

Review: Cardiac resynchronization therapy reduces morbidity and mortality in left ventricular systolic dysfunction

McAlister FA, Ezekowitz J, Hooton N, et al. Cardiac resynchronization therapy for patients with left ventricular systolic dysfunction: a systematic review. *JAMA*. 2007;297:2502-14.

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

QUESTION

In patients with left ventricular systolic dysfunction (LVSD), what is the efficacy and safety of cardiac resynchronization therapy (CRT)?

METHODS

Data sources: Included MEDLINE, EMBASE/Excerpta Medica, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and various trial registries (to November 2006); U.S. Food and Drug Administration reports; lists of conference abstracts; reference lists; and device manufacturers.

Study selection and assessment: Studies in any language that compared CRT with placebo pacing, right ventricular pacing, drug therapy, or implantable cardioverter-defibrillator (ICD) (when the experimental treatment was CRT-ICD) and reported mortality, hospitalization, changes in functional outcomes (New York Heart Association [NYHA] class, 6-min walk test, LV ejection fraction [LVEF], or quality of life), or peri- or postimplantation safety of CRT in patients with LVSD (LVEF \leq 35% with or without symptoms of heart failure [HF]) who were followed for \geq 2 weeks. 14 randomized controlled trials (RCTs) ($n = 4420$, mean age 65 y, 72% men) met the selection criteria for CRT efficacy. 14 RCTs, 2 controlled clinical trials, and 63 prospective and 10 retrospective observational studies ($n = 9677$) met the selection criteria for CRT safety. Quality assessment of individual studies was based

on the 5-point Jadad scale and allocation concealment for RCTs and the Downs and Black checklist for observational studies.

Outcomes: All-cause mortality, hospitalization for HF, functional outcomes (NYHA class, LVEF, 6-min walk test, and quality of life) and safety outcomes (including peri-implantation death, infections at the implant site, or lead problems).

MAIN RESULTS

Meta-analysis showed that CRT led to lower incidences of all-cause mortality and hospitalization for HF; more patients with improvements of \geq 1 NYHA class; and greater improvements in LVEF, 6-minute walk test, and quality of life than did controls

(drug therapy or ICD alone) (Table). CRT led to a 0.3% (95% CI 0.1 to 0.6) incidence of periimplantation death, 1.8% (CI 1.3 to 2.5) rate of hospitalizations for infections at the implant site, and 6.6% (CI 5.6 to 7.4) incidence of lead problems.

CONCLUSION

Cardiac resynchronization therapy reduces mortality and morbidity in patients with left ventricular systolic dysfunction.

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Cardiac resynchronization therapy (CRT) vs control (drug therapy or implantable cardioverter-defibrillator) in left ventricular (LV) systolic dysfunction at a median 6 months*

Outcomes	Number of trials (n)	Weighted event rates		RRR (95% CI)	NNT (CI)
		CRT	Control		
All-cause mortality	14 (3825)	12%	15%	22% (9 to 33)	30 (20 to 72)
Hospitalization for HF	7 (2270)	17%	27%	37% (7 to 57)	11 (7 to 54)
RBI (CI)					
Improvement of \geq 1 NYHA class	3 (1320)	57%	37%	55% (25 to 92)	5 (3 to 11)
Weighted mean difference (CI)					
LV ejection fraction	5 (905)	3% (0.9 to 5.1)			
6-min walk test distance (m)	10 (2385)	24 (13 to 35)			
Quality of life†	11 (3369)	8 (5.6 to 10)			

*NYHA = New York Heart Association; HF = heart failure; other abbreviations defined in Glossary. Weighted event rates, RRR, RBI, NNT, and CI calculated from control event rates and relative risks in article. Analysis based on a random-effects model.

†Minnesota Living With Heart Failure Questionnaire.

COMMENTARY

The meta-analysis by McAlister and colleagues confirms that CRT reduces morbidity and mortality in patients with ischemic and non-ischemic dilated cardiomyopathy. Approximately 20% to 30% of the 5 million patients with congestive HF in the United States have dyssynchronous contractions, which may benefit from CRT (1). The cost of applying this technology to the increasing number of potential recipients has implications for resource-limited health care delivery systems. Unfortunately, only two thirds of candidates meeting current criteria have a favorable response to CRT (2). The challenge is to optimize outcomes and minimize cost by selecting patients who will derive the greatest benefit.

Current guidelines for CRT require NYHA class 3 or 4 HF symptoms and LVEF \leq 35% despite optimal pharmacologic treatment and QRS segment duration \geq 120 msec on electrocardiography. These requirements seem appropriate, given that the review showed that 91% of patients had NYHA class 3 or 4 HF and all patients had a prolonged QRS segment. The initial assumption that CRT benefits patients with

a long QRS duration, consistent with interventricular dyssynchrony, is being challenged by studies suggesting that markers of intra-LV dyssynchrony are more useful. Echocardiographic tissue Doppler imaging and magnetic resonance tissue imaging have shown promise in quantifying intra-LV dyssynchrony and predicting efficacy of CRT (3, 4). Further studies are required to find the optimal criteria to maximize efficacy and minimize cost.

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