

ELECTRIC THERAPY IN HEART FAILURE
(Original language)

The Importance of the COMPANION Trial
(Comparison of Medical Therapy, Pacing, and
Defibrillation in Heart Failure)

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Reference article

Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure. Michael R. Bristow, M.D., Leslie A. Saxon, M.D., John Boehmer, M.D., Steven Krueger, M.D., David A. Kass, M.D., Teresa De Marco, M.D., Peter Carson, M.D., Lorenzo DiCarlo, M.D., David DeMets, Ph.D., Bill G. White, Ph.D., Dale W. DeVries, B.A., Arthur M. Feldman, M.D., Ph.D., for the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Investigators.
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The therapy of heart failure now encompasses many different modalities and approaches, including (1) medications to control volume and decrease preload and afterload (improve symptoms), (2) medications to improve contractility (improve symptoms), (3) medications that affect the neurohormonal perturbations associated with heart failure (improve survival), and, more recently, devices to correct conduction system abnormalities and treat potentially lethal arrhythmias (improve symptoms and survival).

The use of implantable defibrillators (ICD) results in significant improvements in survival^{1,2}. It is also clear that conduction disturbances occur in a large percentage of patients with heart failure³. Left bundle branch block, in particular, results in a dyssynchronous left ventricular (LV) contraction with associated low cardiac output, worsening mitral regurgitation and accelerated cardiac remodeling⁴. Cardiac resynchronization therapy (CRT) synchronizes the ventricular activation, resulting in improvements in symptoms and quality of life^{4,5}. However, before the publication of the COMPANION (The Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure trial)⁶, only an interesting meta-analysis of various CRT studies suggested a trend towards a reduction in mortality⁷.

The COMPANION trial was the first randomized trial that showed that CRT not only improve symptoms, but possibly the risk of death as well, especially when combined with an ICD⁸. This particular study included one of the sickest populations in heart failure trials. Entry criteria were NYHA class III or IV, left ventricular ejection fraction of $\leq 35\%$, a QRS inter-

val of at least 120 msec, and a hospitalization for heart failure in the preceding 12 months. A total of 1520 eligible patients were randomly assigned in a 1:2:2 ratio to optimal pharmacological therapy (OPT) alone or in combination with CRT or CRT-ICD. Most patients were class III (85%), the mean LVEF was 21%, mean blood pressure were 111/67, and most were on good medical therapy by today's standards (89% were on and ACEi or ARB, 68% on beta-blockers and 54% on spironolactone). As compared to the OPT, CRT and CRT-ICD resulted in a 34 and 40% reduction in the primary end-point of death from or hospitalization for heart failure, respectively ($p < 0.002$ and < 0.001). In addition, the CRT-ICD group had a 36% reduction in the secondary end-point of death from any cause ($p = 0.003$). Interestingly, CRT without ICD also resulted in a 24% reduction of all cause mortality. Even though this difference did not reach statistical significance, it showed a strong trend ($p = 0.059$). It is important to note that this study was stopped prematurely because of a marked improvement in mortality in both CRT groups, therefore, it is conceivable that this difference would have reached statistical significance, should the study had been completed. As expected, both CRT groups resulted in improvement in NYHA, quality of life scores, 6-min walk distance and increased in the systolic blood pressure, possibly as a surrogate of improved cardiac performance.

The COMPANION trial was the first study to demonstrate that CRT alone not only improves symptoms, but possibly the risk of death as well. These preliminary results were later validated by the CARE-HF trial⁹. Moreover, even though the COMPANION study was not powered to evaluate endpoints in subgroups, the authors found that patients with non-ischemic cardiomyopathy who received CRT-ICD had a 50% reduction in the risk of death, as oppose to a 27% reduction in the ischemic group. These results were later confirmed by SCD-HeFT

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trial^{10,11}, which showed a significant improvement in survival in patients with HF who received an ICD, irrespective of the etiology.

The lessons learned from the COMPANION trial have affected the current practice in the management of HF. In addition, these lessons, later corroborated by the CARE-HF and SCD-HeFT, were later incorporated into the current guidelines from the ACC/AHA for the management of HF¹². Based on the COMPANION trial, and subsequent confirmatory studies every physician involved in the care of patients with HF and dyssynchrony (defined as a QRS duration of > 120 msec), whom have persistent NYHA Class II or III symptoms despite maximum medical therapy should be considered for CRT-ICD implantation, unless contraindicated.

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