Implantable defibrillators for the prevention of mortality in patients with nonischemic cardiomyopathy: a meta-analysis of randomized controlled trials

Desai A S, Fang J C, Maisel W H, Baughman K L

CRD summary
This review evaluated the efficacy of implantable cardioverter defibrillator (ICD) therapy in reducing mortality in patients with nonischaemic cardiomyopathy (NICM). The authors concluded that ICD therapy significantly reduces mortality in selected patients with NICM. Limitations in the reporting of methodological details mean that it is unclear whether the conclusions are reliable.

Authors' objectives
To evaluate the efficacy of implantable cardioverter defibrillator (ICD) therapy in reducing all-cause mortality in patients with nonischaemic cardiomyopathy (NICM).

Searching
MEDLINE (from 1966 to April 2004), EMBASE (from 1991 to April 2004), and the Cochrane CENTRAL Register (Issue 1, 2004) were searched; the search terms were reported. In addition, the reference lists of identified studies were checked and reviews, commentaries and proceedings from national cardiology meetings (from 2003 to 2004) were searched.

Study selection
Study designs of evaluations included in the review
Prospective randomised controlled trials (RCTs) were eligible for inclusion. The duration of follow-up ranged from 14.8 to 66 months.

Specific interventions included in the review
Studies of ICD therapy in comparison with medical therapy were eligible for inclusion. The types of ICD evaluated in the included studies were transvenous and epicardial. The comparators included medication, with some trials having additional trial arms using either placebo or cardiac resynchronisation therapy (with and without a defibrillator).

Participants included in the review
Studies of patients with NICM, resuscitated cardiac arrest, documented or symptomatic tachyarrhythmia, or depressed left ventricular function at risk of developing lethal cardiac arrhythmia, were eligible for inclusion. The number of participants with NICM in the included studies ranged from 9.6 to 100%. The mean age of the participants ranged from 52 to 67 years, and 68 to 84.5% were male.

Outcomes assessed in the review
Studies reporting all-cause mortality, cardiac death, or arrhythmic mortality were eligible for inclusion. All of the included studies reported total mortality; one study also reported all-cause rehospitalisation.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The criteria used to assess quality were allocation concealment, completeness of follow-up, and objectivity of the outcome assessment. The authors did not state how the papers were assessed for quality, or how many reviewers performed the quality assessment.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data on the occurrence of all-cause mortality were extracted for the subgroup of patients with NICM from the individual studies, where available, and used to calculate risk ratios (RRs) and 95% confidence intervals (CIs).

Methods of synthesis
How were the studies combined?
Logarithmic RRs with 95% CIs were calculated separately for primary and secondary prevention and were combined using both fixed-effect and random-effects meta-analyses, weighted by the inverse variance. Where heterogeneity was not statistically significant, the results of the fixed-effect meta-analysis were used. Studies that did not report the results for NICM patients separately were excluded from the meta-analysis. Publication bias was investigated graphically using a funnel plot and mathematically using an adjusted rank correlation test.

How were differences between studies investigated?
Heterogeneity was assessed statistically using the chi-squared test. Sensitivity analyses were performed by omitting individual studies in sequence. Subgroup analyses were performed on trials with less than (and more than) 3 years’ follow up, to assess the impact of the length of follow-up on primary prevention trials.

Results of the review
Eight RCTs (total n=5,207; 2,146 with NICM) were included in the review. Five studies were primary prevention (total n=3,244; 1,854 with NICM) and three were secondary prevention (total n=1,963; 292 with NICM).

The authors stated that quality was comparable across the 8 studies. None of the studies described the method of allocation generation. Allocation concealment and blinding were not possible, but all trials used either an independent or blinded committee for the adjudication of events. Follow-up, when reported, ranged from 95 to 100%, and all studies used an intention-to-treat analysis. Wide variations in the crossover rates were reported.

Primary prevention (5 studies).
ICD therapy was associated with a statistically significant reduction in all-cause mortality compared with medication (RR 0.69, 95% CI 0.55, 0.87, P=0.002). There was no evidence of statistical heterogeneity (P=0.74).

Subgroup analyses.
A statistically significant reduction in all-cause mortality with ICD therapy, compared with medication, was still seen when a trial that recruited people with more advanced heart failure was excluded from the analysis (RR 0.74, 95% CI 0.58, 0.96, P=0.02), and when a study that recruited patients with heart failure of short duration and low control group mortality was also removed (RR 0.73, 95% CI 0.55, 0.96, P=0.03). When studies with 3 or more years' follow-up were removed from the analysis, there was still a statistically significant reduction in all-cause mortality with ICD therapy (RR 0.63, 95% CI 0.46, 0.88, P=0.006).

Secondary prevention (3 studies).
One study did not report results for NICM patients separately and was not included in the meta-analysis. Two studies found that ICD therapy was associated with a 31% reduction in all-cause mortality compared with medication, although this was not statistically significant (RR 0.69, 95% CI 0.39, 1.24, P=0.22). There was no evidence of statistical heterogeneity (P=0.66).

The authors reported that there was no evidence of publication bias (Begg adjusted rank correlation test, P=0.81).

Authors’ conclusions
ICD therapy appeared to significantly reduce mortality in selected patients with NICM.
CRD commentary
The research question and the inclusion criteria were clearly reported and appeared appropriate. Several sources were searched to identify relevant trials and an attempt was made to identify unpublished studies. Publication bias was assessed graphically and mathematically, and no evidence of bias was suggested. Details of the methodology used at each stage of the review (study selection, quality assessment and data extraction) were lacking, thus the possibility of reviewer error and bias cannot be ruled out. Appropriate measures of effect were calculated. Limitations in the reporting of methodological details mean that it is unclear whether the conclusions can be considered reliable.

Implications of the review for practice and research
Practice: The authors stated that the decision to use ICD therapy must be influenced by patient preference and quality of life.

Research: The authors did not state any implications for further research.

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Other publications of related interest
This additional published commentary may also be of interest. Hernandez AF. Review: implantable cardioverter defibrillators reduce all-cause mortality in nonischemic cardiomyopathy. ACP J Club 2005;142:57.

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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.