The impact of gender on survival amongst patients with implantable cardioverter defibrillators for primary prevention against sudden cardiac death

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CRD summary
The authors concluded that men receiving implantable cardioverter defibrillator therapy, but not women, appear to have a significantly reduced risk of death. The authors' conclusions appear to reflect the evidence presented, but poor reporting of the review methods and study quality make it difficult to assess their reliability.

Authors' objectives
To evaluate the effect of implantable cardioverter defibrillators (ICDs) on survival according to the gender of the patient.

Searching
MEDLINE, EMBASE, CINAHL and the Cochrane CENTRAL Register were searched from inception to October 2003 using the reported search terms. In addition, reference lists were checked and abstracts from three named journals were screened from 2000 to 2005.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies that compared ICDs for primary prevention with standard care were eligible for inclusion. The included studies compared ICD with or without standard medical therapy with standard medical therapy alone. One study evaluated ICD plus biventricular pacemaker or pacemaker defibrillator. Study participants received maximum tolerated doses (unless contraindicated) of appropriate pharmacological treatment in accordance with the standard guidelines for the treatment of patients with heart failure and/or a history of myocardial infarction.

Participants included in the review
Inclusions criteria were not specified for the participants. The included studies were in ischaemic and nonischaemic patients with depressed left ventricular ejection fraction (<30% to <36% where reported). The mean age of the study participants was 62 years (range: 58 to 68).

Outcomes assessed in the review
Studies that presented data on the risk of death for males and females separately were eligible for inclusion. The review assessed death from any cause.

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
Validity was assessed on the basis of randomisation, allocation concealment, masking of allocation, blinding and withdrawals. Three reviewers independently assessed validity and resolved any disagreements by consensus.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. For each study, hazard ratios (HRs) with 95% confidence intervals (CIs) were extracted or estimated from graphs after unsuccessful attempts to obtain numerical values from the original authors (estimates from graphs were used for all but one study). Unadjusted data were used in the analyses.
Methods of synthesis
How were the studies combined?
Weighted average HRs with 95% CIs were calculated, using a random-effects method (DerSimonian and Laird), for male and female patients separately. Publication bias was assessed using a funnel plot and tested using the regression method of Egger.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Q statistic (p<0.1 indicated significant heterogeneity). Analyses were repeated after excluding one study that evaluated ICD plus a biventricular pacemaker.

Results of the review
Five RCTs (n=6,405) were included.

In males, use of an ICD reduced the risk of death by 26% (HR 0.74, 95% CI: 0.60, 0.91; based on 4,830 men). In females, there was no statistically significant difference in the risk of death for women with an ICD compared with control (HR 0.82, 95% CI: 0.60, 1.09; based on 1,575 women). No statistically significant heterogeneity was detected for either analysis (p=0.102 and p=0.523, respectively).

The percentage reduction in the risk of death was similar for men after excluding the study that evaluated ICD plus a biventricular pacemaker (reduction of 24%, HR 0.76, 95% CI: 0.58, 0.99). In females, the risk of death was reduced by 12% after excluding this study (HR 0.88, 95% CI: 0.63, 1.22). Statistically significant heterogeneity was detected for the analysis involving men (p=0.069), but not for the analysis involving women (p=0.554).

There was no strong evidence of publication bias from either the funnel plot or Egger’s test (p>0.80).

Authors’ conclusions
Men, but not women, appear to have a significantly reduced risk of death with ICD therapy.

CRD commentary
The review addressed a clear question that was defined in terms of the participants, intervention, outcomes and study design. Several relevant sources were searched but no attempts were made to minimise publication or language bias. Methods were used to minimise reviewer errors and bias in the assessment of validity, but it was not clear whether similar steps were taken at the study selection and data extraction stages. Validity was assessed using specified criteria, but the results of this assessment were not reported. Adequate information about the included studies was presented. Statistical heterogeneity was assessed and the studies were generally appropriately pooled using meta-analysis. Potential reasons for the lack of a significant effect in women were discussed: for example, the smaller numbers of women available for analysis. The authors’ conclusions appear to reflect the evidence presented, but poor reporting of the review methods and study quality make it difficult to assess their reliability.

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

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