Off-pump surgery is associated with reduced occurrence of stroke and other morbidity as compared with traditional coronary artery bypass grafting: a meta-analysis of systematically reviewed trials

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CRD summary
The authors concluded that off-pump coronary artery bypass grafting is associated with a reduced risk of stroke, atrial fibrillation and surgical wound infection compared with on-pump surgery, but it may increase re-interventions and reduce the number of grafts. Overall, this was a well-conducted review and the authors’ conclusions are likely to be reliable.

Authors' objectives
To compare the effects of off-pump coronary artery bypass grafting (CABG) and on-pump CABG using cardiopulmonary bypass (CPB) on mortality and morbidities.

Searching
MEDLINE, EMBASE and the Cochrane CENTRAL Register were searched from 1980 to February 2006; some details of the search strategy were reported. No language restrictions were applied. In addition, reference lists of RCTs and reviews were screened.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies that compared off-pump CABG with on-pump CABG using CPB were eligible for inclusion. Studies had to use no additional experimental medications or devices. Where reported, most of the studies used normothermic CPB (34 to 36 degrees C) or mild hypothermic CPB (32 to 33 degrees C).

Participants included in the review
Studies of adults were eligible for inclusion. Where reported, patients in the included studies had a mean age of 62 years and 23% were female. Few studies included patients with a reduced ejection fraction.

Outcomes assessed in the review
No restrictions were applied to the outcomes. The review assessed mortality, stroke, atrial fibrillation, 30-day wound infection, renal failure, myocardial infarction, angina recurrence, re-intervention, and number of crossovers from on-pump to off-pump surgery and vice versa. Definitions of these outcomes were reported. The duration of follow-up in most of the included studies ranged from 30 days to 1 year.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies.

Assessment of study quality
Two reviewers independently extracted all data; such data might have included details of the validity assessment. Validity was assessed on the basis of reporting of randomisation, adequacy of randomisation, intention-to-treat analysis and allocation concealment. Studies were classified as ‘high’ quality if they had no flaws and ‘low’ quality if they had multiple flaws.

Data extraction
Two reviewers independently extracted the data. Only explicit reports of outcome events were extracted; descriptions such as no major complications occurred were not considered as zero events. For each study providing relevant data, the
numbers of events of interest were extracted for each treatment arm.

**Methods of synthesis**
How were the studies combined?
Pooled relative risks (RRs) with 95% confidence intervals (CIs) were calculated using fixed-effect methods in the absence of significant heterogeneity and random-effects methods when significant heterogeneity (I-squared >20%) was found. The number-needed-to-treat, with 95% CI, and the number of events averted or induced per 1,000 procedures were also calculated. The potential for publication bias was assessed using funnel plots.

How were differences between studies investigated?
Statistical heterogeneity was assessed using a chi-squared test and the I-squared statistic. Sensitivity analysis was performed by repeating the analysis after including one study with results that differed from the others and by re-classifying studies of intermediate quality as high and low quality. A subgroup analysis was conducted to examine the influence of CABG technique (normothermic or hypothermic bypass) and cardioplegia technique (cold crystalloid, cold blood or warm/tepid blood). Heterogeneity amongst studies evaluating the number of distal grafts was explored using subgroup analysis, with studies grouped by sample size.

**Results of the review**
Forty-one RCTs (n=3,996) were included.

The randomisation method was not described in 24 of the 41 RCTs and only 12 concealed the treatment allocation.

Compared with on-pump surgery, off-pump CABG was associated with a statistically significant reduction in the risk of stroke (RR 0.50, 95% CI: 0.07, 0.73), representing 10 fewer strokes per 1,000 CABG patients (27 RCTs, n=3,062), atrial fibrillation (RR 0.30, 95% CI: 0.16, 0.43) and wound infection (RR 0.48, 95% CI: 0.26, 0.63). It was also associated with a statistically non significant reduction in the risk of renal failure and myocardial infarction, and a statistically non significant increase in the risk of re-intervention. There was no statistically significant difference in mortality or angina recurrence.

There was increased crossover from off-pump to on-pump CABG (RR 3.82, 95% CI: 2.12, 6.88), representing 50 additional crossovers from off-pump to on-pump CABG (23 RCTs, n=2,804).

Off-pump CABG was associated with a statistically significant reduction in the number of distal grafts compared with on-pump surgery (weighted mean difference -0.27 per patient, 95% CI: 0.37, 0.17; 29 RCTs, n=2,457); significant heterogeneity was found (p<0.00001; I-squared 69.6%).

Funnel plots showed no evidence of publication bias.

**Authors’ conclusions**
Off-pump CABG is associated with a reduced risk of stroke, atrial fibrillation and surgical wound infection compared with on-pump surgery, but it may increase re-interventions and reduce the number of grafts.

**CRD commentary**
The review addressed a clear question and inclusion criteria were specified for the intervention and study design. Inclusion criteria were not defined for the outcomes and this resulted in the inclusion of a few studies that provided no data for any of the reported outcomes. Several relevant sources were searched and attempts were made to minimise language bias. The potential for publication bias was assessed and no evidence of it was found. Methods were used to minimise reviewer errors and bias in the study selection and data extraction processes, but it was unclear whether similar steps were taken in the assessment of validity. Validity was assessed using specified criteria and the results for individual studies were reported. Statistical heterogeneity was assessed and the studies were appropriately pooled using meta-analysis, although it was not always clear how many studies the pooled results were based on. Overall, this was a well-conducted review and the authors’ 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 the need for longer-term follow-up to evaluate the effects of off-pump CABG on the requirement for re-intervention.

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