Effects of cardiac resynchronization therapy on overall mortality and mode of death: a meta-analysis of randomized controlled trials

CRD summary
This review evaluated the effects of cardiac resynchronisation therapy (CRT) alone, compared with optimal medical therapy, on mortality in patients with advanced heart failure. The authors concluded that CRT reduces all-cause mortality and predominantly mortality due to worsening heart failure, but does not affect sudden cardiac death. These conclusions reflect the results, but the possible influence of bias cannot be entirely excluded.

Authors' objectives
To evaluate the effects of cardiac resynchronisation therapy (CRT) alone, compared with optimal medical therapy, on mortality and different modes of death in patients with advanced heart failure (HF).

Searching
MEDLINE (1985 to 2005) and the Cochrane CENTRAL Register (Issue 3, 2005) were searched; the search terms were reported. In addition, the website of the U.S. Food and Drug Administration and reference lists of retrieved papers were searched, as were scientific sessions of the major cardiac conferences over the preceding 5 years. The search was restricted to English language publications.

Study selection
Randomised controlled trials (RCTs) comparing the effects of CRT alone against optimal pharmacological therapy in patients with advanced symptoms of HF were eligible for inclusion. RCTs were required to have a follow-up of at least 3 months and report mortality and mode of death as outcome measures (crossover RCTs in which the first treatment period was at least 3 months were included, and only this first period was included in the analyses). The participants in the included studies were predominantly older (mean age 64 to 68 years) and male (mean 67 to 81%), with New York Heart Association functional class III HF (mean 82 to 100%).

Two reviewers independently screened papers for inclusion and any discrepancies were resolved through consensus.

Assessment of study quality
Studies were assessed as to whether they used blinding and an intention-to-treat analysis.

It appears that two reviewers independently extracted these data.

Data extraction
Odds ratios (ORs) with 95% confidence intervals (CIs) for the outcomes of overall mortality, worsening HF mortality and sudden cardiac death were calculated, where reported.

Two reviewers independently extracted data on an intention-to-treat basis.

Methods of synthesis
Both fixed-effect and random-effects models were used to pool the ORs. Statistical heterogeneity was investigated using the $\chi^2$ and $I^2$ statistics. Where heterogeneity was significant, the random-effects model was used.

Results of the review
Eight publications from five RCTs (n=2,371) were included in the review. Two of these were crossover RCTs (n=101).

One trial was double-blind, two were single-blind and two were not blinded.
CRT alone significantly reduced all-cause mortality by 29% (OR 0.71, 95% CI: 0.57, 0.88) and mortality due to worsening HF by 38% (OR 0.62, 95% CI: 0.45, 0.84). However, CRT alone did not significantly impact on sudden cardiac death (OR 1.04, 95% CI: 0.73, 1.46).

No significant heterogeneity was detected.

Authors' conclusions
CRT alone reduces all-cause mortality in patients with advanced symptoms of HF. It predominantly reduces mortality due to worsening HF and does not affect sudden cardiac death.

CRD commentary
This review answered a clearly defined question. The search for relevant studies covered two electronic databases plus other sources, but the restriction to English language publications may mean that relevant trials were missed, thereby introducing language bias. Study quality was addressed, but only a limited number of aspects relating to study quality (e.g. blinding) were assessed and these were not used in the synthesis. However, the authors made attempts to minimise error and bias in the study selection and data extraction processes, and the statistical methods used to synthesise the included studies appear appropriate. The authors’ conclusions reflect the results presented in the review, but the possible influence of bias on these results cannot be entirely excluded.

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

Research: The authors stated that there is a need to determine to what extent, and in which patients, there will be a benefit of combining an additional defibrillator function with CRT.

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