

THERAPEUTICS

Cardiac resynchronization reduced death and hospitalization in heart failure and cardiac dyssynchrony

Cleland JG, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med*. 2005;352:1539-49.

Clinical impact ratings: Hospitalists ★★★★★★ Cardiology ★★★★★★☆

QUESTION

In patients receiving standard medical therapy for moderate or severe heart failure (HF) with cardiac dyssynchrony, does cardiac resynchronization (CR) decrease the risk for complications and death?

METHODS

Design: Randomized controlled trial (Cardiac Resynchronization—Heart Failure [CARE-HF]).

Allocation: {Allocation concealed}†.*

Blinding: Unblinded.*

Follow-up period: Mean 29.4 months.

Setting: 82 centers in Europe.

Patients: 813 patients who were ≥ 18 years of age (median age 67 y and 66 y for CR and usual-care groups, respectively; 73% men); had had HF for ≥ 6 weeks; had received standard pharmacologic therapy; were classified as New York Heart Association class III or IV; and had a left ventricular ejection fraction ≤ 35%, a left ventricular end-diastolic dimension ≥ 30 mm, and a QRS interval ≥ 120 msec on electrocardiography. Patients with a QRS interval of 120 to 149 msec also had to have 2 of the following: aortic pre-ejection delay > 140 msec, intraventricular mechanical delay > 40 msec, or delayed activation of the posterolateral left ventricular wall. Exclusion criteria were a major cardiovascular event in the previous 6 weeks, conventional indications for pacemaker or implantable defibrillator, HF requiring continuous intravenous therapy, or atrial arrhythmia.

Intervention: Medical therapy plus CR ($n = 409$) or medical therapy alone ($n = 404$). CR consisted of an InSync or InSync III device (Medtronic, Minneapolis, MN, USA), which used standard right ventricular leads, and Attain (Medtronic, Minneapolis, MN, USA), which used left ventricular leads, to provide atrial-based, biventricular stimulation. The devices did not have a defibrillator function.

Outcomes: Composite endpoint of death from any cause or unplanned hospitalization for major cardiovascular event. Secondary outcomes include death from any cause.

Patient follow-up: 100% (intention-to-treat analysis).

MAIN RESULTS

Fewer patients in the CR group than in the usual-care group died or had an unplanned hospitalization (Table).

CONCLUSION

In patients with heart failure and cardiac dyssynchrony, cardiac resynchronization reduced death and hospitalization for major cardiovascular events.

Source of funding: Medtronic.

For correspondence: Dr. J.G. Cleland, Castle Hill Hospital, Kingston-upon-Hull, England, UK. E-mail j.g.cleland@hull.ac.uk. ■

*See Glossary.

†Information provided by author.

Cardiac resynchronization vs usual care in heart failure and cardiac dyssynchrony at mean 29.4 months‡

Outcomes	Cardiac resynchronization	Usual care	RRR (95% CI)	NNT (CI)
Composite endpoint [§]	39%	55%	28% (16 to 39)	7 (5 to 12)
All-cause death	20%	30%	32% (13 to 48)	11 (8 to 26)

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

[§]All-cause death or hospitalization for major cardiovascular event.

COMMENTARY

Today, standard therapy of HF includes ≥ 3 medications, such as angiotensin-converting enzyme inhibitors, β-blockers, and diuretics. Pharmacologic therapy has tackled most of the pathophysiologic mechanisms of HF. However, when long-term inotropic agents were tested in clinical trials, they improved cardiac output and contractility at the price of increased mortality. In the mid-1990s, the astute identification of a prolonged QRS complex duration as a marker of mortality in patients with HF determined the rapid development of CR and paved the way to finally completing the foundations for HF therapy. Several observational and clinical trials have shown the safety and efficacy of CR as additional therapy in patients with refractory HF (1). Early studies focused on improvement in functional capacity and surrogate physiologic markers. More recently, clinical trials have focused on “harder” outcomes, such as prevention of hospital admissions and progression of HF. However, the true test of efficacy of new therapeutic advances is the reduction of mortality.

The CARE-HF trial puts the final nail in the coffin of the question of whether CR reduces mortality in patients with moderate-to-severe medically refractory HF, regardless of the cause. An impressive 28% relative risk reduction (RRR) in the composite outcome and a 32% RRR

in all-cause mortality definitely supports the use of this technology in carefully selected patients. This trial also highlights the importance of introducing finer selection tools, such as echocardiographic markers of cardiac dyssynchrony, which may in part be responsible for the impressive results of this trial by selecting responders to CR. The numbers needed to treat of 7 to prevent 1 composite endpoint and 11 patients to prevent 1 death are indeed economically attractive and comparable to other usual forms of therapy, such as dialysis.

CR therapy is here to stay in selected patients with HF. The question of whether implantable-cardioverter therapy alone or combined with CR will further reduce mortality is currently being addressed by the Resynchronization/Defibrillation for Advanced Heart Failure (RAFT) and Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT) trials.

*Carlos A. Morillo, MD, FRCPC, FACC
McMaster University-Hamilton Health Sciences
Hamilton, Ontario, Canada*

Reference

- Bradley DJ, Bradley EA, Baughman KL, et al. Cardiac resynchronization and death from progressive heart failure: a meta-analysis of randomized controlled trials. *JAMA*. 2003;289:730-40.