Atrioventricular nodal ablation in atrial fibrillation: a meta-analysis of biventricular vs. right ventricular pacing mode
Chatterjee NA, Upadhyay GA, Ellenbogen KA, Hayes DL, Singh JP

CRD summary
This review concluded that compared to right ventricular pacing, biventricular pacing was not associated with improved survival in people with refractory atrial fibrillation undergoing atrioventricular node ablation. However, it was associated with modest improvements in other outcomes. Considering concerns about possible missed trials, and quality of included trials, the authors' conclusions should be treated with caution.

Authors' objectives
To assess the effects of biventricular pacing, compared to right ventricular only pacing, in people with atrial fibrillation undergoing atrioventricular nodal ablation.

Searching
MEDLINE (including in-process), CINAHL, Cochrane Controlled Trials Register (CENTRAL), the Cochrane Database of Systematic Reviews, DARE and the American College of Physicians Journal Club were searched to November 2011. Search terms were reported. The bibliographies of reviews were checked. Only published studies were sought.

Study selection
Randomised controlled trials (RCTs), or subgroups of RCTs, that compared biventricular pacing to right ventricular pacing in people with atrial fibrillation undergoing atrioventricular nodal ablation were eligible for inclusion. The outcomes of interest were mortality, adverse events, echocardiographic data (such as ejection fraction) and functional outcomes (New York Heart Association functional class, exercise stress duration, quality of life.

In the included studies between 38 and 73% were men, and mean ages ranged from 67 to 73 years. All studies included people with persistent or permanent atrial fibrillation. Between 10 and 42% had coronary artery disease. Mean left ventricular ejection fraction ranged from 37 to 57, and where reported, mean New York Heart Association class from 2 to 2.6. Three studies included people with left ventricular systolic dysfunction. Biventricular pacing mode was dual-chamber and rate-responsive.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
Quality was assessed using the Jadad scale.

Two reviewers independently assessed quality. Disagreements were resolved by consensus.

Data extraction
Data were extracted to calculate odds ratio (OR) and 95% confidence intervals (CI) for dichotomous data; mean differences and 95% confidence intervals were calculated for continuous data. For continuous data where only baseline and follow-up data were reported, change and standard deviation were calculated. Data for adverse events was restricted to up to 30 days, with the exception of lead failure which could occur at any time during follow-up. For the cross over study, for mortality analyses, group size was taken as half those participating to prevent double counting.

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

Methods of synthesis
A random-effects model was used to calculate pooled risk ratio and 95% confidence intervals, and pooled weighted mean differences and 95% confidence intervals. Heterogeneity was assessed with $I^2$. Subgroup analyses investigated studies including participants with left ventricular systolic dysfunction.
Results of the review
Four RCTs (534 participants) were included. One (56 participants) was a crossover study. Follow-up appeared to range from six to 24 months.

There was no statistically significant difference between biventricular pacing and right ventricular pacing, in all-cause mortality ($I^2=31\%$, four trials), procedure related adverse events ($I^2=27\%$, three trials) or six minute walk test duration ($I^2=0\%$, three trials). There was a small increase in mean left ventricular ejection fraction associated with biventricular pacing ($+2.6\%$, 95% CI 1.7 to 3.4, $I^2=53\%$, four trials).

In two trials, biventricular pacing was associated with modest but statistically significant reduction in quality of life (Minnesota Living with Heart Failure Questionnaire 2.72 fewer points, 95% CI 1.45 to 3.99, $I^2=0\%$). A third trial reported no change in quality of life using the SF-36 Health Status Scale.

In subgroup analyses, including only those studies with baseline left ventricular systolic dysfunction, results were similar to the main analyses for all-cause mortality ($I^2=0\%$, three trials), and for mean left ventricular ejection fraction ($I^2=58\%$). These studies also reported on cardiac mortality; there was some reduction favouring biventricular pacing but this did not reach statistical significance ($I^2=0\%$, three trials).

Authors’ conclusions
In patients with refractory atrial fibrillation undergoing atrioventricular node ablation, biventricular pacing was not associated with improved survival when compared with right ventricular-only pacing. However, it was associated with modest improvements in quality of life and left ventricular ejection fraction.

CRD commentary
The aims of this review were clearly stated in terms of the inclusion criteria. It wasn't clear whether any language restrictions were applied to the search, and only published studies were eligible. It was possible that studies were missed, and that publication bias may have affected the review. It wasn’t possible to rule out language bias. The methods of data extraction and quality assessment were those aimed at reducing possible reviewer error or bias. Those for study selection weren't clear. Although quality was assessed the results were not presented so it was difficult to independently comment on the quality of included data. The methods of synthesis generally appeared appropriate, and heterogeneity was assessed. However it wasn't entirely clear whether the inclusion of data from the crossover study was appropriately dealt with.

The authors note that participants were those with relatively preserved left ventricular ejection fraction and results may not therefore be generalisable to other populations. They also acknowledge that data came from a small number of relatively small studies, some with short follow-up times. Given this it may not be possible to rule out any benefits of biventricular pacing.

As there were questions about possible missed studies, and the quantity and quality of included data, the authors’ conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The authors stated that their results supported the recommendations outlined in the European Society of Cardiology guidelines (further details reported in paper).

Research: The authors stated that RCTs were needed to assess the effects of biventricular pacing in people with atrial fibrillation undergoing atrioventricular node ablation. These should take into account longer follow-up times, selection of clinical endpoints and heterogeneity of ventricular function, and in particular look at participants with heart failure who do not meet indications for cardiac resynchronisation therapy.

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