Cardiac resynchronization in patients with atrial fibrillation: a meta-analysis of prospective cohort studies

Upadhyay GA, Choudhry NK, Auricchio A, Ruskin J, Singh JP

CRD summary
This review concluded there were benefits to treating heart failure with cardiac resynchronisation; patients with atrial fibrillation had greater improvement in ejection fraction, but smaller improvements in functional outcomes than those in sinus rhythm. Mortality was similar in both groups. Given some problems with the review and less reliable data from observational studies, these conclusions should be treated with caution.

Authors' objectives
To determine the effects of cardiac resynchronisation therapy in patients with atrial fibrillation compared with those in sinus rhythm.

Searching
MEDLINE, CINAHL, Cochrane Database of Systematic Reviews, DARE, Cochrane Central Register of Controlled Trials (CENTRAL) and the American College of Physicians Journal club were searched to May 2007. Search terms were reported. Bibliographies of relevant reviews were checked. Only published studies were eligible for inclusion.

Study selection
Studies that assessed the effects of implantable cardiac resynchronisation therapy for heart failure in patients with atrial fibrillation compared with those in sinus rhythm were eligible for inclusion. Studies in which most patients developed atrial fibrillation after enrolment, or where patients had intermittent or paroxysmal atrial fibrillation, or studies with less than 25 participants, were excluded.

The outcomes of interest were mortality at one year, echocardiographic data (ejection fraction) and functional outcomes. Functional outcomes were measured using the New York Heart Association (NYHA) functional class and the six-minute walk test. Quality of life was measured by the Minnesota Living with Heart Failure questionnaire.

In the included studies, the majority of participants were men (between 68 and 92%), and their mean ages ranged from 63 to 73 years. Between 77 and 100% had NYHA Class III to V heart failure; mean ejection fractions ranged from 20 to 26%. All participants were taking a combination medical therapy before enrolment, including beta-blockers, angiotensin inhibitors and diuretics. Overall, 56% of those with atrial fibrillation had undergone atroventricular junction ablation. Two studies used implantable cardiac resynchronisation therapy in combination with defibrillators. Participants in sinus rhythm were programmed to atrial-synchronous sequential pacing, and the majority of those in atrial fibrillation to biventricular rate adaptive mode.

The authors did not state how the papers were selected for the review.

Assessment of study quality
The authors discussed the quality of studies, in terms of study design, inclusion criteria and comparability of baseline characteristics.

Two authors extracted data on study quality. Disagreements were resolved by consensus.

Data extraction
When studies reported outcomes at multiple time points, the six month or 12 month data were used. Relative risks (RR) and 95% confidence intervals (CI) were calculated for dichotomous outcomes and mean differences for continuous outcomes.

Two authors extracted data independently. Disagreements were resolved by consensus.
Methods of synthesis
For dichotomous outcomes, pooled relative risks and 95% confidence intervals were calculated using a random-effects model. For continuous outcomes, where three or more studies reported the outcome, weighted mean differences (WMD) and 95% confidence intervals were calculated using a fixed-effect model.

Heterogeneity was assessed using the $I^2$ statistic.

Results of the review
Five prospective cohort studies (1,164 participants) were included in the review. Study size ranged from 37 to 673 participants. Of included participants, 797 were in sinus rhythm and 367 had atrial fibrillation. Those with atrial fibrillation were older (1.6 years on average) and had worse heart failure (NYHA Class III to IV 99.6% compared with 89%) than those in sinus rhythm.

There was no difference in mortality between patients with atrial fibrillation and those in sinus rhythm after cardiac resynchronisation therapy (RR 1.57, 95% CI 0.87 to 2.81; $I^2=47.5$%).

Both groups showed improvements with cardiac resynchronisation therapy for all other outcomes; the improvement was greater in the atrial fibrillation group for ejection fraction (WMD 0.39%, 95% CI 0.22 to 0.55; $I^2=97$%); improvement was greater in the sinus rhythm group for change in NYHA functional Class (WMD 0.06, 95% CI 0.04 to 0.08), six-minute walk test (WMD 11.6 minutes, 95% CI 10.4 to 12.8) and quality of life scores (WMD 3.94 points, 95% CI 3.35 to 4.54).

Authors' conclusions
Patients in atrial fibrillation showed significant benefits after cardiac resynchronisation therapy, with a similar or improved ejection fraction than sinus rhythm patients, but with smaller benefits in functional outcomes. There was no difference in mortality at one year between the two patient groups.

CRD commentary
The aims of the review were clearly stated for the participants, treatment and outcomes, although they were less clear for study design. The search covered a number of relevant sources, but it was limited to published studies, so there was a possibility of publication bias. There was no mention of whether any language restrictions were applied, so it was unclear whether language bias had an effect on results. The methods used for data extraction were aimed at reducing the risk of reviewer error or bias, but no information was given about methods used for study selection.

Quality did not seem to have been formally assessed, although the authors did discuss the limitations of observational studies, and differences in participants' characteristics at baseline. Heterogeneity was assessed and considerable heterogeneity was observed for some of the outcomes, so it may not have been appropriate to combine these results. As the authors acknowledged, the data came from observational studies, which are less reliable than RCTs because their results may be affected by factors not necessarily related to the treatment.

Given these limitations, the authors' conclusions should be treated with caution.

Several of the authors disclosed financial links with Biotronik, Boston Scientific, Medtronic and/or the Sorin Group (manufacturers of cardiac resynchronisation devices).

Implications of the review for practice and research
Practice: The authors stated that cardiac resynchronisation therapy may be associated with clinical benefit in patients with atrial fibrillation.

Research: The authors stated that there is a need for RCTs to assess the impact of cardiac resynchronisation therapy treatment for heart failure with atrial fibrillation, in particular using optimal medical management as a comparator. They also stated that cardiac resynchronisation therapy treatment in older patients should be assessed.
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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.