Estimating the risk of complications related to re-exploration for bleeding after adult cardiac surgery: a systematic review and meta-analysis

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CRD summary
The review found that re-exploration for major bleeding after cardiac surgery significantly increased the risk of postoperative mortality and morbidity. The review had some methodological limitations and it was difficult to determine the clinical value of these findings.

Authors' objectives
To assess the prognostic impact of re-exploration for major bleeding after adult cardiac surgery and determine whether it is an independent risk factor for adverse events.

Searching
PubMed, Scopus, Science Direct and The Cochrane Library were searched to January 2011. Search terms were reported. Reference lists of retrieved articles were checked. The search was restricted to full-length articles published in English since 1980.

Study selection
Observational studies of adults who underwent re-exploration for major postoperative bleeding after cardiac surgery were eligible for inclusion. The primary review outcome was immediate postoperative mortality (during hospital stay or within 30 days following surgery). Secondary outcomes were sternal wound infection, stroke, acute renal failure, need for aortic balloon pump and prolonged mechanical ventilation. Outcomes were defined in the review.

Most participants in most of the included studies underwent isolated coronary artery bypass grafting. Participants in the intervention groups were older, more likely to be male and were more likely to have peripheral vascular disease, to have had preoperative aspirin and to have undergone urgent or emergency surgery (where reported). Studies reported few details of the timing of aspirin use and use of other pre-, intra- or postoperative antithrombotic drugs. Criteria for re-exploration varied but in all cases involved severe postoperative bleeding and/or cardiac tamponade. In 20% of cases diffuse bleeding was found on re-exploration and no surgical cause was identified. Outcomes in participants who underwent re-exploration of bleeding were compared with outcomes in those who did not undergo the intervention. Two studies reported only propensity score matched pairs analysis. Studies were set in USA or European countries.

A single reviewer selected the studies.

Assessment of study quality
Study quality was assessed using the Newcastle-Ottawa scale for cohort studies to allocate points based on the quality of participant selection (zero to 4 points), baseline comparability (zero to 2 points) and ascertainment of outcomes (zero to 3 points).

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

Data extraction
Risk ratios (RR) and risk differences (RD) were calculated for dichotomous outcomes, with 95% confidence intervals (CIs). To obtain risk-adjusted data for the primary outcome, adjusted odds ratios and standard errors were extracted from multivariate analysis or propensity score-matched pairs.

Four reviewers independently extracted data. Disagreements were resolved by consensus.

Methods of synthesis
Unadjusted data were combined using a Mantel-Haenszel model to calculate pooled risk differences and risk ratios, with 95% confidence intervals. Adjusted odds ratios and their standard errors were pooled using generic inverse
variance analysis to calculate pooled risk ratios and 95% confidence intervals for the primary outcome. Heterogeneity was assessed using the $I^2$ statistic. Where important heterogeneity was detected ($I^2>40\%$) a random-effects model was used; otherwise a fixed-effect model was used. Subgroup analyses were performed according to the type of surgery (isolated coronary artery bypass versus other), age of study (published during previous decade versus older) and timing of re-exploration (within 12 hours of surgery versus later). Sensitivity analysis was conducted among studies that reported adjusted data, including only those that used multivariate analysis.

**Results of the review**

Eight observational studies were included: five prospective and three retrospective. The review included 557,923 participants. In six studies the sample size ranged from 3,220 to 528,686. The other two studies only included the findings of matched pairs (168 and 464 participants). The two matched-pairs studies scored 9 out of 9 for quality. The other studies failed to meet criteria for comparability of groups at baseline and all scored 7 for quality.

Re-exploration for bleeding was associated with a significantly increased risk of immediate postoperative mortality (RD 0.06, 95% CI 0.04 to 0.09, $I^2=82\%$ and RR 3.27 95% CI 2.44 to 4.37; eight studies), stroke (RR 2.18, 95% CI 1.96 to 2.43; four studies), need for intra-aortic balloon pump (RR 3.34, 95% CI 1.95 to 5.72; five studies), acute renal failure (RR 3.70, 95% CI 2.91 to 4.69; five studies), sternal wound infection (RR 4.52, 95% CI 3.95 to 5.18; four studies) and prolonged mechanical ventilation (RR 3.39, 95% CI 2.28 to 5.05; four studies).

When risk-adjusted data were pooled, re-exploration for bleeding was associated with a significantly increased risk of immediate postoperative mortality (RR 2.56, 95% CI 1.46 to 4.50; four studies; $I^2=55\%$). The authors stated that this was clear evidence that the intervention had an independent negative effect on postoperative mortality.

The increased risk in the intervention group persisted in all subgroup and sensitivity analyses. The risk was particularly high when re-intervention was performed more than 12 hours after surgery (RR 5.22, 95% CI 2.43 to 11.21; $I^2=0\%$)

**Authors' conclusions**

Re-exploration for major bleeding after cardiac surgery significantly increased the risk of postoperative mortality and morbidity.

**CRD commentary**

The review objectives centred around patients with major bleeding so no evidence was sought to inform decisions about whether to perform re-explorations for lesser bleeds. Relevant sources were searched for studies. Search restrictions by publication status and language meant that some studies may have been missed. Study selection was conducted by a single reviewer, which increased risks of reviewer bias and error, and it was unclear whether this also applied to the process of quality assessment.

It was unclear to what extent the adjusted analyses corrected for all likely confounders. In six out of eight studies the groups did not appear comparable at baseline although other quality criteria were rated as satisfactory. This made it unclear whether the adverse outcomes resulted from re-exploration or from excessive bleeding. Relevant methods were used to combine data and assess and explore heterogeneity but effect estimates and $I^2$ values were not reported for all analyses.

The review had some methodological limitations and it was difficult to determine the clinical value of these findings.

**Implications of the review for practice and research**

**Practice:** The authors stated that re-exploration for excessive bleeding after adult cardiac surgery was a serious and preventable complication and effort to avoid such bleeding may lead to significantly improved clinical outcomes and cost savings.

**Research:** The authors stated that future studies should examine the risks of re-exploration for bleeding associated with different types of cardiac surgery, the prognostic impact of different types of bleeding (surgical versus diffuse non-surgical) at re-exploration, the impact of the timing of re-exploration and its effect on pre- and postoperative cardiac function and the impact of re-exploration on stroke risk. They suggested use of propensity score analysis and of regression adjustment, especially for the evaluation of observational studies.
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