Does systemic leukocyte filtration affect perioperative hemorrhage in cardiac surgery: a systematic review and meta-analysis


CRD summary
This review of the use of systemic leukofiltration in cardiopulmonary bypass found that it had no clinically significant effect on perioperative blood loss during cardiac surgery, but that studies in this area are of poor quality and further research may be warranted. The conduct and reporting of this review was good and these conclusions are likely to be reliable.

Authors' objectives
To determine the effect of systemic leukofiltration on haemorrhage and blood transfusion requirements in patients undergoing cardiopulmonary bypass assisted cardiac surgery.

Searching
MEDLINE, EMBASE, Google Scholar, Web of Science and The Cochrane Library were searched from inception to January 2007. Search terms were reported. Reference lists were searched manually. There were no language restrictions.

Study selection
Comparative studies of humans undergoing open-heart surgery that used systemic leukofiltration (filter within the arterial or venous line of the cardiopulmonary bypass circuit) were eligible for the review. Studies that assessed additional leukodepleting strategies were included if systemic leukofiltration occurred in one arm. Studies where filtration occurred alongside cardioplegic and/or cell-saver line filtration were excluded. Duplicate publications, unblinded studies, studies with no events in either treatment group and those not providing sufficient data for data extraction were excluded.

Studies had to report at least one clinical outcome relating to haemorrhage to be included. The included studies were single or double-blind randomised controlled trials (RCTs) or blinded case-control studies. Surgical procedures were mostly coronary artery bypass grafting or coronary artery bypass grafting with valve replacement. The proportion of men ranged from 64% to 90%. Mean age ranged from 58.9 to 71 years, where stated. Two reviewers independently assessed studies for inclusion. Discrepancies were resolved by consensus.

Assessment of study quality
Study validity was assessed using the JADAD scale for RCTs (maximum score of 5) and assessment was performed by two reviewers independently with disagreements resolved by consensus.

Data extraction
Data were extracted by two reviewers independently. Disagreements were confirmed by consensus. Study authors were contacted if necessary to confirm queries. Means and standard deviations were extracted for each treatment group for 24-hour chest tube drainage (postoperative blood loss) and total amount of packed red cell blood transfused; these were used to calculate the mean difference and 95% confidence interval (CI) for each study.

Methods of synthesis
Studies were pooled in a random-effects meta-analysis. Statistical heterogeneity was explored with X² tests and the I² statistic; I² over 50% indicated significant heterogeneity. Sensitivity analyses were also used to further explore any possible heterogeneity by repeating analyses using a fixed-effect model, removing outlying studies from the analyses and undertaking three a priori subgroup analyses. The three a priori subgroups were: studies using seven or more matching criteria between groups; studies of only arterial filtration; and higher-quality studies (defined as JADAD score of 2 or more). Publication bias was assessed using funnel plots.
Results of the review
Thirteen studies were included in the review (n=710; range from 20 to 159): 10 studies were single-blind RCTs; two were double-blind RCTs; and one was a prospective blinded case-control study. Most RCTs were of low quality: nine scored 1 on the JADAD scale; two scored 2; and one scored 3. Studies matched on between four and nine criteria to produce well-balanced groups at baseline.

There was no evidence that systemic leukofiltration had an effect on chest tube drainage in the first 24 hours (weighted mean difference was -23.9mL, 95% CI: -95.5 to 47.6mL, p=0.51; 11 studies) or on the total packed red cell blood transfusion requirements (weighted mean difference was 7.84mL, 95% CI: -80.1 to 95.8mL, p=0.85; six studies). There was significant heterogeneity ($I^2=90.8\%$) for the chest tube drainage analysis. When the outlying study was removed a statistically significant reduction in chest tube drainage was observed (weighted mean difference was -15.8mL, 95% CI: -30.5 to -1.0mL, p=0.04; 10 studies).

Subgroup analyses showed a statistically significant reduction in chest tube drainage for the systemic leukofiltration group for the six studies that matched on seven or more criteria (weighted mean difference was -18.1mL, 95% CI: -28.3 to -8.0mL, p<0.001) but no evidence of a difference for total packed red cell transfusion. No significant differences were seen for either outcome in those studies with arterial filtration only, or higher-quality studies scoring 2 or more on JADAD. Most of the subgroup analyses reduced the heterogeneity observed in the full analyses.

Authors’ conclusions
Systemic leukofiltration did not have a clinically significant effect on peri-operative blood loss in cardiac surgery. The research in this area was heterogeneous, due partly to poor study designs and inadequate matching of study groups. Further good-quality trials may be needed and other strategies to reduce coagulopathy associated with cardiopulmonary bypass should be sought and evaluated.

CRD commentary
This review had a well-defined research question and study inclusion and exclusion criteria. The search strategy appeared appropriate. Grey literature was sought. There was no risk of language bias and the authors investigated publication bias. All aspects of the review were performed by two reviewers independently, which should have minimised any error or bias. Study quality was assessed using a recognised tool for RCTs, although the JADAD scale has limitations as it only covers a small number of relevant criteria. The methods of meta-analysis were appropriate and a thoughtful exploration of the impact of outlying studies with reasons for possible heterogeneity was performed. The authors stated that they also performed meta-analyses using fixed-effect models, but the results were not reported in the paper (it would have been useful to report whether fixed-effect models lead to any changes in the results). The authors highlighted the limitations of the studies and considered the clinical as well as the statistical significance of the results. The conduct and reporting of this review was good. Its conclusions appeared 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 that further good quality trials on systemic leukofiltration may be needed as well as research into other possible strategies for reducing coagulopathy associated with cardiopulmonary bypass.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.