Extending the boundaries of cardiac resynchronization therapy: efficacy in atrial fibrillation, New York Heart Association class II, and narrow QRS heart failure patients

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CRD summary
This review found that patients with less severe chronic heart failure may benefit from cardiac resynchronisation therapy. Methodological flaws and a lack of information about the quality of the included studies mean that the authors’ conclusions may not be reliable.

Authors’ objectives
To evaluate the effects of cardiac resynchronisation therapy (CRT) by comparison of the groups: patients with narrow QRS (<120ms) versus those with wide QRS intervals; patients with atrial fibrillation versus those with sinus rhythm; and patients with New York Heart Association (NYHA) Class II symptoms versus patients with NYHA Class III/IV symptoms.

Searching
MEDLINE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to December 2008 for relevant English-language studies; search terms were reported. Reference lists of retrieved articles were checked to identify additional references.

Study selection
Comparative studies that evaluated the effects of CRT between of 15 or more patients with narrow or wide QRS intervals, atrial fibrillation or sinus rhythm or NYHA class II or NYHA Class III/IV symptoms were eligible for inclusion. Studies that assessed benefits of CRT in patients with narrow QRS, atrial fibrillation or NYHA Class II compared to similar groups who did not receive CRT were excluded from the analysis. Narrow QRS was defined as up to 120ms; and studies that did not define narrow QRS using this method were excluded.

Outcomes examined included left ventricular ejection fraction, left ventricular end-systolic volume, exercise capacity measured by the six-minute walk test, change in NYHA class and quality of life. Patients in most trials were reported to have received optimal medical therapy.

Three reviewers independently performed the study selection. Any disagreements were resolved by a fourth reviewer.

Assessment of study quality
The authors reported that three reviewers independently assessed methodological quality. Methods by which quality was assessed and the results of the assessment were not reported.

Data extraction
Data were extracted to calculate standardised mean differences (SMD) and corresponding 95% confidence intervals (CI) for each outcome measure.

Three reviewers independently performed data extraction. Any disagreements were resolved by discussion with a fourth reviewer.

Methods of synthesis
Pooled standardized mean differences and 95% CIs were calculated for each outcome using a DerSimonian and Laird random-effects model. The results were summarised narratively grouped by comparison: wide QRS versus narrow QRS, atrial fibrillation versus sinus rhythm and NYHA Class II versus NYHA Class III/IV.

Results of the review
Thirteen studies (2,882 patients) were included in the review: one randomised controlled trial (RCT); eight prospective observational studies; and four retrospective observational studies. Follow-up ranged from three months to 68 months. Sample sizes in the studies ranged from 22 to 952 patients.

There were statistically significant higher levels of benefit after CRT observed for patients with a wide QRS interval compared with patients with QRS intervals less than 120ms for the six-minute walk test (pooled SMD 1.27, 95% CI 0.59 to 1.96; four studies) and for NYHA class improvement (pooled SMD 1.24, 95% CI 0.72 to 1.75; three studies). There were no significant differences between these groups for left ventricular ejection fraction or left ventricular end-systolic volume.

Patients with sinus rhythm achieved significantly greater benefits of treatment with CRT than patients with atrial fibrillation in the six-minute walk test (pooled SMD 1.67, 95% CI 0.55 to 2.79; three studies) and quality of life (pooled SMD 1.24, 95% CI 0.55 to 1.94; three studies). There were no differences between these groups for left ventricular ejection fraction or NYHA class improvement.

There were no significant differences between patients with NYHA Class II symptoms and patients with NYHA Class III/IV symptoms in left ventricular end-diastolic diameter or left ventricular end-systolic diameter after treatment with CRT (three studies).

**Authors' conclusions**

There may be a place for the use of cardiac resynchronisation therapy in patients with heart failure who do not meet current standard indications for this type of therapy. More research is required on this intervention, in particular for patients with narrow QRS intervals, NYHA II symptoms and/or sinus rhythm.

**CRD commentary**

The review addressed a clear question. Criteria for inclusion of studies in the review were stipulated. The search was limited to two electronic databases. The review was restricted to studies published in English, so there was a risk of publication bias. Steps were taken to minimise errors and bias for study selection and data extraction. The authors reported that they assessed methodological quality, but did not report the results. There was no examination of statistical heterogeneity, although data was combined in a random effects model. It may not have been appropriate to combine the results in a meta-analysis because of the heterogeneity of the study designs used. Findings from uncontrolled studies are associated with a number of potential biases and confounders that can lead to an overestimation of treatment effect.

Methodological flaws and the lack of information about the included studies mean that the authors' conclusions should be interpreted with caution and may not be reliable.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that adequately powered randomised controlled trials were necessary to evaluate the role of CRT in patients with NYHA II symptoms, atrial fibrillation and narrow QRS intervals.

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**Bibliographic details**


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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.