Meta-analysis of thoracic epidural anesthesia versus general anesthesia for cardiac surgery
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CRD summary
The review found that thoracic epidural analgesia with general anaesthesia in patients who underwent cardiac surgery reduced supraventricular arrhythmia and respiratory complications. The effects on mortality, myocardial infarction and stroke were uncertain. These conclusions appear reliable in most respects but the findings about supraventricular arrhythmia should be interpreted with caution due to heterogeneity between the studies and possible bias.

Authors' objectives
To compare the benefits and harms of general anaesthesia with thoracic epidural anaesthesia versus general anaesthesia alone in cardiac surgery.

Searching
PubMed, Science Citation Index, EMBASE, CINHAL, Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science were searched to January 2010. Search terms were reported. The search was restricted to published studies. There were no language restrictions.

Study selection
Randomised Controlled Trials (RCTs) that compared general anaesthesia plus thoracic epidural anaesthesia versus general anaesthesia alone in adults (aged at least 18 years) who had cardiac surgery were eligible for inclusion. Outcomes of interest were mortality, acute myocardial infarction, supraventricular tachyarrhythmia and respiratory and neurological complications (such as stroke, epidural haematoma and abscess). Respiratory complications were defined as respiratory insufficiency that required reintubation or prolonged ventilation and ventilator-associated pneumonia. Primary study definitions of stroke and myocardial infarction were used.

Various epidural drugs were used and these included bupivacaine, morphine, ropivacaine, fentanyl and sufentanil given alone or in combination, usually as a bolus plus infusion. Most studies did not report whether prophylactic medications were used for postoperative arrhythmias. As most of the included studies were designed to evaluate intermediate outcomes rather than clinical events, few events occurred that were relevant to the review. Studies were conducted during a period that spanned 30 years.

Two reviewers independently selected the studies. Disagreements were resolved with the help of a third reviewer.

Assessment of study quality
Criteria used to assess study validity were methods of randomisation and allocation concealment, blinding of data collection, analysis and outcomes ascertainment and completeness of follow-up.

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Data extraction
Risk ratios (RRs) and 95% confidence intervals (CIs) were calculated by dividing the number of events in each treatment group by the number of participants randomised. Where no events occurred in the control group, data were adjusted to permit calculation of a risk ratio using a correction proportional to the size of the treatment arm.

Two reviewers extracted data. Disagreements resolved with the help of a third reviewer.

Methods of synthesis
Studies were combined to calculate pooled risk ratios and 95% CIs using a fixed effect (Mantel-Haenszel) model where data were homogeneous and a random-effects model otherwise. Heterogeneity was assessed using the I² statistic and
DerSimonian Laird estimator. Data were displayed in L’Abbe plots, Galbraith plots and forest plots. Funnel plots and Peters’ regression test were used to assess publication bias. Subgroup analyses and metaregression were used to investigate the impact of time to extubation, year of study publication and study quality. The effect of using different continuity corrections and weighting models was investigated.

Results of the review
Twenty-eight RCTs were included (n=2,731 participants, range 16 to 654). All were rated as having satisfactory allocation concealment. Twelve trials reported blinding. Reported losses to follow-up ranged from nil to 16 participants.

No statistically significant difference was found between intervention and control arms in rates of mortality (28 RCTs, $I^2=0\%$), myocardial infarction (15 RCTs, $I^2=0\%$) and stroke (13 RCTs, $I^2=0\%$). No studies reported events of epidural haematoma or abscess.

The intervention was associated with a significantly lower rate of supraventricular tachyarrhythmias (RR 0.68, 95% CI 0.50 to 0.93, $I^2=62\%$; 14 RCTs). Statistical heterogeneity in this analysis was attributed partially to selective use of clonidine in one RCT, which may have biased results in favour of the intervention. The intervention was associated with a significantly lower rate of respiratory complications (RR 0.53, 95% CI 0.40 to 0.69, $I^2=0\%$; 13 RCTs).

No evidence was found of significant publication bias. None of the variables investigated in meta-regression had a significant effect on outcomes.

Authors’ conclusions
Thoracic epidural anaesthesia with general anaesthesia in patients who underwent cardiac surgery reduced supraventricular arrhythmia and respiratory complications. The effects on mortality, myocardial infarction and stroke were uncertain.

CRD commentary
The objectives and inclusion criteria of the review were clear and relevant sources were searched for studies. The restriction to published studies meant that some studies might have been missed, although formal assessment of publication bias did not find evidence of this. Steps were taken to minimise risks of reviewer bias and error by having more than one reviewer independently select studies and undertake validity assessment; it was not explicitly reported whether or not this also applied to data extraction. It was unclear whether or not the numerator for calculating risk ratios was events or participants who had events.

Statistical techniques used to combine the studies and to assess and explore heterogeneity appeared valid. There was substantial heterogeneity in the analysis of supraventricular tachyarrhythmias: it was unclear to what extent this was explained by selection bias in one of the RCTs. The authors noted that the review was limited by the age of some of the studies and in most studies there was a high risk of observer bias associated with lack of clearly defined clinical outcomes. Meta-analyses were underpowered due to low event rates. Rare but serious complications (such as epidural haematoma) were not reported. The authors questioned whether the risk-benefit profile of thoracic epidural anaesthesia could be adequately explored in RCTs.

The authors’ conclusions appear reliable in most respects, but their findings with regard to supraventricular arrhythmia should be interpreted with caution due to heterogeneity between the studies and possible bias.

Implications of the review for practice and research
Practice: The authors stated that use of thoracic epidural anaesthesia remained controversial in view of a lack of a significant effects on mortality, stroke and myocardial infarction and because there may have been rare but potentially very serious harms. Thoracic epidural anaesthesia should be used with caution until its benefit-harm profile was clearer.

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

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