Epidural analgesia reduces postoperative myocardial infarction: a meta-analysis
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Authors' objectives
To determine the effect of post-operative epidural analgesia on post-operative myocardial infarction (PMI).

Searching
MEDLINE was searched from 1966 to December 1998 for studies published in any language. The MeSH terms used were 'pain, postoperative', 'anesthesia, epidural', 'postoperative complications', 'myocardial infarction', 'congestive heart failure' and 'death'. All anaesthesia journals published in English since 1987 were handsearched, and the Science Citation Index was searched under the reference 'Yeager et al., Anesthesiology 1987'.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible. None of the included RCTs were double-blind.

Specific interventions included in the review
Administrations of post-operative epidural anaesthesia for 24 hours or more after surgery were eligible. Studies that used epidural anaesthesia for less than 24 hours post-operatively were excluded. The included studies used high lumbar, lumbar and thoracic epidurals, and compared epidural with systemic analgesia. The dosing of the epidural, where reported, was with a local anaesthetic or narcotic; the drugs were administered as a continuous infusion and in bolus form.

Participants included in the review
Post-operative patients were eligible. The included patients had undergone peripheral vascular, aortic, mixed vascular, or abdominal surgery. Twenty-eight per cent (stated as across 6 studies in the text, but as 7 studies in the tables) of the included participants had a history of MI; 21% of those with a previous infarction had angina; 22% received beta-blockers before surgery; 6% (across 6 studies) had congestive cardiac failure; 27% (across 4 studies) had chronic obstructive pulmonary disease; and 19% (across 5 studies) had diabetes.

Outcomes assessed in the review
Studies that assessed PMI or deaths were eligible. Other effects of epidural anaesthesia (pain relief and coagulation), and post-operative ST changes measured by continuous Holter monitoring, were also assessed.

How were decisions on the relevance of primary studies made?
Two authors reviewed all citations, and any disagreements were resolved by consensus.

Assessment of study quality
The validity of the included studies was graded using the 3-item, 5-point scale of Jadad et al. (see Other Publications of Related Interest no.1), which assesses randomisation, blinding and withdrawals. The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
One reviewer extracted the following data: author; sample size; patient characteristics; details of the surgical and analgesic interventions; cardiac outcomes and other effects of epidural anaesthesia.

Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis, in which a pooled Peto odds ratio was calculated using a fixed-effect model (see Other Publications of Related Interest no.2). A pooled event rate difference with 95% confidence intervals (CIs) was also calculated.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the method of Breslow and Day (see other Publications of Related Interest no.3). Subgroup analysis of the level of epidural placement (thoracic or lumbar) was also performed. Two sensitivity analyses were conducted: one excluding a controversial study (see other Publications of Related Interest no.4), and the other using a random-effects model.

Results of the review
Eleven RCTs (1,173 patients) were included.

The quality scores ranged from 1 to 3 out of a possible 5 points. All but one RCT were graded 2 or 3.

Deaths (11 RCTs).

There was no statistically significant difference in the death rates between treatment groups (rate difference -1.3%, 95% CI: -3.8, 1.2, p=0.091). No significant heterogeneity was detected.

PMI (8 RCTs).

MI was significantly less common in the epidural group than in the systemic analgesia group (rate difference -3.8%, 95% CI: -7.4, -0.2, p=0.049). No significant heterogeneity was detected.

There was a statistically-significant reduction in PMI for post-operative thoracic epidural analgesia when compared with systemic analgesia (rate difference -5.3%, 95% CI: -9.9, -0.7, p=0.04).

There was no significant difference in the death rates between thoracic epidural and systemic analgesia (rate difference -2.0, 95% CI: -5.3, 1.2, p=0.11).

A non significant difference between the treatments was found when using a random-effects model. Exclusion of the controversial study led to wide CIs and a non significant difference between the treatments.

Analgesia (4 RCTs).

Three of the four RCTs showed a statistically significantly better analgesia for epidural compared with systemic analgesia. No figures were reported.

Post-operative ST changes (3 RCTs): there was a non statistically- significant reduction in post-operative ischaemia in the epidural compared with the systemic analgesia group (rate difference -7.5%, p=0.19).

Post-operative coagulation (2 RCTs): both RCTs showed a statistically-significant reduction in the variables favouring epidural analgesia.

Authors’ conclusions
Post-operative epidural analgesia continued for more than 24 hours after surgery reduces PMI. The findings suggested that thoracic epidural analgesia was superior to lumbar epidural in reducing PMI.

CRD commentary
The aims were clearly stated, and the inclusion criteria were defined in terms of the study design, intervention and outcomes. Several literature sources were searched with no language restrictions applied, and the methods used to select the studies were described. The included studies were restricted to RCTs, and validity was formally assessed and scored.
using a validated scale.

Relevant data were extracted and tabulated. However, the abstraction was undertaken by one reviewer, and it was not reported whether the primary analyses were undertaken on an intention to treat basis. Statistical heterogeneity was assessed, the studies were appropriately combined in a meta-analysis, and the results were presented graphically. Sensitivity analyses were undertaken to determine the influence of the type of model used (fixed versus random) and the influence of one controversial RCT on the results. Neither side-effects nor unsuccessful epidurals were considered. In addition, the lack of a significant difference in the death rates between treatment groups was not discussed.

Aside from these reservations, the evidence presented appears to support the authors' conclusions.

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

Practice: The authors state that in high-risk cardiac patients, epidural post-operative analgesia is warranted and should be used more widely.

Research: The authors state that further studies should add risk stratification, according to a predetermined risk index, to the randomisation process to avoid skewing of the patient populations.

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