Review: Cardiac resynchronization therapy reduces mortality and hospitalization for heart failure

McAlister FA, Ezekowitz JA, Wiebe N, et al. **Systematic review: cardiac resynchronization in patients with symptomatic heart failure.** Ann Intern Med. 2004;141:381-90.

Nichol G, Kaul P, Huszti E, Bridges JF. **Cost-effectiveness of cardiac resynchronization therapy in patients with symptomatic heart failure.** Ann Intern Med. 2004;141:343-51.

QUESTION

In patients with symptomatic heart failure (HF), how effective is cardiac resynchronization therapy (CRT)?

METHODS

Data sources: Cochrane Library, MEDLINE, EMBASE/Excerpta Medica, Web of Science, several trial registries, primary authors of included studies, FDA reports, reference lists of included studies, and companies that produce biventricular devices up to May 2004.

Study selection and assessment: Randomized controlled trials (RCTs) of CRT in patients with symptomatic HF. Health-related quality of life (QOL) and cost data were gathered from publicly available data.

Outcomes: All-cause mortality, hospitalization for HF, or both. Secondary outcomes were HF mortality, overall cardiac mortality, noncardiac mortality, 6-minute walk test, improvement in New York Heart Association (NYHA) class, and QOL. The economic analysis determined incremental cost per quality-adjusted life-year (QALY) using 2003 U.S. dollars . The willingness-to-pay threshold was $100 000/QALY.

MAIN RESULTS

9 RCTs (n = 3574, mean age 64 y, 74% men, all had prolonged QRS durations and left ventricular ejection fraction < 35%) were included. 10 additional cohort studies were included in a safety analysis. Most patients were receiving angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers. Fewer patients who received CRT died from any cause or had hospitalization for HF than did patients who received control treatment (Table). CRT was associated with an increase in 6-minute walk distance (8 RCTs, weighted mean difference 28 m, 95% CI 16 to 40), improvement in ≥ 1 NYHA class (4 RCTs, relative risk 1.6, CI 1.3 to 1.9), and improvement in QOL (7 RCTs, 7.6-point improvement on Minnesota Living with Heart Failure Questionnaire, CI 3.8 to 11.5). The periimplantation mortality rate was low (0.4%). The median incremental cost-effectiveness of CRT was $107 800/QALY (inter-quartile range 79 800 to 156 500).

CONCLUSION

In patients with systolic heart failure and evidence of electromechanical dyssynchrony who remain symptomatic despite optimal pharmacotherapy, cardiac resynchronization therapy (CRT) reduces all-cause mortality and heart failure hospitalization and improves quality of life and functional status.

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Cardiac resynchronization therapy vs control for symptomatic heart failure*

Outcomes	Number of trials	RRR (95% CI)	NNT (CI)
All-cause mortality	9	21% (4 to 34)	24 (15 to 124)†
Heart failure hospitalization	6	33% (8 to 52)	16 (9 to 56)

*Control treatment was usually a pacemaker turned off. Follow-up ranged from 1 to 12 months. Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article using a random-effects model. All outcomes favor cardiac resynchronization therapy.
†Data provided by author.

COMMENTARY

The reviews by McAlister and Nichol and their colleagues provide a helpful construct for discussing the financial analysis of biventricular (BiV) pacing. BiV is a costly but effective alternative for patients in whom all currently available medical treatments have failed. The authors estimated a conservative $30 000/patient; however, most BiV implants in the United States are now coupled with an implantable defibrillator (ICD), resulting in a cost often in excess of $50 000. Many of the trials in the review by McAlister and colleagues used less expensive and possibly less effective BiV pacemakers. Previous RCTs of ICDs showed a benefit in most patients with decreased left ventricular function (1, 2). The MIRACLE trial (3) showed a 77% reduction in the number of days hospitalized for CHF with CRT, a difference that will likely translate into a lower cost per hospital visit. This cost differential and the financial effects of CRT on office visits are difficult to quantify and were not included in the analysis by Nichol and colleagues.

Most of the cost associated with BiV implants occurs at implantation. The devices can be maintained at minimal cost with long-lasting batteries. However, device-related complications incur additional costs. Many studies had only 6-month follow-up, making long-term cost estimates challenging. Longer studies are required to determine whether benefits of BiV pacing will increase with minimal incremental cost in years 2 to 6.

The implantation of resynchronization devices is a highly technical procedure. The leads and delivery systems currently available dramatically improve implant success and shorten procedure duration. These improvements have theoretical but unproven effects on periprocedural complication rates, efficacy, and lead dislodgement rate. An intention-to-treat comparison of costs of modern resynchronization equipment would certainly assist in patient selection for CRT.

McAlister and Nichol and their colleagues help us ponder whether patients with end-stage HF should be resynchronized at high cost or have therapy limited by cost and remain symptomatic until they die.

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