Dual versus single chamber pacemaker therapy in atrioventricular block and sick sinus syndrome


Authors' objectives
To systematically review the evidence for both the short- and long-term clinical effectiveness of dual-chamber pacemakers, compared with single-chamber ventricular pacemakers, in adults with sick sinus syndrome (SSS), atrioventricular (AV) block or both.

Searching
MEDLINE, EMBASE, the Science Citation Index and the Cochrane Controlled Trials Register were searched from 1980 to June 2001, without any language restrictions. A comprehensive list of search terms were used (full details given in the report). Additional sources searched were the National Research Register, MRC-funded projects, UK Department of Health, British Heart Foundation, clinicaltrials.gov, controlled-trials.com, CentreWatch.com and the websites of relevant professional associations. Experts were contacted and the reference lists of retrieved papers were examined.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials (RCTs) of parallel or crossover design were eligible. The length of study ranged from 7.2 to 60 months for the included parallel RCTs, and from 1 week to 3 months for each crossover period in the included crossover studies.

Specific interventions included in the review
The inclusion criteria stated permanent rate-adaptive or non rate-adaptive pacemakers capable of sensing and pacing in both the atrium and ventricle (e.g. DDD, DDDR, DDI, DDIR, VDD or VVDR; see Other Publications of Related Interest no.1 for details of these modes). The minimum pacing duration was 48 hours. The comparators were permanent rate-adaptive or non rate-adaptive pacemakers capable of sensing and pacing in either the ventricle or the atrium (single-chamber pacemakers, VVI, VVIR, AAI, AAIR). Studies that compared more than one type of single- or dual-chamber pacemaker were included provided that a single-pacing mode was compared to a dual-pacing mode as part of the study. The review did not compare atrial versus ventricular pacing, nor differences between rate-adaptive and non-rate adaptive pacemakers. Some of the included studies used 'physiological' pacemakers, rate-adaptive pacemakers and pacemakers with mode switching. Some participants were taking additional drugs (beta-blockers, calcium antagonists, angiotensin-converting enzyme inhibitors, diuretics, nitrates, anti-arrhythmic drugs, cardiac glycosides or antiplatelets).

Participants included in the review
The inclusion criteria specified participants aged 18 years or older where the majority of the population had SSS, AV block or both. In the included studies a small proportion of participants also had 'other/unknown' indications for pacing. Cardiovascular co-morbidities included hypertension, coronary heart disease, dilated cardiomyopathy, heart failure and arrhythmias. However, some studies excluded participants with these or other co-morbidities (full details provided in the report). The mean ages of the participants ranged from 52 to 81 years. Both male and female participants were included.

Outcomes assessed in the review
The primary outcomes were cardiovascular mortality and morbidity (symptoms of pacemaker syndrome as defined by the author of the trial), onset of atrial fibrillation, stroke or other thromboembolic events, or heart failure. The secondary outcomes included quality of life (measures of psychological or mental functioning, social functioning, physical status, symptoms), exercise assessment (exercise duration or walking distance), and complication rate (device complications severe enough to warrant additional hospital visits, surgical procedure or reimplantation). The symptoms assessed in the included studies were dizziness, fatigue, chest pain, breathlessness and palpitations.
How were decisions on the relevance of primary studies made?
One reviewer assessed the papers for inclusion. A random sample (10%) was also assessed by a second reviewer. Any disagreements were resolved by a third reviewer.

Assessment of study quality
Quality was assessed, and a score calculated, using a checklist based on the Jadad scale (see Other Publications of Related Interest no.2). The checklist items included method of randomisation, concealment, blinding, completeness and intention-to-treat analysis. For parallel studies, additional quality items were assessed: whether randomisation was by mode or device; the comparability of the study arms at the beginning of the study; the comparability of treatment throughout the trial; and adequacy of statistical power. For crossover studies, the additional items included washout periods, period effect tests and unscheduled crossover rates. A study was considered to be inadequate if there was evidence of failure on two or more quality criteria. Data concerning the quality of the studies was extracted by one reviewer. In addition, a second reviewer independently extracted data from a 10% sample of the studies.

Data extraction
A data extraction form was designed and piloted on a sample of studies, then modified and used to extract data. The data were extracted by one reviewer and authors were contacted for missing information. The data extracted included general study characteristics: year and country or studies, the number of participants, indication for pacing, details of cardiovascular co-morbidities, mean age, details of intervention devices and comparators, drugs used, length of study and full details on all outcomes(further information is provided in the report).

