Survival advantage of kidney transplantation over dialysis in patients with hepatitis C: a systematic review and meta-analysis

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CRD summary
The review concluded that hepatitis C virus-infected end-stage renal disease patients who remained on maintenance dialysis has a higher risk of death than those who received kidney transplantation. Most included studies were small retrospective studies of unknown quality and some relevant studies may have been missed, so the authors’ conclusions may not be reliable.

Authors’ objectives
To compare five-year mortality rates between waiting list maintenance dialysis and kidney transplantation in patients with end-stage renal disease and hepatitis C virus infection.

Searching
MEDLINE, EMBASE and Scopus were searched from inception up to June 2011 for studies in English; search terms were reported. Reference lists of eligible studies were also searched for other potentially relevant studies.

Study selection
Cohort studies of adults (aged 19 or older) with end-stage renal disease and hepatitis C virus infection that compared death rates between kidney transplantation and waiting list (treated with maintenance dialysis) were eligible for inclusion. The primary outcome of interest was death from any cause. Studies of patients with other multiple organ transplantations (such as liver-kidney) and patients who had co-infections with hepatitis B or HIV virus were excluded.

The included studies were published from 1997 to 2011 and conducted in the USA, Taiwan, Turkey, Serbia and Australia. All included patients had end-stage renal disease and hepatitis C virus infection. The average age of patients ranged from 33 to 55 years; most were men (where reported). Patients either underwent kidney transplantation or waiting list control; no further details were reported. The duration of dialysis ranged from 31.6 to 58.7 months among the waiting list group and 23 to 41 months among the kidney transplant group (where reported). Around half of the studies reported that diabetes was present in 2% to 43% of included patients.

It was unclear how many reviewers assessed the studies for inclusion.

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

Data extraction
Two reviewers independently extracted data on the total number of deaths per treatment group at the end of each study to calculate the relative risk of death; disagreements were resolved by discussion. Where numbers of deaths were not reported, death rates at five years were extracted from survival curves or the hazard ratio of death (along with 95% confidence intervals) was extracted.

Methods of synthesis
Relative risks were pooled using the DerSimonian and Laird random-effects model in the presence of heterogeneity, or a fixed-effect model in the absence of heterogeneity. The number needed to treat was also calculated. Statistical heterogeneity was assessed using the Cochran’s Q test and quantified using $I^2$; heterogeneity was considered as being present if $I^2$ was 25% or higher.

Meta-regression was used to explore sources of heterogeneity. Subgroup analyses were performed.

Publication bias was assessed using the Egger test and assessment of a funnel plot.
Results of the review
Nine cohort studies (one prospective; eight retrospective) were included in the review, with 1,734 participants (range 52 to 502). The length of follow-up ranged from four to 20 years.

The risk of death at five years was statistically significantly higher for patients who remained on a waiting list (treated with maintenance dialysis) than those who underwent kidney transplantation (RR 2.19, 95% CI 1.50 to 3.20). There was evidence of substantial heterogeneity between study results (I²=64.8%). Eight patients would need to be treated with kidney transplantation to prevent one extra death (NNT 8, 95% CI 5 to 11).

The proportion of patients in each treatment group dying from cardiovascular disease, infection and liver disease were presented.

The meta-regression analysis identified age as a potential source of heterogeneity. A subgroup analysis, in which patients aged 45 years or less were pooled, resulted in a non-statistically significant difference between treatment groups (RR 1.19, 95% CI 0.91 to 1.56), whilst patients aged over 45 years still had a statistically significantly higher risk of death in the waiting list group than the kidney transplantation group (RR 2.57, 95% CI 2.04 to 3.23). Pooling within age groups removed heterogeneity (I²=0% for both groups).

There was no evidence of publication bias suggested by the Egger test.

Authors' conclusions
Hepatitis C virus-infected end-stage renal disease patients who remain on maintenance dialysis had a higher risk of death at five years compared with those who received kidney transplantation.

CRD commentary
The review question and inclusion criteria were clear. A limited search of relevant sources was undertaken. Only studies in English were sought and no attempts were made to identify unpublished studies, so some relevant studies may have been missed. Data extraction was undertaken in duplicate, which reduced the risk of reviewer bias and error. However, it was unclear whether similar methods were employed in the selection of studies.

The authors did not appear to assess the quality of the included studies, so the reliability of the results of the included studies was unclear. Most studies were retrospective, which have certain limitations. The methods used to pool studies and explore heterogeneity appear to have been appropriate. The authors acknowledged that they did not have details on the severity of hepatitis C virus amongst patients, which may have affected treatment response and patient survival. There was significant heterogeneity between study results, although the direction of effect was consistent.

Whilst the authors' conclusions were supported by the evidence presented, most of the included studies were small retrospective studies of unknown quality (due to the lack of quality assessment) and some relevant studies may have been missed. Therefore, the authors' conclusions may not be reliable.

Implications of the review for practice and research
Practice: The authors stated that the results from their study supported the concept that kidney transplantation was not contraindicated in hepatitis C virus-infected end-stage renal disease patients.

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

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