Epidural analgesia improves outcome in cardiac surgery: a meta-analysis of randomized controlled trials

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CRD summary
This well-conducted review concluded that an anaesthetic regimen including thoracic epidural analgesia did not reduce mortality or myocardial infarction after cardiac surgery; there was evidence of reductions in renal impairment, duration of postoperative ventilation and the composite endpoint of death/myocardial infarction. Overall, as most data came from small lower quality trials, the authors’ conclusions should be treated with some caution.

Authors’ objectives
To assess the impact of thoracic epidural analgesia on clinical outcomes in patients undergoing cardiac surgery.

Searching
PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and BioMed Central were searched to January 2008; search terms were not reported. Conference proceedings from four relevant cardiology associations were searched (2005 to 2008). Bibliographies of identified studies and reviews were checked. Experts were contacted. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) that compared an anaesthesia plan including thoracic epidural analgesia versus an anaesthesia plan without epidural anaesthesia in of adults undergoing cardiac surgery were eligible for inclusion. There were no restrictions on dosage or timing of analgesia administration. Trials had to report on myocardial infarction or death.

Primary outcomes were in-hospital myocardial infarction (as defined by trial) and mortality at longest available follow-up. Other outcomes were time on mechanical ventilation, acute renal failure, and a composite of myocardial infarction and death.

In the included trials, most participants underwent coronary artery bypass graft; some were off-pump. Other surgery included mitral valve replacement (one trial) and ‘cardiac surgery’ (one trial). Catheters were positioned either the day before surgery or immediately before surgery; puncture levels ranged variously from 7th cervical to 10th thoracic levels. Local anaesthetics (epidural) used in the operating room included ropivacaine, bupivacaine, lidocaine and mepivacaine; other epidural drugs included sufentanil, fentanyl, morphine, and clonidine in varying doses. Catheters were removed between day one and day five.

Studies were selected by at least two authors independently. Disagreements were resolved by consensus or with a third author.

Assessment of study quality
Quality was assessed using the Cochrane Collaboration methods for assessing risk of bias (selection, performance, attrition and adjudication biases). Assessments were classified as low, moderate or high risk of bias, or incomplete reporting for each aspect. Additionally allocation concealment was categorised as adequate, unclear, inadequate or not used.

Quality was assessed by at least two authors independently. Disagreements were resolved by consensus or with a third author.

Data extraction
Odds ratio (OR) and 95% confidence intervals (CI) were calculated for binary outcomes, and mean differences and
95% CI for continuous outcomes. For the combined outcome of death and myocardial infarction, where data were reported individually for both outcomes, a conservative approach was taken so that possible double counting was avoided.

Data were extracted by at least two authors independently. Disagreements were resolved by consensus or with a third author.

**Methods of synthesis**

Pooled odds ratios and 95% confidence intervals for binary outcomes, and weighted mean differences (WMD) and 95% confidence intervals for continuous outcomes, were calculated using a fixed-effect method for those outcomes where statistical heterogeneity was low ($I^2 \leq 50\%$), otherwise a random-effects method was used. Heterogeneity was assessed using the Cochran Q test and $I^2$ statistic.

Forest plots were ordered to investigate any effect of year of publication.

Publication bias was assessed using funnel plots

**Results of the review**

Thirty-three RCTs were included in the review (2,366 participants). Trial size ranged from 16 to 408 participants, with 26 trials having less than 100 participants. Most trials appeared to be classed as moderate risk of bias, with a general lack of reporting on methods of randomisation and allocation concealment. No trials were double-blind design. Most trials reported follow-up of 12 hours to the length of hospital stay, but some reported follow-up between 14 days to 13 years.

No serious adverse complications of epidural analgesia were reported.

Compared with control, thoracic epidural analgesia had no statistically significant effect on myocardial infarction or mortality, but there was a reduced risk for the combined outcome of death or myocardial infarction (OR 0.61, 95% CI 0.40 to 0.95; $I^2=0\%$).

Twelve trials reported on renal failure, with five reporting no events. In the remaining seven trials, epidural analgesia was associated with a reduced incidence of renal failure (OR 0.56, 95% CI 0.34 to 0.93; $I^2=0\%$).

Time of mechanical ventilation was reduced with epidural analgesia (WMD -2.48 hours, 95% CI -2.64 to -2.32; $I^2=99\%$; 1,236 participants).

Rearrangement of forests plots showed no association between results and year of publication.

There was no evidence of publication bias.

**Authors’ conclusions**

An anaesthetic regimen including thoracic epidural analgesia did not appear to reduce mortality or myocardial infarction after cardiac surgery, but there was evidence of reductions in renal impairment, duration of postoperative ventilation and the composite endpoint of death/myocardial infarction.

**CRD commentary**

The aims of the review were clearly stated for participants, intervention and study design. The search covered a number of relevant sources, which included searching for unpublished studies and those in any language; this was likely to have reduced the risk of language and publication bias. However, search terms were not reported, so it was not possible to clearly assess the validity of the search. Appropriate methods were used to reduce reviewer error or bias.

Trial quality was assessed appropriately. There were some discrepancies between numbers reported in the text and tables. The methods of synthesis generally appeared appropriate. Substantial heterogeneity was found for the one
outcome (time to mechanical ventilation), so it may not have been appropriate to pool this data. The largest contribution to the outcomes of mortality and myocardial infarction was from a trial where follow-up was up to 13 years; it was unclear how appropriate it was to include outcomes from such a long follow-up from a perioperative analgesic intervention.

The review was well conducted but, as data generally came from small lower quality trials, the authors’ conclusions should be treated with some caution.

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

**Practice:** The authors stated that thoracic epidural analgesia should only be used after careful consideration and discussion of alternatives with the patient because of the potential adverse effects of epidural haematoma and paraplegia and the need for further research.

**Research:** The authors suggested that a large multicentre RCT is needed to assess clinical relevant outcomes of thoracic epidural analgesia used for patients undergoing cardiac surgery.

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