Methods of synthesis
How were the studies combined?
The results were collated in separate summary tables for parallel and crossover studies. A vote counting approach was used initially to show the direction of effect for all studies, as not all studies could be pooled because of missing data. Where sufficient appropriate data were available, a meta-analysis was carried out using the fixed-effect model since there was no statistical evidence of heterogeneity. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for the binary data, whereas standardised mean differences and 95% CIs were calculated for the continuous data. Funnel plots were generated to assess publication bias. Where possible, the results for patients with SSS and AV block were presented separately.

How were differences between studies investigated?
The authors stated that there was no statistical evidence of heterogeneity, but gave no further details of this. In addition, the studies were ranked according to quality criteria in order to assess the feasibility of carrying out sensitivity analyses of the impact of quality of clinical effectiveness results.

Results of the review
Thirty studies were included: 4 parallel design (3,383 participants) and 26 crossover (495 participants).

None of the studies was considered to be ‘adequate’ in quality. In particular, the washout period was considered inadequate in 25 of the 26 crossover studies. Differences in quality were not deemed significant enough to merit sensitivity analyses.

Parallel studies: there was significant benefit of dual-chamber pacing compared with single-chamber pacing for the incidence of pacemaker syndrome (mean OR 0.1, 95% CI: 0.06, 0.16). For the other primary outcomes, there was a non significant trend towards benefit from dual/physiological pacing compared with single-chamber ventricular pacing: the OR was 0.9 (95% CI: 0.70, 1.15) for atrial fibrillation, 0.66 (95% CI: 0.39, 1.12) for stroke, 0.78 (95% CI: 0.53, 1.14) for heart failure, and 0.93 (95% CI: 0.71, 1.21) for mortality. Only one study assessed quality of life. No statistically-significant difference was observed in the two treatment groups, except for mental health at 9 months and cardiovascular functioning status at 18 months; these favoured dual-chamber pacing.
Crossover studies: the only primary outcome reported on was incidence and symptoms of pacemaker syndrome, because the duration of follow-up was short for all of these studies (up to 3 months). The direction of effect was divided between fewer symptoms in a dual mode, and no significant differences between dual and single modes. Only one study showed fewer symptoms in the single mode. There was a statistically significant reduction in pacemaker symptoms in dual pacing compared with single pacing (-0.74 standard deviation units, 95% CI: -0.95, -0.52). Four studies assessed quality of life. The pooling of data was deemed inappropriate and individual studies found either no significant difference or a significantly higher quality of life in dual mode.

There was insufficient information to compare treatments for AV block and SSS as subgroups in the parallel studies. A lack of statistical power meant that no conclusions could be drawn from the crossover studies. Further details of other results are detailed in the report.

Cost information
An economic evaluation was carried out. The initial costs of implantation were generally higher for dual-chamber than for single-chamber pacemakers: the average UK cost was £5,418 for a dual-chamber rate-adaptive pacemaker and £3,044 for a single-chamber pacemaker. It remains unclear from the identified studies whether this higher cost would be offset by future savings because of fewer complications, pacemaker failures and differences in follow-ups with dual-chamber pacemakers, compared with single-chamber pacemakers.

Authors' conclusions
Whilst evidence is of a variable nature in terms of quality and effectiveness, there is a trend towards greater effectiveness in dual pacing.

CRD commentary
This was a long and detailed review. The aims were clearly stated, a very comprehensive search was carried out, and the quality assessment was thorough. Full details of the included studies were tabulated. The methods of the review, where described, would seem to be satisfactory. However, the authors acknowledged that they counted the same study twice within the review, as different outcomes were reported in different papers. The authors were right not to combine the results from parallel and crossover studies, and the meta-analysis was appropriate. As the authors point out, the participants in the crossover trials may not be representative of the pacemaker population as a whole, so it may be difficult to generalise from these results. In addition, randomisation was by mode (rather than device) in these studies and this could have introduced bias. This, and the acknowledged poor quality of the included studies, could have influenced the effect size and direction. Overall, the authors' conclusions follow on from the results.

Implications of the review for practice and research
Practice: The recommendation for the preferential use of dual-chamber pacemakers over single-chamber pacemakers for AV block and SSS is borderline.

Research: Further clinical evidence is needed, particularly on patient-related quality of life and long-term adverse outcomes. The authors note that five large RCTs are currently ongoing.

Bibliographic details

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Other publications of related interest

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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.