Off-pump coronary artery bypass surgery may reduce the incidence of stroke in patients with significant left main stem disease


CRD summary
The review found that off-pump coronary artery bypass surgery may reduce neurological adverse events and early mortality in patients with significant left main stem disease, compared to on-pump coronary artery bypass surgery. However, further research was recommended. Although the review had a number of limitations and included only observational evidence, the authors' cautious conclusions appear justified.

Authors' objectives
To compare early outcomes of off-pump coronary artery bypass surgery versus on-pump coronary artery bypass surgery in patients with significant left main stem disease, focusing on major neurological events such as stroke.

Searching
EMBASE, MEDLINE, the Cochrane Library, Google Scholar and CINAHL were searched from 1965 to December 2006. Search terms were reported. The PubMed related articles function was used and the reference lists of retrieved articles were checked. Only peer-reviewed publications were included.

Study selection
Studies that compared off-pump coronary artery bypass with on-pump coronary artery bypass among patients with left main stem disease were eligible for inclusion. Eligible studies had to report early outcomes.

Outcomes of interest in the review included major neurological complications, such as stroke (primary outcome). Secondary outcomes included 30-day mortality, atrial fibrillation, length of stay in hospital, acute renal failure, blood loss, re-operation, transfusion, use of intra-aortic balloon pump, postoperative myocardial infarction, and postoperative inotropic requirement. Outcomes were defined in detail in the review. Secondary outcomes were included only if they were reported in at least three studies.

The studies in the review matched comparison groups for nine to thirteen predictor variables including age, sex, and past and current clinical characteristics. The mean ejection fraction of participants ranged from 40 to 52% across study groups and the proportion with an ejection fraction of 30% or less ranged from 13 to 82% (where reported). The studies defined left main stem stenosis as at least or more than 50% of the vessel stenosed. Overall, less than a quarter of participants received off-pump coronary artery bypass and the rest received on-pump coronary artery bypass. Off-pump coronary artery bypass was associated with significantly fewer grafts than on-pump coronary artery bypass.

Neurological outcomes reported in the review were stroke and transient ischaemic attack. The definition of stroke was consistent across studies, but stroke timing, severity and type were not reported.

The authors did not state how the papers were selected for the review.

Assessment of study quality
The Newcastle-Ottawa Scale for non-randomised studies was used to evaluate the following components of study quality: patient selection, comparability of groups for predictor variables, and measurement of outcomes. Studies were graded as lower quality (0 to 7 points out of a possible 9 points) or higher quality (8 to 9 points).

Two reviewers independently assessed study validity.

Data extraction
Odds ratios (ORs) were extracted or calculated for dichotomous outcomes and mean differences for continuous outcomes, with 95% confidence intervals (CIs).
Two reviewers independently extracted the data.

**Methods of synthesis**
Studies were combined to calculate pooled odds ratios and weighted mean differences (WMDs) with 95% confidence intervals. Both fixed-effect and random-effects models were used (fixed-effect results data were presented in the review). Heterogeneity was assessed using the $\chi^2$ test and publication bias was assessed with funnel plots.

Sensitivity analyses were conducted according to study quality.

**Results of the review**
Nine retrospective observational studies were included (n=4,411 patients). Quality scores were 9 (three studies), 8 (two studies), 7 (three studies) and 6 (one study) out of a possible 9 points. All studies reported satisfactory selection methods, clearly defined outcomes, and over 90% follow-up rate, but scores varied for group comparability.

**Primary outcomes:** The off-pump coronary artery bypass group had a significantly lower incidence of stroke than the on-pump coronary artery bypass group (OR 0.17, 95% CI 0.05 to 0.60). Transient ischaemic attack rates did not differ significantly between the groups. Neither of these analyses had significant statistical heterogeneity.

**Secondary outcomes:** The off-pump coronary artery bypass group had significantly lower rates of early mortality (OR 0.55, 95% CI 0.31 to 0.99), with no significant statistical heterogeneity. The off-pump coronary artery bypass group also had a shorter mean hospital stay (WMD -1.23 days, 95% CI -2.42 to -0.03), lower blood loss (WMD -185.36mL, 95% CI -303.72 to -67.01), and a lower risk of inotropic requirement (OR 0.31, 0.19 to 0.51). However, these three analyses had significant statistical heterogeneity ($\chi^2$ test, mean hospital stay $p<0.00001$; lower blood loss $p=0.03$; inotropic requirement $p=0.0001$). There was no statistically significant difference between the groups for rates of atrial fibrillation, re-operation, acute renal failure, myocardial infarction, or intra-aortic balloon pump use.

Findings did not differ significantly when analyses were restricted to higher quality studies, or with use of random-effects models.

Funnel plots were presented but were not interpreted.

**Authors' conclusions**
Off-pump coronary artery bypass surgery may reduce neurological adverse events and early mortality in patients with significant left main stem disease, compared with on-pump coronary artery bypass surgery, but further research is required.

**CRD commentary**
The objectives and inclusion criteria of the review were clear and relevant sources were searched for studies. It was unclear whether the search was restricted by language. The apparent restriction to published studies meant that the review may have been subject to publication bias. This was assessed with funnel plots, but these were not specifically interpreted in the text. Steps were taken to minimise the risk of reviewer bias and error by having more than one reviewer independently assess study quality and extract data, but the process used for study selection was not described.

Study quality was assessed using appropriate criteria; quality was limited in some cases by methodological flaws such as questionable comparability of groups. There appeared to be clinical heterogeneity between study populations, but the distribution of predictor variables in each study group was reported as raw numbers rather than proportions, which made the data difficult to interpret. Appropriate statistical techniques were used to combine the studies and check for heterogeneity, but where significant heterogeneity was detected, it was not acknowledged or explored further in the text. The reviewers acknowledged numerous limitations in the review, including poor study design and lack of long-term data.

Although the review had a number of limitations and included only observational evidence, the authors’ cautious conclusions appear justified.
Implications of the review for practice and research

Practice: The authors stated that off-pump coronary artery bypass surgery may be of neurological benefit and reduce early mortality in patients with significant left main stem disease.

Research: The authors stated that a multi-centre randomised controlled trial is needed to compare outcomes after off-pump and on-pump coronary artery bypass among patients with left main stem disease, to determine which patient groups may particularly benefit from off-pump coronary artery bypass, and to report on longer-term outcomes.

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