Acute renal failure in the intensive care unit: a systematic review of the impact of dialytic modality on mortality and renal recovery

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Authors' objectives
To determine the effectiveness of intermittent haemodialysis (IHD) therapy, compared with continuous renal replacement therapy (CRRT), for patients with acute renal failure (ARF) in the intensive care unit (ICU).

Searching
MEDLINE was searched from 1969 to 2002. In addition, the Cochrane Library and DARE were searched (the search terms were provided). This was supplemented by searching the abstracts of the American Society of Nephrology (1990 to 2001), checking the contents pages of seven journals (2000 to 2002) and contacting field experts. The Science Citation Index was also used to identify articles, and the reference lists of included studies and reviews were checked. No language restrictions were imposed.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the main analysis. Non-randomised controlled trials were eligible only for the sensitivity analysis.

Specific interventions included in the review
Studies were included if they compared concurrent groups of patients receiving some form of IHD or CRRT. Studies were excluded if they involved multiple interventions in the study groups. Various techniques were used in the included studies.

Participants included in the review
Studies in adult patients with ARF who were treated in an ICU were eligible for inclusion. The characteristics of the participants in each of the included studies were not given.

Outcomes assessed in the review
The primary outcome of interest was mortality, either in-hospital or at ICU discharge. The secondary outcomes were renal death (death or dependence on dialysis at the end of the study) and dialysis dependence among survivors, at hospital or ICU discharge.

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
Study validity was assessed in terms of randomisation, concealment of allocation, and the use of an intention-to-treat analysis. The authors did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment.

Data extraction
Two independent reviewers extracted the data using a standardised form, and resolved any discrepancies by consensus with a third reviewer. If insufficient data were given in the paper, additional information was sought from the trial investigator.

Data on mortality, renal death and dialysis dependence were extracted from the individual studies and used to calculate a relative risk (RR), using intention-to-treat when possible. If both in-hospital and ICU discharge mortality rates were
given then in-hospital rates were used. The Baseline Acute Physiology and Chronic Health Evaluation II (APACHE II) scores and the IHD and CRRT techniques used (including membrane and dose) were also noted.

Methods of synthesis
How were the studies combined?
The results from the individual studies were combined using fixed- and random-effects (DerSimonian and Laird) meta-analyses. The RR results were presented along with 95% confidence intervals (CIs).

The possibility of publication bias was investigated using the fail-safe N technique for RCTs and funnel plots for non-randomised trials.

How were differences between studies investigated?
The homogeneity of the included studies was assessed statistically using the Cochran Q test and through visual examination of the distribution of mortality rates for IHD and CRRT. Sensitivity analyses were performed on the basis of study quality (randomised or non-randomised), the year the study was conducted and the CRRT technique used (haemodialysis, haemofiltration, or haemodiafiltration). Meta-regression was used as a formal test of interaction, and was also used to test for interaction between baseline severity according to the APACHE II score and mortality.

Results of the review
Six RCTs (n=624) were included in the main analysis. Twelve non-randomised studies (n=1,252) were included in additional sensitivity analyses.

Mortality.
There was no significant difference in survival between IHD and CRRT (RR 0.96, 95% CI: 0.85, 1.08, P=0.50) based on the 6 RCTS (fixed-effect). There was no evidence of statistically-significant heterogeneity across the studies (P=0.09). Similar results were obtained regardless of the inclusion of non-randomised studies, the CRRT technique used, the year of publication, or by controlling for baseline severity of illness. It was estimated that an additional trial with at least 1,250 patients would be required to detect a significant improvement (RR 1.2) in mortality with CRRT in comparison with IHD.

Renal recovery.
There was no statistically-significant difference in renal death between IHD and CRRT (RR 1.02, 95% CI: 0.89, 1.17, P=0.78) based on 371 patients in 4 RCTs (fixed-effect). There was no evidence of statistically-significant heterogeneity across the studies (Q=0.79, d.f.=3, P=0.85). Similarly, no statistically-significant difference in dialysis dependence was found (RR 1.19, 95% CI: 0.62, 2.27, P=0.60) and there was no evidence of statistical heterogeneity (Q=2.6, d.f.=3, P=0.78). It was estimated that, for renal death, the addition of a very large trial would be required to detect a significant difference between the therapies (number of patients provided). In contrast, one additional trial with 190 patients would be needed to show a statistically-significant difference in dialysis dependence in favour of CRRT if that trial showed around 50% reduction in dialysis dependence with CRRT.

Cost information
The authors stated that, according to other reports, CRRT is at least twice as expensive as IHD.

Authors' conclusions
There was no evidence that CRRT confers a benefit in either survival or renal recovery, in comparison with IHD, for ARF in unselected critically ill patients.

CRD commentary
This was a relatively well-conducted review with a clear question and inclusion criteria. A comprehensive search
strategy was adopted to identify both published and unpublished data without language restrictions. The fail-safe N for mortality and renal death suggest that it is unlikely that studies that might not have been identified would have had sufficient data to change the findings. The authors used procedures to minimise bias when extracting the data from the included studies; however, the presence of bias in the selection of studies for inclusion cannot be ruled out. Appropriate criteria were used to assess the validity of the RCTs, but the potential impact on the findings was not explored in depth. The authors provided sufficient details of the included studies. The studies were summarised using appropriate quantitative methods. The conclusion of the review was appropriate given the results presented.

Implications of the review for practice and research
Practice: The authors stated that although no significant difference was observed between IHD and CRRT, it is important to consider long-term outcomes (including those arising from chronic dialysis therapy) when considering whether patients should receive IHD or CRRT. Furthermore, the absence of specific inclusion criteria for the patients in the studies included in the review may mean that CRRT could be more efficacious in subsets of patients with ARF, for example those with hypotension, although this remains to be confirmed.

Research: The authors stated that further studies evaluating mortality would require a large number of participants and should account for contamination (crossover) of treatment and variations in the dialysis techniques, and stratify by disease severity. In addition, the trials should assess the outcomes at discharge or later. Future trials should also evaluate renal recovery.

Bibliographic details

PubMedID
12407631

DOI
10.1053/ajkd.2002.36318

Indexing Status
Subject indexing assigned by NLM

MeSH
APACHE; Acute Kidney Injury /mortality /therapy; Clinical Trials as Topic; Dialysis /methods; Humans; Intensive Care Units; Randomized Controlled Trials as Topic; Treatment Outcome

AccessionNumber
12002002646

Date bibliographic record published
29/02/2004

Date abstract record published
29/02/2004

Record Status
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.