Off-pump coronary artery bypass surgery and acute kidney injury: a meta-analysis of randomized controlled trials
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CRD summary
This generally well-conducted review found that compared to on-pump coronary artery bypass graft (CABG) surgery, off-pump CABG surgery may be associated with a lower rate of acute kidney injury but may not affect dialysis requirement. Clinical variations across the trials precluded firm conclusions. The authors' cautious conclusions are likely to be reliable.

Authors' objectives
To compare the effect of off-pump coronary artery bypass grafting (CABG) to on-pump CABG on the development of acute kidney injuries including kidney problems that require treatment with dialysis.

Searching
MEDLINE was searched from 1966 to February 2010. Search terms were reported. There were no language restrictions. ClinicalTrials.gov and abstracts from annual meetings of the American Society of Nephrology (2000 to 2009), American College of Chest Physicians (2003 to 2009) and American Heart Association (2003 to 2009) were searched for completed trials. References from retrieved narrative and previous systematic reviews were checked for additional studies.

Study selection
Randomised controlled trials (RCTs) that compared off-pump CABG surgery to on-pump CABG in adults and in which postoperative primary or secondary kidney endpoints were evaluated were eligible for inclusion. Duplicate publications were excluded. The primary outcome was occurrence of acute kidney injury as defined in the included trials. The secondary outcome was all-cause mortality.

Patients' mean age ranged from 48 to 76 years. Where reported, the proportion of patients with diabetes ranged from zero to 56% and those with hypertension from 42% to 86%. Around half the participants were men. Various definitions of acute kidney injury were used and included requirement for dialysis, absolute or relative increases in serum creatine and decreases in globular filtration rate and/or urine output. Mean preoperative serum creatine ranged from 1.0 to 1.5mg/dL. Most trials enrolled patients who were to undergo elective CABG surgery; one trial enrolled patients who required urgent CABG surgery. One trial restricted enrolment to patients with pre-existing chronic kidney disease.

Two reviewers independently screened the studies for inclusion; a third reviewer screened the abstracts for the scientific meetings.

Assessment of study quality
Methodological quality was evaluated by one reviewer using the five-point Jadad scale of randomisation, concealment, blinding and follow-up.

Data extraction
Two reviewers independently extracted data to calculate odds ratios (OR) and 95% confidence intervals (CI) for the outcomes. The reviewers contacted trial authors for missing data. Any disagreements between the reviewers were resolved by consensus.

Methods of synthesis
Pooled odds ratios and 95% CIs were calculated using a Peto fixed-effect model. Statistical heterogeneity was evaluated using $I^2$ and $\chi^2$. A random-effects model was used in a sensitivity analyses. Potential sources of heterogeneity were investigated and included age, definition of acute kidney injury, prevalence of diabetes mellitus, sample size, acute kidney injury incidence, death rate in off-pump CABG surgery, surgical setting (elective or urgent), Jadad quality score and prevalence of hypertension. Publication bias was assessed by visual appraisal of funnel plots.
Results of the review
Twenty-two RCTs (4,819 participants) were included in the review. Sample sizes ranged from 20 to 2,203 patients. The reviewers reported that randomisation was adequately described in 12 out of 14 trials that described randomisation procedures. Concealment of allocation was adequate in only three trials. Intention-to-treat analyses were performed in 11 trials. Attrition rates were as high as 13% and there were crossover rates of 11% reported in the trials.

There was a statistically significantly lower odds of postoperative acute kidney injury observed with off-pump CABG compared to on-pump CABG surgery (OR 0.60, 95% CI 0.43 to 0.84, $I^2=0\%$; 22 trials). Non-significant benefits of off-pump CABG surgery were observed with lower odds of both requiring dialysis treatment (OR 0.67, 95% CI 0.40 to 1.12, $I^2=0\%$; 20 RCTs) and mortality (OR 0.79, 95% CI 0.50 to 1.25, $I^2=28\%$).

In the subgroup analyses, larger effects were found for acute kidney injury in the off-pump CABG surgery group among studies with a lower mean age (<65 years) (OR 0.50, 95% CI 0.32 to 0.76), elective CABG surgery (OR 0.39, 95%CI 0.24 to 0.64), lower Jadad quality scores (OR 0.43, 95% CI 0.19 to 0.97), higher prevalence (≥66%) of hypertension (OR 0.44, 95% CI 0.28 to 0.73) and where the definition of acute kidney injury included biochemical parameters, urine output and requirements for dialysis (OR 0.58, 95% CI 0.40 to 0.85).

Funnel plots suggested publication bias was present for all three outcomes.

Authors' conclusions
Use of off-pump CABG may be associated with a lower risk of postoperative acute kidney injury, but may not affect the requirements for dialysis. However, the definition of acute kidney injury varied substantially across the trials and the low quality of the included trials precluded definitive conclusions.

CRD commentary
The review addressed a clear question. Criteria for inclusion of studies were clearly stipulated. One electronic database was searched without language restrictions and the authors made attempts to identify unpublished studies. Steps were taken to minimise errors and bias for study selection and data extraction, although only one reviewer performed the assessment of methodological quality. Pooling of the study results appeared justified as there was little statistical heterogeneity across the results for the primary outcome. Appropriate subgroup analyses were undertaken on variables that were determined a priori. There were some discrepancies between the results reported in the text and those presented in forest plots, most notably for the subgroup analysis that evaluated acute kidney injury on the basis of definition of dialysis requirement. The authors correctly acknowledged limitations in the review due to variable definitions of the primary outcome, small sample sizes of many of the included studies with low to zero event rates and the risk of publication bias.

The review was generally well conducted and the authors' cautious conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors stated that a well-designed RCT of patients with high preoperative risk of renal dysfunction was required to validate the potential advantage of off-pump compared to on-pump CABG surgery in this population.

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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.