Effectiveness of prophylactic implantation of cardioverter-defibrillators without cardiac resynchronization therapy in patients with ischaemic or non-ischaemic heart disease: a systematic review and meta-analysis

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CRD summary
This review concluded that there was strong evidence for improved survival with implantable cardioverter defibrillators in people with left ventricular ejection fraction of 35% or more due to ischaemic or non-ischaemic heart disease where patients were 40 days from myocardial infarction and three months from coronary revascularisation. The data quality was unclear and the conclusions should be treated with caution.

Authors' objectives
To assess the efficacy of implantable cardioverter defibrillators (ICD) alone for primary prevention of sudden cardiac and arrhythmic death in people with heart failure due to coronary artery disease or dilated cardiomyopathy.

Searching
MEDLINE (January 1980 to January 2009), EMBASE (1991 to last quarter 2008) and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to the last quarter of 2008. Search terms were reported. Only studies published in English were sought. References of identified papers and proceedings from international cardiology meetings were checked.

Study selection
Randomised controlled trials (RCTs) that assessed ICD-only therapy (cardiac resynchronisation therapy was excluded) compared to conventional medical therapy in people with left ventricular dysfunction deemed at high risk of sudden cardiac death were eligible for inclusion. Studies on survivors of sudden cardiac death or unstable arrhythmias and people with inherited arrhythmic disorders were excluded. The outcomes of interest were all-cause mortality, cardiac mortality and arrhythmic mortality. Trials with crossover rates of more than 50% were excluded.

Between 67% and 92% of participants in the included studies were men. Mean age ranged from 52 to 64 years. Coronary artery disease was present in 73% of participants. Mean left ventricular ejection fraction (LVEF) ranged from 21% to 28%. Fifty-nine per cent of participants had New York Heart Association (NYHA) Class II heart failure symptoms and 26% had Class III. Some participants were additionally on amiodarone (2% to 13%), betablockers (4% to 87%), digoxin (42% to 86%) or angiotensin converting enzyme inhibitors/angiotensin receptor blockers (55% to 97%). Follow-up ranged from 20 to 66 months.

Two authors independently selected studies for inclusion.

Assessment of study quality
Two authors independently assessed study quality based on items such as randomisation, description of crossover, withdrawals and drop-outs, completeness of follow-up and objectivity of outcome assessment.

Data extraction
Two authors independently extracted all-cause mortality data to enable calculation of risk ratios (RR) and 95% confidence intervals (CI).

Methods of synthesis
Studies were grouped according to aetiology of cardiomyopathy. Where there was no heterogeneity, pooled risk ratios and 95% CI were calculated using a fixed-effect model; otherwise, a random-effects model was used. Heterogeneity was assessed using $I^2$. Where statistical heterogeneity was evident, sensitivity analyses were undertaken by removal of each study individually.
Funnel plots were used to assess publication bias.

**Results of the review**

Eight RCTs (6,188 participants) were included. Study size ranged from 103 to 2,521 participants. Four trials were on people with coronary artery disease, three were on people with non-ischaemic heart disease and one was on both.

Tests showed no evidence of publication bias.

Pooling of data on all-cause mortality in people with coronary artery disease revealed considerable heterogeneity ($I^2=74.9\%$, five trials). Heterogeneity was reduced ($I^2=61.5\%$) when two trials that recruited participants who were recovering from acute myocardial infarction and participants who underwent coronary artery bypass surgery were removed. Results then showed an association between ICD therapy and a reduction in mortality (RR 0.67, 95% CI 0.51 to 0.88; three trials). In people with dilated cardiomyopathy, ICDs were associated with a reduction in all-cause mortality (RR 0.74, 95% CI 0.59 to 0.93, $I^2=0\%$; four trials). Pooled data from all six trials showed a reduction in mortality with ICDs (RR 0.73, 95% CI 0.64 to 0.82, $I^2=0\%$).

Compared to controls, ICDs were associated with a reduction in arrhythmic mortality (RR 0.40, 95% CI 0.31 to 0.50, $I^2=0\%$; eight trials).

The mean proportion of people who received appropriate ICD therapy from implanted devices was 23% (range 17.8% to 31.4%). Inappropriate therapy was observed in 16.5% of participants (six trials).

**Authors’ conclusions**

There was strong evidence to support the beneficial effect on survival of ICD-only therapy on survival of people with LVEF of 35% or more due to ischaemic or non-ischaemic heart disease if they were 40 days from myocardial infarction and at least three months from a coronary revascularisation procedure.

**CRD commentary**

The aims of the review were clearly stated in terms of the inclusion criteria. The search covered several relevant sources and included unpublished studies, which reduced the risk of publication bias. Tests appeared to confirm this, but were likely to have been unreliable because of the number of available studies. Only studies in English were sought and language bias may have affected the review. The review methods were aimed at reducing reviewer error or bias. The authors stated that they assessed study quality, but did not present the results. The methods of synthesis and assessment of heterogeneity were generally appropriate. However, even after removal from the analysis of two trials that reported no effect on all-cause mortality in people with coronary artery disease, there was still moderate heterogeneity. It would have been interesting to see the full analyses before removal of these studies. There were some discrepancies between numbers of participants in tables and text. Baseline characteristics and concomitant therapies were described overall in each trial and gave no indication of similarities or differences between groups. The authors reported a high level of crossover in some studies, but it was unclear which studies these were. Two of the authors have received grants from medical device companies.

Questions about the quality of included data mean the authors’ conclusions should be treated with caution.

**Implications of the review for practice and research**

The authors did not state any implications for practice and research.

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