Cardiac resynchronization was effective for moderate-to-severe heart failure with intraventricular conduction delay

Abraham WT, Fisher WG, Smith AL, et al., for the MIRACLE Study Group. **Cardiac resynchronization in chronic heart failure.** N Engl J Med. 2002;346:1845-53.

QUESTION

In patients with moderate-to-severe heart failure and an intraventricular conduction delay, does cardiac resynchronization improve clinical outcomes?

DESIGN

Randomized (unclear allocation concealment*), blinded (unclear),* controlled trial with 6-month follow-up (Multicenter InSync Randomized Clinical Evaluation [MIRACLE]).

SETTING

45 centers in the United States and Canada.

PATIENTS

453 patients (mean age 64 y, 68% men) who had moderate or severe (New York Heart Association [NYHA] functional class III or IV) chronic heart failure resulting from ischemic or nonischemic cardiomyopathy; received stabilized doses of medication for ≥ 1 month (≥ 3 mo for β-blockers); and had left ventricular ejection fraction ≤ 35%, a QRS interval ≥ 130 msec, and a 6-minute walking distance ≤ 450 m. Exclusion criteria included use of pacemakers or cardioverter-defibrillators, a cardiac or cerebral ischemic event in the previous 3 months, and atrial arrhythmia in the previous month. Follow-up was ≥ 90% for all outcomes.

INTERVENTION

All patients received implantation of a cardiac-resynchronization device (InSync model 8040, Medtronic, Minneapolis, MN, USA) with 3 pacing leads: a standard right atrial lead, a standard right ventricular lead, and a specialized left ventricular lead. Patients were allocated to atrial-synchronized biventricular pacing (n = 228) or no pacing (n = 225).

MAIN OUTCOME MEASURES

Change in NYHA class, death or worsening heart failure, quality of life (Minnesota Living with Heart Failure score), and distance walked in 6 minutes.

MAIN RESULTS

Analysis was by intention to treat. More patients in the resynchronization group than in the no-pacing group had an improvement in NYHA class (Table). Resynchronization led to fewer patients who died or had worsening of heart failure (Table). Patients in the resynchronization group had a greater improvement in quality of life (median score change −18 vs −9, P = 0.001) and were able to walk further in 6 minutes (median change in distance from baseline 39 vs 10 m, P = 0.005) than patients in the no-pacing group.

CONCLUSION

In patients with moderate-to-severe heart failure and an intraventricular conduction delay, cardiac resynchronization reduced death or worsening of heart failure and improved quality of life and walking ability.

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*See Glossary.

Atrial-synchronized biventricular pacing vs no pacing in heart failure†

Outcomes at 6 mo	Resynchronization	No pacing	RBI (95% CI)	NNT (CI)
Improved by ≥ 2 NYHA classes	16%	6.1%	163% (43 to 391)	11 (7 to 26)
Improved by 1 NYHA class	52%	32%	63% (29 to 109)	5 (4 to 10)
			RRR (CI)	
Death or worsening of heart failure‡	12%	20%	37% (3.6 to 60)	14 (9 to 143)

†NYHA = New York Heart Association. Other abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.
‡Event rates, RRR, NNT, and CI calculated from Cox proportional hazards ratio.

COMMENTARY

The MIRACLE trial shows that 1 in 5 patients with advanced symptomatic congestive heart failure and an intraventricular conduction delay have incremental improvement of ≥ 1 NYHA symptom class at 6 months with biventricular pacing. Limited information is available at present to predict the subset of patients with congestive heart failure and an intraventricular conduction delay who will benefit from resynchronization pacing therapy. Given the relatively low rate of short-term response to biventricular pacing, the more mundane initial management efforts at correcting modifiable underlying factors (e.g., ischemia and valvular disease) and optimizing medical therapy should not be overlooked.

The effect of biventricular pacing on long-term outcomes including mortality is unknown. Hence, the incremental effectiveness and cost-effectiveness of this expensive technology remains uncertain. Furthermore, the addition of defibrillation capability to resynchronization therapy was not addressed in this study.

Despite these limitations, resynchronization therapy should be considered for patients who have depressed left ventricular systolic function, NYHA class III or IV congestive heart failure symptoms despite optimal medical therapy, and a QRS duration ≥ 130 msec. Additional data suggest that patients with left bundle-branch block in fact receive greater benefit than those with right bundle-branch block. If longer-term data show benefit and additional study allows more precise selection of those patients who will respond, the MIRACLE trial will probably be viewed as a landmark initial step in the development of an effective new treatment method for a small but important subset of patients with advanced congestive heart failure.

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