Do miniaturized extracorporeal circuits confer significant clinical benefit without compromising safety? A meta-analysis of randomized controlled trials
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CRD summary
The review concluded that miniaturised extracorporeal circulation was not associated with increased cerebrovascular injury and may confer and advantage, reducing post-operative arrhythmia, blood loss, and transfusion. However, there were a number of confounding factors which require further research. The review was generally well conducted; the authors' conclusions reflect the uncertainty in the evidence base and seem reliable.

Authors' objectives
To determine the safety and efficacy of miniaturised extracorporeal circulation (miniaturised treatment) compared with conventional extracorporeal circulation (conventional treatment) in patients undergoing cardiac surgery.

Searching
PubMed, EMBASE and The Cochrane Library were searched up to July 2010 for articles published in any language. Search terms were reported. Reference lists of retrieved articles and reviews were searched. Google Scholar and cardiac journals, including published conference proceedings, were also searched.

Study selection
Randomised controlled trials (RCTs) of miniaturised treatment compared with conventional treatment in patients undergoing cardiac surgery were eligible for inclusion. Trials with two or more arms that compared other interventions (such as off-pump coronary artery bypass grafting) were included. The primary outcomes were 30-day mortality, neurocognitive disturbance, cerebrovascular event, renal failure, post-operative myocardial infarction, and all-cause sustained arrhythmia. A number of secondary outcomes were also specified including length of hospital stay, blood loss, and transfusion. Trials were excluded if they had duplicate data or data were inconsistent.

The included trials studied miniaturised treatment versus conventional treatment in patients primarily undergoing coronary artery bypass grafting; some trials also looked at aortic surgery, or isolated aortic surgery plus combined aortic valve and graft surgery. The type of miniaturised treatment varied across the trials; over half of the included trials used Jostra miniaturised treatment. Sixteen trials included only elective cases, one trial included cases irrespective of urgency, one trial included elective and urgent cases, and the rest of the trials did not specify. All included trials matched groups on the basis of patient age; some trials also matched on other criteria.

Three reviewers independently performed study selection; disagreements were resolved by discussion with a senior reviewer.

Assessment of study quality
Two reviewers independently assessed trial quality using the Cochrane Risk of Bias tool, which appraised allocation concealment, blinding, randomisation, incomplete outcome data, selective reporting, and other biases.

Data extraction
Data were extracted on primary and secondary outcomes; these were used to calculate odds ratios (ORs) and mean differences, with 95% confidence intervals (CIs). Trial authors were contacted for missing data.

Two reviewers performed data extraction; disagreements were resolved by consensus.

Methods of synthesis
Fixed-effect or random-effect meta-analysis was used to calculate pooled odds ratios and weighted mean differences (WMDs), with 95% confidence intervals. Statistical heterogeneity was assessed using $X^2$ and $I^2$.

Sensitivity analyses were conducted for all trials, for trials including only coronary artery bypass grafting, for trials
including only aortic valve repair, higher quality trials, larger trial sample size, and eight or more matching demographic criteria.

Publication bias was assessed using funnel plots.

**Results of the review**

Twenty-nine trials (2,355 patients; 1,181 conventional treatment patients and 1,174 miniaturised treatment patients) were included in the review. There was a moderate risk of bias within the included trials, mainly due to not specifying trial outcomes in the methodology or the method of randomisation or allocation concealment.

**Primary outcomes:**

There was no statistically significant difference in 30-day mortality or neurocognitive events with conventional treatment compared with miniaturised treatment.

For end organ dysfunction, there was a statistically significant reduced risk of arrhythmia (OR 0.69, 95% CI 0.49 to 0.97; I²=22%; nine trials) with miniaturised treatment compared with conventional treatment, but there was no significant difference in postoperative myocardial infarction or renal failure.

**Secondary outcomes:**

There was no statistically significant difference between the two treatments for the length of hospital stay, the length of intensive care unit stay, ventilation time, the number of cases for revision for bleeding, chest tube drainage over 24 hours, or number of units transfused per patient.

Compared with conventional treatment, miniaturised treatment was associated with a statistically significantly reduced mean blood loss (WMD -131.32mL, 95% CI -187.87 to -74.76; I²=89%; 12 trials) and number of patients transfused (OR 0.35, 95% CI 0.23 to 0.53; I²=0%; 10 trials).

Sensitivity analyses based on trial size and quality significantly altered a number of the analyses, generally in favour of miniaturised treatment.

Other results were presented in the review.

**Authors’ conclusions**

Miniaturised extracorporeal circulation was not associated with increased cerebrovascular injury and may confer an advantage, reducing post-operative arrhythmia, blood loss, and transfusion. However, there are a number of confounding factors which require further research.

**CRD commentary**

Inclusion criteria for the review were clearly defined. Several relevant data sources were searched, with no language restrictions. Attempts were made to reduce reviewer error and bias throughout the review process.

Quality assessment indicated that there was a moderate risk of bias in the included trials. The authors also noted that many of the trials had small sample sizes. Trials were combined using standard statistical methods; statistical heterogeneity was assessed. Some of the outcomes had moderate to high levels of statistical heterogeneity, and sensitivity analyses indicated that the results were sensitive to a number of factors including trial size and quality.

The review was generally well conducted; the authors’ conclusions reflect the uncertainty in the evidence base and seem reliable.

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

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

**Research:** The authors stated that further large, RCTs were needed to produce more homogenous data, that focused not only on coronary artery bypass grafting, but also on isolating vascular surgery.
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