Impact of implantable defibrillators and resynchronization therapy on outcome in patients with left ventricular dysfunction: a meta-analysis

Abdulla J, Haarbo J, Kober L, Torp-Pedersen C

CRD summary
The authors concluded that both cardiac resynchronisation therapy and implantable cardioverter defibrillator improve outcomes for selected patients with left ventricular systolic dysfunction; combination of the two may provide further benefit. The review was well-conducted in many respects but, given the lack of a systematic validity assessment, poor reporting of study details and limitations of the primary studies, these conclusions may need to be viewed with some caution.

Authors' objectives
To evaluate the clinical benefits of cardiac resynchronisation therapy (CRT) and primary prophylactic implantable cardioverter defibrillator (ICD) in patients with left ventricular systolic dysfunction (LVSD).

Searching
MEDLINE, EMBASE, the Cochrane Library and the Science Citation Index were searched to June 2005; the search terms were reported. The proceedings of conferences and scientific meetings were handsearched for abstracts. The reference lists of relevant articles, reviews and meta-analyses were also checked. The search was restricted to articles in English.

Study selection
Randomised controlled trials (RCTs) and non-RCTs that compared CRT, or primary prophylactic ICD, with conventional treatments for at least 1 month in patients with LVSD were eligible for inclusion. Participants in the CRT studies were required to be symptomatic. The included studies compared biventricular pacemakers, ICD, or a combination of these with univentricular pacemakers, conventional therapy for heart failure, amiodarone, or each other. Most of the studies included patients with mixed cardiomyopathy, with or without atrial fibrillation; patients with prior myocardial infarction, non-ischaemic cardiomyopathy and coronary bypass grafts were also included. The duration of follow-up ranged from 1 to 48 months. The mean age of the participants was 61 years for ICD trials and 65.5 year for CRT trials and most were male. The outcomes reported in the review were all-cause and cardiac mortality, hospitalisation for heart failure, change in New York Heart Association (NYHA) class, and exercise tolerance (peak oxygen consumption and 6-minute walk test).

Three reviewers selected the studies.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Odds ratios (ORs) were calculated for binary data, while mean differences and standard deviations were calculated for continuous data. Only data from the first period were included for crossover studies.

Three reviewers extracted the data.

Methods of synthesis
Pooled ORs and weighted mean differences (WMDs) were calculated. Both the DerSimonian Laird random-effects model and the Peto-Yusuf fixed-effect model were used. Statistical heterogeneity was evaluated using the $\chi^2$ test. Where heterogeneity was found, it was investigated by sensitivity analyses. P-values of less than 0.05 were considered
Results of the review
Twenty studies (n=10,853; range: 13 to 2,521) were included: 18 RCTs (n=10,603) and 2 non-RCTs (n=250). Six RCTs were crossover in design.

Three studies were described as double-blind and three as single-blind.

CRT significantly reduced all-cause mortality (OR 0.73, 95% CI: 0.60, 0.89, p=0.002; 9 RCTs, 1 non-RCT) and hospitalisation for heart failure (OR 0.60, 95% CI: 0.45, 0.80, p=0.001). It also improved functional status in terms of peak oxygen consumption (WMD -0.64, 95% CI: -0.73, -0.54, p<0.0001; 2 RCTs, 1 non-RCT), but not 6-minute walk test.

ICD significantly reduced all-cause mortality (OR 0.75, 95% CI: 0.59, 0.96, p=0.025; 8 RCTs) and cardiac mortality (OR 0.63, 95% CI: 0.48, 0.82, p=0.001; 5 RCTs).

Combining ICD and CRT reduced mortality further in comparison with CRT alone (OR 0.69, 95% CI: 0.53, 0.91, p=0.008; 1 RCT, 1 non-RCT).

Significant heterogeneity was observed for the analyses of mortality for ICD and ICD combined with CRT.

Authors' conclusions
CRT and ICD both improve outcomes for selected patients with LVSD; combination of the two may provide further benefit.

CRD commentary
The review question and inclusion criteria were clear. Relevant sources were searched but the search was restricted to studies in English, thus potentially introducing language bias. Three reviewers selected the studies and extracted the data, but it was not clear how any discrepancies were resolved. Although some important details of study design were reported, such as blinding and randomisation, there was no indication that study validity was systematically assessed and there were insufficient details about the included studies to permit the reader to make their own assessment of study quality. It was reported, however, that several of the studies were small with few events and a relatively short duration of follow-up. The lack of detail makes it difficult to evaluate the reliability of the data presented, in particular the meta-analyses from which selected studies of ICD were excluded (post hoc) because of potential confounding. It is unclear whether the pooling of studies was justified, given the evident clinical heterogeneity between them. However, this is difficult to assess without more detailed information about the studies. Appropriate statistical methods were used to assess heterogeneity, though it was unclear whether random-effects or fixed-effect models were presented in the publication. It does not appear that potential publication bias was assessed. The potential for bias and confounding in the studies was acknowledged in general terms in the text. The review was well-conducted in many respects but, given the lack of a systematic validity assessment, poor reporting of study details and limitations of the primary studies, the authors’ conclusions may need to be viewed with some caution.

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

Research: The authors stated that research is needed to determine which patients benefit most from CRT, ICD, or both.

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Bibliographic details
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.