optimal medical therapy (OMT), cardiac resynchronization with a pacemaker (CRT-P), or cardiac resynchronization with a pacemaker-defibrillator (CRT-D). In this study, there was a significant mortality benefit only when comparing patients with a CRT-D with those randomized to OMT (36% relative risk reduction, *P* value .003). When comparing CRT-P with OMT, there was nonsignificant trend for mortality benefit as well (25% relative risk reduction, *P* value .059). Subgroup analysis of this cohort demonstrated that much of the significance in treatment was observed in patients who had a QRS of greater than 147 ms and an left bundle branch block (LBBB).[3]

In 2005, the CARE-HF study investigators presented a similar trial in which they enrolled 813 patients with cardiomyopathies with an EF less than 0.35, a QRS greater than 120 ms, and an NYHA class of III or IV. Of note, the subjects who had a QRS between 120 and 149 ms were required to have additional evidence of ventricular dyssynchrony. These subjects were randomized in a 1:1 manner to OMT or CRT-P. In this study, there was a 10% absolute risk reduction in mortality (*P* value .03). Patients with CRT-P also had improved EF, decreased left ventricular end-diastolic volumes, improved NYHA class, and improved quality of life scores when compared with patients with OMT.[6]

Since then, 2 other large trials have been published that have further expanded the use of CRT in patients with less-symptomatic heart failure. In 2009, the results of Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) were published; this trial enrolled 1820 patients with NYHA class I (ischemic) and II (ischemic and nonischemic) symptoms, EF less than 0.3, and a QRS duration greater than 130 ms. These patients were randomized in a 3:2 manner to receive either CRT-D or implantable cardioverter-defibrillator (ICD). There was an 8.1% absolute risk reduction in the primary end point of death from any cause or from heart failure event in the CRT-D group, with heart failure events being the primary cause. Subgroup analysis showed that patients with a QRS greater than 150 ms were the most likely to benefit from this therapy.[2]

Similarly, in 2010, a total of 1798 patients with NYHA class II and III symptoms, EF less than 0.3, and a QRS greater than 120 ms or paced QRS greater than 200 ms were enrolled in the Resynchronization–Defibrillation for Ambulatory Heart Failure Trial (RAFT). These patients were randomized in a 1:1 manner to either a CRT-D or an ICD. In this study, patients who received a CRT-D had a 5% absolute risk reduction in death of any cause (*P* value of .003) when compared with those who had an ICD alone. Subgroup analyses demonstrated that only patients with sinus rhythm, LBBB, and a QRS greater than 150 ms benefited from the addition of CRT to the ICD.[4]

It is clear from these data that at initial implant the patient described above met all criteria for the appropriate implantation of a CRT device. He had an ischemic cardiomyopathy with an EF that was less than 0.3 and an LBBB QRS in sinus rhythm of greater than 150 ms. The only trial that included a treatment arm with either CRT-D or CRT-P was the COMPANION trial. Despite a significant trend for mortality benefit in the CRT-P trial, which was confirmed in the CARE-HF trial, CRT-D was the only therapy that was statistically significant when compared with OMT. As such, implantation of a CRT-D device at the time of implant was reasonable. This, however, does not answer the question of whether at generator exchange a device with defibrillation capacity should be reimplanted now that there is normalization of LVEF.