Meta-analysis of mortality in dialysis patients with an implantable cardioverter defibrillator

CRD summary
This review concluded that in patients with implantable cardioverter defibrillators, there was a 2.7 fold increased risk of death in those receiving dialysis compared with those not receiving dialysis. Beta-blockers appeared to be less protective in patients on dialysis than in patients not on dialysis. Data came from small observational studies, so these conclusions should be treated with caution.

Authors' objectives
To assess the effects of implantable cardioverter defibrillators in patients receiving dialysis.

Searching
MEDLINE, EMBASE and Web of Science were searched from January 1999 to July 2008. Search terms were reported. Google Scholar was also searched. Bibliographies of relevant papers and abstracts from meetings of five relevant societies were checked. Studies not available in English, or those unable to be translated, were excluded.

Study selection
Studies that reported the effects of implantable cardioverter defibrillators in patients receiving dialysis compared with those not receiving dialysis were eligible for inclusion. Eligible studies had to report the mortality outcomes in relation to renal function.

The primary outcome of interest was all-cause mortality in patients with implantable cardioverter defibrillators receiving dialysis compared with patients not on dialysis.

In the included studies, indications for implantable cardioverter defibrillator were both primary and secondary. The mean ages of participants ranged from 63 to 67 years, and between 69 and 84% were men. Where stated, 34 to 86% of patients were taking beta-blockers. Chronic kidney disease in patients not receiving dialysis was defined as glomerular filtration rate of less than 60ml/min/1.73m².

Four authors independently selected studies for inclusion. Disagreements were resolved by consensus.

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

Data extraction
The number and percentages of deaths were extracted and risk ratio (RR) and 95% confidence intervals (CI) were calculated. Where necessary investigators were contacted for additional information.

Four authors independently extracted data. Disagreements were resolved by consensus.

Methods of synthesis
Risk ratios and 95% confidence intervals were pooled, weighted by the inverse of the variance using a random-effects model. Heterogeneity was assessed using Q test and the I² statistic.

Subgroup analyses were performed based on beta-blocker usage (over 75% of patients on beta-blockers; less than 75% of patients on beta-blockers; studies not reporting the number of patients on beta-blockers) and studies on primary prevention versus primary plus secondary prevention. Sensitivity analyses were performed by removing one study at a time from the analysis. Meta-regression was used to investigate any effect of length of follow-up and study size.

Publication bias was assessed using a funnel plot, Duval and Tweedie's Trim-and-Fill method, and calculating the fail-
Results of the review
Seven studies were included in the review (2,516 participants, 89 on dialysis), including one case controlled study and six retrospective observational studies. Mean follow-up ranged from 12 to 48 months.

For patients with implantable cardioverter defibrillators, 49% of those receiving dialysis and 17.7% of those not receiving dialysis died (RR 2.67, 95% CI 1.68 to 4.25; seven studies; random-effects model). There was evidence of statistical heterogeneity ($I^2=76.4\%$).

In those studies where over 75% of patients were on beta-blockers, the risk of death was increased for those on dialysis compared with those not receiving dialysis (RR 3.54, 95% CI 1.75 to 7.16; two studies; random-effects model), and in those studies where less than 75% of patients were on beta-blockers (RR 1.55, 95% CI 1.06 to 2.27; two studies; random-effects model). Studies not reporting on the percentage on patients on beta-blockers showed similar findings to those with over 75% on beta-blockers (three studies).

When comparing patients receiving dialysis with those not receiving dialysis with chronic kidney disease (glomerular filtration rate of less than 60ml/min/1.73m$^2$), the risk of death was similar for both groups (five studies; random-effects model).

Subgroup analysis by primary and primary plus secondary prevention studies showed similar results to the main analysis. Meta-regression showed no apparent effect on results of mean follow-up time or study size. Sensitivity analyses excluding single studies showed no effect on the results.

Tests showed no evidence of publication bias; fail safe N showed that more than 25 unpublished studies would have to be added to alter the results.

Authors’ conclusions
In patients with implantable cardioverter defibrillators there was a 2.7 fold increased risk of mortality for those receiving dialysis compared with those not receiving dialysis. Beta-blockers may be less protective in people with implantable cardioverter defibrillators on dialysis than in patients not on dialysis.

CRD commentary
The inclusion criteria were clearly stated in terms of participants, intervention and outcomes. The search, covering a number of relevant sources, was likely to have reduced the risk of publication bias. Studies not written in English were excluded and this may have resulted in language bias. However, the authors’ tests suggested that it was unlikely that missing studies would have significantly effected overall results. The methods of study selection and data extraction were aimed at reducing reviewer error or bias.

The quality of included studies did not appear to have been assessed, so it was not possible to comment on the validity of included data. The methods of synthesis overall appeared appropriate, although there was considerable heterogeneity. The authors investigated possible sources of heterogeneity.

Evidence came from small observational studies and, as the authors commented, data from these studies may be unreliable. It is possible that other confounding factors may have had an effect on study outcomes. In view of this, the conclusions should be treated with caution.

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

Research: The authors stated that one trial is already underway, but that other prospective RCTs with broader inclusion criteria are needed to assess the effects of implantable cardioverter defibrillators in patients on dialysis. Further trials are needed to assess the value of beta-blockers in patients receiving dialysis.
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