Is there any difference between blood and crystalloid cardioplegia for myocardial protection during cardiac surgery? A meta-analysis of 5576 patients from 36 randomized trials

Sa MP, Rueda FG, Ferraz PE, Chalegre ST, Vasconcelos FP, Lima RC

CRD summary
The authors concluded that there was evidence to suggest no superiority between blood and crystalloid cardioplegia in terms of risk of death, myocardial infarction or low cardiac output syndrome in patients undergoing cardiac surgery. This conclusion seems reliable based on the evidence presented.

Authors’ objectives
To compare the efficacy of blood versus crystalloid cardioplegia for myocardial protection in patients undergoing cardiac surgery.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), ClinicalTrials.gov, Scientific Electronic Library Online, LILACS and Google Scholar were searched (with dates spanning from 1966 to 2011). Search terms were reported. The reference lists of relevant articles were scanned.

Study selection
Eligible for inclusion were randomised controlled trials that compared blood and crystalloid cardioplegia in patients undergoing cardiac surgery. The outcomes of interest were in-hospital death (primary outcome), perioperative myocardial infarction or perioperative low cardiac output syndrome.

Most included trials used intermittent cardioplegia at cold temperature, and comprised patients undergoing coronary artery bypass surgery. Four trials were conducted in infants who underwent surgery to correct congenital heart defects. Surgery was elective in most cases.

One reviewer screened and selected the abstracts of potentially relevant studies. Two independent reviewers assessed the eligibility of full text articles. Disagreements were resolved with the involvement of a third reviewer.

Assessment of study quality
Trial quality was assessed on type of randomisation, whether multicentre enrolment had taken place, participant/personnel characteristics and blinding, outcome assessment and the treatment of incomplete outcome data.

Two independent reviewers carried out quality assessment. Disagreements were resolved with the involvement of a third reviewer.

Data extraction
Data were extracted to enable the presentation of risk ratios and 95% confidence intervals.

Two independent reviewers extracted the data. A third reviewer checked data and resolved any disagreements.

Methods of synthesis
Weighted random-effects (DerSimonian and Laird) and fixed-effect (Mantel-Haenszel) meta-analyses were carried out. Statistical heterogeneity was assessed with X² and I². Publication bias was assessed using a funnel plot, followed by Begg and Mazumdar's test and Egger's test. Subgroup/meta-regression analyses were carried to evaluate the influence on outcomes of route of delivery (antegrade versus retrograde), temperature (cold versus warm) and timing of delivery (continuous versus intermittent).

Results of the review
Thirty-six trials (5,576 patients; sample size range 20 to 1,440) were included. Overall, the authors stated that there was moderate risk of bias across trials. All except one trial were single centre, and the processes of randomisation and
blinding were not reported in most cases.

There were no statistically significant differences (using fixed-effect meta analyses) between blood and crystalloid cardioplegia for risk of mortality (RR 0.95, 95% CI 0.6 to 1.51; 24 trials; I²=0%), perioperative myocardial infarction (RR 0.80, 95% CI 0.55 to 1.12; 25 trials; I²=0%) or perioperative low cardiac output syndrome (RR 0.77, 95% CI 0.58 to 1.14; nine trials; I²=18.6%). Random-effects meta-analyses showed similar results.

There was no evidence of publication bias, and subgroup/meta-regression analyses did not alter the main findings.

**Authors' conclusions**
There was evidence to suggest no superiority between blood and crystalloid cardioplegia in terms of risk of death, myocardial infarction or low cardiac output syndrome in patients undergoing cardiac surgery.

**CRD commentary**
The review question and inclusion criteria were clearly reported. Several relevant data sources were searched and publication bias was assessed. The review process was carried out with attempts to minimise reviewer error and bias. Detailed results of the quality assessment were reported. Study details were clearly presented, but patient characteristics were sparse.

Statistical heterogeneity was assessed, and the chosen methods of synthesis seemed appropriate. The impact of clinical heterogeneity was acknowledged by the authors, and they proposed a cautious interpretation of the outcome for low cardiac output syndrome due to limited data. Given these limitations, some firm research recommendations would have been helpful.

Overall, the authors' conclusion seems reliable based on the evidence presented.

**Implications of the review for practice and research**
*Practice:* The authors did not state any implications for practice.

*Research:* The authors did not state any implications for research.

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