Why the Authors Use Cardiac Resynchronization Therapy with Defibrillators

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KEYWORDS

• Cardiac resynchronization therapy • Heart failure • Systolic • Defibrillators • Implantable • Death • Sudden

KEY POINTS

- Randomized trial evidence directly comparing cardiac resynchronization therapy (CRT) with a pacemaker (CRT-P) and with an implantable defibrillator (CRT-D) is not available.
- Indirect evidence suggests that CRT-D may reduce mortality to a greater degree because of greater sudden death reduction.
- CRT-D is more costly and possibly subject to more complications than CRT-P.

INTRODUCTION

Powerful Therapies for an Increasing Incidence of Heart Failure

One irony of modern cardiology is that our success in treating patients with acute cardiovascular disease has led to an increasing incidence of chronic left ventricular (LV) dysfunction.[1–3] As patients with cardiovascular disease live longer, their decreased mortality has translated to an increased opportunity for heart failure progression. We now face an expanding population of patients who meet the criteria for an intracardiac device.[4–7]

Two therapies indicated for patients with heart failure include cardiac resynchronization (CRT) and implantable-cardioverter defibrillators (ICDs). Both have been proven to benefit patients with chronic LV systolic dysfunction.[8–15] ICDs decrease the rate of sudden cardiac death (SCD) by attempting to terminate potentially fatal ventricular tachyarrhythmia (VTA). CRT seeks to improve LV function by decreasing mechanical dyssynchrony typically brought on by chronic right ventricular pacing or left bundle branch block (LBBB).

Although there is natural overlap in the patient populations indicated to receive either therapy, there are no randomized controlled trials (RCTs) that directly compare CRT only (CRT-P) to CRT plus defibrillator (CRT-D) (**Fig. 1**). When deciding which device or combination of devices to offer patients, a clinician must rely on indirect evidence. This review seeks to present data that will provide guidance to device placement for this growing population of patients.

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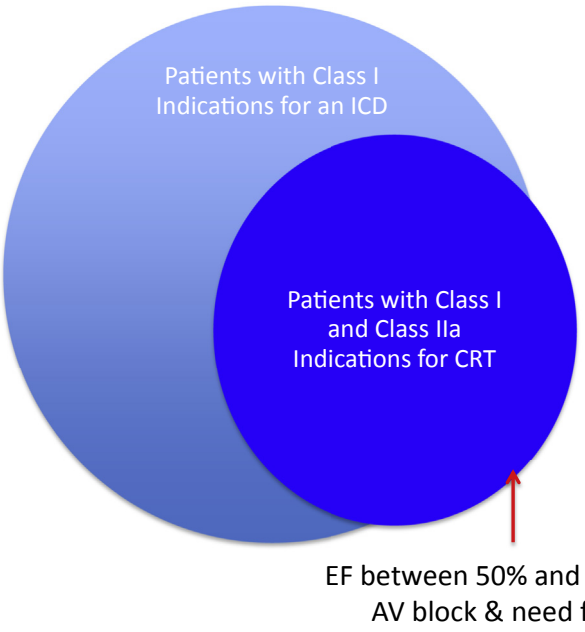

Fig. 1. The substantial but not complete overlap of indications for implantable defibrillator therapy and for CRT. AV, atrioventricular; EF, ejection fraction. (*Adapted from* Brignole M, Auricchio A, Baron-Esquivias G, et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). Eur Heart J 2013;34(29):2281–329; and Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2012;126(14):1784–800.)

The Case for Cardiac Resynchronization Therapy Only

The logic for implanting CRT-P is straightforward. First, if CRT-P is effective in inducing LV reverse remodeling, a patient's ejection fraction (EF) may improve to the point that it obviates ICD therapy. This reasoning is supported by an echocardiogram substudy from Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT) that reported significantly less VTA in patients determined to be high responders to CRT (defined as a >25% reduction to LV end-systolic volume [LVESV]).[16]

Second, in certain populations, such as those with nonischemic cardiomyopathy (NICM), the benefit of ICDs is less clear. In DEFINITE (Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation), the largest RCT to examine the effect of ICDs in patients with NICM, ICDs provided a highly significant reduction of SCD but did not demonstrate an overall survival benefit.[17,18] Furthermore, an analysis from SCD-HeFT examined the benefits of ICDs in patients with NICM and found a nonsignificant survival benefit.[8] Both of these trials had relatively limited follow-up times, potentially obscuring the long-term benefits of ICD therapy. A meta-analysis from 2004 evaluated the efficacy of ICDs in patients with NICM by reviewing 5 prospective RCTs for primary prevention and 3 prospective RCTs for secondary prevention.[19] This study found a significant benefit for primary prevention (relative risk [RR] 0.69, $P = .002$) but an insignificant benefit for secondary prevention (RR 0.69, $P = .22$).[19] Nevertheless, the question arises: if these patients received CRT, would any effect have been seen with ICD implantation?

Researchers from the University of Pittsburgh addressed the question of relative benefit of CRT-D in patients with NICM when they conducted a retrospective study of 157 patients. Their study followed patients who had LVEF of 35% or less, were pacemaker dependent, had no prior VTA, but were all upgraded to CRT-D. Among the 82 who had NICM, only 1 patient received an appropriate shock in 5 years of follow-up. This finding compared with 11 appropriate shocks in the 75 patients with ischemic disease.[17] The seemingly small risk of SCD in nonischemic patients suggests that, in the right population, we should consider the benefits of implanting CRT-P instead of CRT-D: less upfront costs to implantation; a smaller device size and smaller pocket size; less risk for implantation complications; longer average battery life; and zero risk for inappropriate shocks, shown in Multicenter Automatic Defibrillator Implantation Trial-Reduction in Inappropriate Therapy (MADIT-RIT) to be detrimental to cardiovascular outcomes.[17,20]

THE CASE FOR CARDIAC RESYNCHRONIZATION THERAPY PLUS DEFIBRILLATOR

Greater Protection from Sudden Cardiac Death

The obvious benefit of CRT-D is greater protection from SCD. Data from Cardiac Resynchronization—Heart Failure (CARE-HF), which compared