Cardiac resynchronization therapy after atrioventricular junction ablation for symptomatic atrial fibrillation: a meta-analysis

Stavrakis S, Garabelli P, Reynolds DW

CRD summary
This review concluded that cardiac re-synchronisation therapy may be superior to right ventricular pacing in patients undergoing atrioventricular junction ablation for atrial fibrillation, but that further research was needed as the included trials were underpowered. Although the possibility of missed trials could not be ruled out, the authors’ conclusions appear reasonable as they include the need for further research.

Authors’ objectives
To assess the effectiveness of cardiac re-synchronisation therapy versus right ventricular pacing after atrioventricular junction ablation for patients with atrial fibrillation.

Searching
MEDLINE and EMBASE were searched up to November 2011. Search terms were reported. Bibliographies of retrieved papers were checked. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) that compared cardiac re-synchronisation therapy with right ventricular pacing after atrioventricular junction ablation in patients with persistent or permanent atrial fibrillation were eligible for inclusion. The outcomes of interest were total mortality, hospitalisation for heart failure, quality of life (Minnesota Living with Heart Failure questionnaire score), six-minute walking distance, and changes in left ventricular ejection fraction, left ventricular end systolic and end diastolic diameter.

In the included trials, the mean age of patients ranged from 65 to 72 years; the proportion of men ranged from 43% to 81%. Where reported, duration of atrial fibrillation ranged from 21 to 79 months, left ventricular ejection fraction ranged from 25 to 46%, and from 31% to 95% of patients had Class III New York Heart Failure or higher (moderate to severe). Some patients had ischaemic heart disease, hypertension or diabetes. Additional treatments included beta-blockers, angiotensin converting enzyme inhibitors/angiotensin receptor blockers, digoxin, or anti-arrhythmic agents.

Two reviewers independently selected studies for inclusion. Disagreements were resolved by discussion.

Assessment of study quality
Trial quality was assessed using methods of randomisation, double blinding, and descriptions of withdrawals and drop-outs.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Data were extracted on an intention-to-treat basis to calculate risk ratios and 95% confidence intervals for dichotomous data, and mean differences and 95% confidence intervals for continuous data. Heterogeneity was assessed using the Q statistic and $I^2$. Sensitivity analyses investigated the removal of each trial individually.

Two reviewers independently extracted data. Disagreements were resolved by discussion.

Methods of synthesis
Pooled risk ratios with 95% confidence intervals were calculated using a random-effects method. Mean differences were pooled using the inverse variance method, based on a random-effects model.

Results of the review
Five RCTs were included in the review (638 patients, taken from table 1, 686 cited in text). Follow up ranged from six...
months (mean) to 20 months (median), where reported. In all trials, the methods of randomisation were appropriate, drop-outs and crossover rates were reported, and outcomes assessors were blinded.

Compared with right ventricular pacing, cardiac re-synchronisation therapy reduced the risk of heart failure-related hospitalisation (RR 0.38, 95% CI 0.17 to 0.85; three trials; I²=15%), but had no statistically significant effect on mortality (five trials; I²=9%), six-minute walking distance (four trials; I²=0%), or quality of life (three trials; I²=0%).

There was a statistically significant, but small, difference in left ventricular ejection fraction with cardiac re-synchronisation therapy (mean difference 1.97%, 95% CI 1.52 to 2.42; three trials; I²=13%).

Sensitivity analyses showed no major impact of any individual trial.

Adverse events were similar between groups in individual trials.

**Authors’ conclusions**
Cardiac re-synchronization therapy may be superior to right ventricular pacing in patients undergoing atroventricular junction ablation for atrial fibrillation. Further studies were required, adequately powered to detect clinical outcomes and specifically examining patients with preserved left ventricular systolic function.

**CRD commentary**
The aims of this review were clearly stated in the inclusion criteria. The search was not restricted by language, so language bias was unlikely. However it was not clear whether unpublished studies were sought, so publication bias may have affected the review. The methods of study selection and data extraction were aimed at reducing possible reviewer error or bias, but it was not clear if this extended to quality assessment.

Trial quality was assessed based on the Jadad scale. The authors mentioned the possibility of imbalances between groups due to drop-outs/withdrawals, but did not report further details, so it was not possible to evaluate the risk of attrition bias affecting the results. The methods of synthesis appeared appropriate; heterogeneity was assessed. The authors acknowledged that the included trials were small with relatively short follow up; this meant that it may not be possible to rule out more significant effects of treatment. The possibility of missed trials could not be ruled out.

As authors’ conclusions include the need for further research, their conclusions appear reasonable.

**Implications of the review for practice and research**
**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that large-scale multicentre RCTs, with longer follow up, were needed to compare cardiac re-synchronisation therapy with right ventricular pacing in patients undergoing atroventricular junction ablation for symptomatic atrial fibrillation. Future trials should stratify patients according to preserved versus decreased left ventricular ejection fraction, QRS duration, and presence versus absence of heart failure. Given that a cardiac re-synchronisation device is much more expensive than a pacemaker, an analysis of the costs was warranted.

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