Prevention and treatment of acute kidney injury in patients undergoing cardiac surgery: a systematic review

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CRD summary
The authors concluded that most studies were underpowered to demonstrate a beneficial effect on acute renal replacement therapy and mortality. More thorough research was needed. The authors’ cautious conclusions appeared to reflect the limited evidence base, but the reliability of these findings remains unclear due to substantial shortcomings in the review.

Authors' objectives
To assess strategies to prevent or treat acute kidney injury in cardiac surgery.

Searching
PubMed (from 1950), SCOPUS (from 1966) and Cochrane Renal Library databases and Google Scholar were searched for English-language studies to 2008; search terms were reported. Reference lists from relevant articles and reviews were searched.

Study selection
Randomised controlled trials (RCTs) in patients aged over 19 years of age with all degrees of renal function undergoing cardiac surgery (coronary artery bypass grafting and/or valve surgery; elective, emergent or not specified) compared with no therapy, placebo or standard care for the institution (such as maximal hydration) were eligible for inclusion. Studies were eligible if kidney injury was assessed by methods of serum creatinine or creatinine clearance/glomerular filtration rate (GFR). Eligible interventions included methods of prevention or treatment of acute kidney injury administered any time before, during or after surgery and included medical therapies as well as procedure-based therapies (such as cardiopulmonary bypass modification and early renal replacement therapy). Relevant outcomes included incidence of acute kidney injury or change in serum creatinine, creatinine clearance, glomerular filtration rate, incidence of acute renal replacement therapy and mortality. Renal outcomes were abstracted regardless of whether they were a primary or secondary trial outcome. Studies that described outcomes for patients who were on renal replacement therapy prior to surgery or who had received a kidney transplant were excluded.

In the included studies, acute kidney injury definitions varied. Criteria for the initiation of acute renal replacement therapy were not comparable across studies. Some studies included patients with chronic kidney disease. Studies analysed the effects of vasodilators, interventions that primarily induced natriuresis or diuresis or both, anti-inflammatory agents and interventions that worked through other mechanisms of action. Interventions were given preoperatively, intraoperatively and postoperatively. Where reported, frequency of assessing kidney function was variable between studies (range eight hours to measurements on days one, five and 15). Studies were in 21 countries. Sixty-four studies involved coronary artery bypass grafting and 27 involved valvular surgeries. Mean age ranged from 35.1 to 82.5 years. In most studies the proportion of males was over 50%.

Two reviewers independently selected studies for inclusion in the review.

Assessment of study quality
Trial quality was assessed using the Jadad scale of randomisation, allocation concealment, blinded outcome assessment, intention-to-treat and patients excluded and lost to follow-up (maximum score 5). Studies were classed as good, moderate, and low quality.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Two reviewers independently extracted outcomes for creatinine, creatinine clearance/GFR and incidence of acute renal replacement therapy and mortality. For studies that reported a continuous outcome the standard difference in means in
treatment and control groups were compared. For continuous outcomes the standard difference in means was converted to log odds ratios so that these outcomes could be combined with categorical outcomes.

Disagreements were resolved by consensus.

**Methods of synthesis**
The studies appeared to be pooled using methods that accounted for within-study and between-study heterogeneity, but details of the methods used were not reported clearly.

Heterogeneity was assessed using the Cochrane Q and I² statistics.

**Results of the review**
Seventy studies (5,554 patients, range 14 to 388) were included in the review: 66 studies assessed prevention strategies and four assessed treatment. Twenty studies scored the maximum 5 on the Jadad scale, eight studies scored 4, 24 scored 3 and 18 scored 1 or 2 (figures taken from the table presented, which differed slightly from the text). Forty-seven studies had 5% or fewer patients excluded or lost to follow-up, 34 studies had no patients excluded, 15 had more than 5% excluded or lost to follow-up and seven studies did not report numbers.

**Acute kidney injury incidence:** A reduction in acute kidney injury was associated with fenoldopam and angiotensin-converting enzyme inhibitors from the vasodilator group and atrial natriuretic peptide, B-natriuretic peptide and urodilatin from the natriuretic and/or diuretic cohort. Off-pump surgical techniques and pulsatile flow techniques also reduced the incidence of acute kidney injury. Detailed statistics for the pooled studies were not reported.

**Acute renal replacement therapy:** None of the individual trials showed a clear benefit in terms of reducing the incidence of acute renal replacement therapy in the cardiac surgery setting (21 studies).

**Mortality:** None of the interventions demonstrated a reduction in mortality (18 studies).

**Authors’ conclusions**
Most studies were underpowered to demonstrate a beneficial effect on acute renal replacement therapy and mortality. The beneficial effect on acute kidney injury alone was enough impetus for a more thorough investigation into prophylaxis and treatment strategies.

**CRD commentary**
The review question and supporting inclusion criteria were stated clearly. The literature search was limited to English-language articles, so language bias may have been introduced. Study quality was assessed using appropriate criteria. Most studies were of low quality. Procedures to minimise bias and error in study selection and data extraction were used; it was unclear whether this extended to the quality assessment process. Pooling of studies was undertaken and the authors investigated sources of heterogeneity, but the findings were not reported and this made it difficult to assess whether pooling was appropriate. The authors acknowledged some of the limitations of the evidence base (such as small sample sizes, underpowered studies and methodological and statistical heterogeneity) that suggested it may not have been appropriate to pool these studies.

The authors’ cautious conclusions appeared to reflect the poor quality of the evidence base, but given substantial shortcomings in the review it is uncertain whether these findings can be considered reliable.

**Implications of the review for practice and research**
**Practice:** The authors stated that few studies assessed treatment strategies, which made it difficult to draw conclusions about their efficacy.

**Research:** The authors stated that large good-quality multicentre trials were required to demonstrate benefits of prevention of acute kidney injury and reduction in rates of acute renal replacement therapy and mortality in cardiac surgery settings.

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