Heparin-bonded circuits versus nonheparin-bonded circuits: an evaluation of their effect on clinical outcomes
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CRD summary
The authors concluded that heparin-bonded cardiopulmonary bypass circuits were associated with positive effects on some outcomes in patients undergoing open heart surgery and only slight differences in other outcomes. This was generally a well-conducted review, but a more cautious conclusion may have been appropriate in view of the differing results between studies.

Authors' objectives
To compare heparin-bonded cardiopulmonary bypass circuits (HBCs) with nonheparin-bonded circuits (NHBCs).

Searching
MEDLINE, EMBASE, the Cochrane Library and the Web of Science were searched from inception to December 2004; the search terms were reported. No language restrictions were applied. In addition, links to related studies were followed and reference lists, abstracts of scientific meetings and related journals were screened.

Study selection
Study designs of evaluations included in the review
Blinded and non-blinded randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies that compared HBCs with NHBCs were eligible for inclusion. Studies were excluded if modifications were applied to the circuit in only one treatment arm, or if auto-transfusion methods were used to treat post-operative bleeding.

Participants included in the review
Studies of patients undergoing open heart surgery were eligible for inclusion. Studies of patients undergoing surgery for congenital heart disease or transplantation were excluded. Most of the included studies were in non-emergency and low-risk patients; almost all of the studies were in patients undergoing coronary artery bypass grafting (CABG).

Outcomes assessed in the review
Studies that assessed at least one of the specified outcomes were eligible for inclusion. The primary review outcomes were the number of patients requiring a post-operative blood transfusion, the amount of blood product transfused and loss of blood (24 hours post-operatively and just prior to drain removal). The secondary outcomes were all-cause 30-day mortality, post-operative incidence of myocardial infarction, stroke, re-sternotomy, wound infection and atrial fibrillation, and duration of ventilation, length of stay (LOS) in the intensive care unit (ICU) and total LOS in the hospital.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies and resolved any disagreements by consensus.

Assessment of study quality
Two reviewers independently assessed validity using the Jadad scale, which considers randomisation, blinding and withdrawals. Studies scoring 3 of more out of the maximum 5 points were considered to be high quality. Any disagreements were resolved by consensus. The review also assessed the comparability of treatment groups.

Data extraction
Two reviewers independently extracted the data and resolved any disagreements by consensus. Authors of multiple studies or studies with unclear data were contacted for clarification.
Methods of synthesis

How were the studies combined?
Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using the Mantel-Haenszel method for dichotomous data, while pooled weighted mean differences (WMDs) and 95% CIs were calculated for continuous data. Studies with zero events in both treatment groups were excluded from the meta-analyses. Fixed-effect and random-effect models were used. A funnel plot was used to assess publication bias.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Q statistic and I-squared statistic. Sensitivity analysis was conducted for the following subgroups defined a priori: isolated CABG, elective surgery, circuit type, high-quality studies and double-blind studies. Post hoc analysis was used to explore potential sources of significant statistical heterogeneity.

Results of the review

Forty-one RCTs (n=3,434) were included.

In 13 studies, treatment groups were comparable for 4 or more of 8 prognostic criteria for blood loss. Thirteen studies were double-blinded. Seven studies used low-dose heparin in the HBC group. The median Jadad score was 2.7 (range: 2 to 5). Sixteen studies were classified as high quality.

There was no statistically significant difference in the amount of post-operative blood loss at 24 hours for patients allocated to HBCs compared with NHBCs; the WMD was -83.7 mL (95% CI: -217.6, 50.2), based on 7 studies (n=537). The amount of blood loss until drain removal was significantly less for patients allocated to HBCs than for those allocated to NHBCs; the WMD was -164.2 mL (95% CI: -262.1, -66.3; p=0.001), based on 13 studies (n=562).

There was no statistically significant difference between treatments in the amount of post-operative blood product transfused (packed red blood cells, fresh frozen plasma and platelets analysed separately; results were reported). The proportion of patients who received a blood product transfusion was significantly less for patients allocated to HBCs compared with NHBCs; the OR was 0.8 (95% CI: 0.6, 0.9, p=0.004), based on 22 studies (n=2,415).

There was no statistically significant difference between groups in specific adverse events, apart from re-sternotomy which was significantly reduced in patients allocated to HBCs (OR 0.6, 95% CI: 0.4, 0.8, p=0.002).

HBCs were associated with a significant reduction in the duration of ventilation, ICU LOS and hospital LOS (data were reported).

Statistically significant heterogeneity was detected for blood loss, blood product transfusion and ICU LOS. There was no significant difference in blood loss up to drain removal in the double-blind studies.

Funnel plots showed no clear evidence of publication bias.

Authors’ conclusions

HBCs were associated with positive effects on some outcomes in patients undergoing open heart surgery and only slight differences in other outcomes.

CRD commentary

The review addressed a clear question that was defined in terms of the participants, intervention, outcomes and study design. Several relevant sources were searched and attempts were made to minimise publication and language bias. A formal assessment of publication bias suggested that this was not present. Validity was assessed using specified criteria and the results of this assessment reported. Details of the individual studies were not always reported clearly. Methods were used to minimise reviewer error and bias in the study selection, validity assessment and data extraction processes.

The data were combined in a meta-analysis and statistical heterogeneity was assessed. Where significant heterogeneity was found, potential causes were explored statistically or discussed. For some outcomes, specific factors associated with heterogeneity could not be identified; the authors acknowledged and discussed this problem. This was generally a well-
conducted review, but a more cautious conclusion may have been appropriate in view of the differences in results between studies.

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

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that an evaluation of the cost-effectiveness of HBCs in routine cases is required. They also highlighted the lack of studies in high-risk patients.

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