Paravertebral block versus thoracic epidural for patients undergoing thoracotomy (Protocol)

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[Intervention Protocol]

Paravertebral block versus thoracic epidural for patients undergoing thoracotomy

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To compare the two regional techniques of thoracic epidural blockade (TEB) and paravertebral block (PVB) in adults undergoing elective thoracotomy with respect to:

1. analgesic efficacy;
2. the incidence of major complications (including mortality);
3. the incidence of minor complications;
4. length of hospital stay;
5. cost effectiveness.

BACKGROUND

Description of the condition

Operations on structures in the chest (usually the lungs) involve cutting between the ribs (thoracotomy). Post-thoracotomy pain results from pleural (lung lining) and muscular damage, costovertebral joint (ribcage) disruption and intercostal nerve (nerves that run along the ribs) damage during surgery (Ng 2007). It is one of the most severe types of postoperative pain. Poor pain relief can lead to immobility and ineffective breathing and clearing of secretions, resulting in susceptibility to lung collapse (atelectasis), chest infections (pneumonia) and blood clots (pulmonary embolism) (Richardson 1994). The risk of respiratory complications has been reported to be between 15% and 32.5% (D'Arsigny 1998; Wang 1999) and has been observed to account for more than half of the 30-day mortality after surgery to remove a lung (Powell 2009). In the same observational study, cardiac arrhythmias were reported in 20% of patients (Powell 2009). Pain relief after thoracic surgery is therefore important for patient comfort and for reduction of postoperative pulmonary and cardiac complications.

Pain can often persist after thoracotomy and the incidence of chronic pain is high, with studies revealing that 30% to 50% of patients still experience pain up to five years after surgery (De Cosmo 2009; Rogers 2000). The exact mechanism of chronic post-thoracotomy pain is unknown but intercostal nerve damage at thoracotomy is believed to be a major factor, as demonstrated by neurophysiological studies (Benedetti 1998). Electromyography and somatosensory evoked responses demonstrated that intercostal nerve damage led to decreased pain threshold of the operative scar. A 'wind up' phenomenon of repeated stimulation of peripheral nerve fibres can cause a wide range of nerve fibres to become hyperexcitable and is associated with chronic pain. Aggressive management of acute pain following thoracotomy may reduce the likelihood of developing chronic pain (Katz 1996). A multi-modal approach to analgesia is widely employed by thoracic anaesthetists using a combination of regional anaesthetic blockade and systemic analgesia, with both non-opioid and opioid medications and local anaesthesia blockade.

There is some evidence that blocking the nerves as they emerge from the spinal column (paravertebral block) maybe associated with a lower risk of major complications in thoracic surgery but the majority of thoracic anaesthetists still prefer to use a thoracic epidural as analgesia for their patients undergoing thoracotomy. Previous systematic reviews of analgesic techniques in thoracic surgery have only evaluated short-term complications (Davies 2006; Joshi 2008; Kotze 2009). In order to bring about a change in practice, anaesthetists need a review that evaluates the risk of all major complications associated with thoracic epidural and paravertebral block in thoracotomy.

Description of the intervention

Thoracic epidural blockade

Thoracic epidural blockade (TEB) using local anaesthetic and opioid agents has been widely regarded as the gold standard for analgesia and the reduction of associated complications following thoracotomy. Good analgesia from an epidural can result in early extubation, better ventilatory mechanics and gas exchange and reduced rates of lung collapse, pneumonia and pain (De Cosmo 2009). However, the technique requires highly trained medical staff not only for insertion and removal of the epidural catheter but also for the management of the continuous infusion of pain medication. The risks associated with insertion of the epidural include accidental dural puncture, inadvertent high block, local anaesthetic toxicity and total spinal anaesthesia (inadvertent spinal injection of an epidural dose of local anaesthetic leading to local anaesthetic depression of the cervical spinal cord and the brainstem). Nerve injury, epidural haematoma and abscess are rare but serious complications. The UK National Audit Project led by the Royal College of Anaesthetists reported a low rate of permanent harm from all central blocks of 4.2 per 100,000, with rates twice as high in epidurals compared other central neuraxial blocks (Cook 2009). A thoracic epidural blocks nerves bilaterally and sympathetic nerve block can result in hypotension due to both vasodilatation and cardiac depression. This requires cautious fluid administration in order to avoid fluid overload in susceptible patients (Marret 2005). Failure rates have been described as from 14% to 30% and can be influenced by the skills of the practitioner inserting the catheter and accidental dislodgement of the catheter (Davies 2006).

An epidural is not a suitable technique for all patients and is contraindicated in patients with local infection, previous spinal surgery, disorders of blood clotting and in those taking anti-coagulant and anti-platelet therapy. The epidural is inserted through the skin rather than placed under vision and requires a highly skilled practitioner to perform the technique. Trained staff are also needed to look after the patients postoperatively in order to avoid accidental dislodgement of catheters and to observe for side effects. These staff add to the cost of the technique to the healthcare system.

Paravertebral blockade

Paravertebral block (PVB) involves injecting local anaesthetic into the paravertebral space to block nerves after leaving the spinal cord. PVB can be given as a 'single shot' technique but is often given as a continuous infusion of local anaesthetic via a catheter placed directly through the skin (percutaneously) or under direct vision during thoracotomy. Thoracic paravertebral anaesthesia has a number of advantages over the thoracic epidural technique. PVB is a one-side (unilateral) technique and so respiratory and sympathetic function is preserved on the other (contralateral) side (Ng

2007) and this may be associated with less hypotension, fewer pulmonary complications and less urinary retention (Davies 2006). The failure rate in adults has been reported as 10.1% (Lonnqvist 1995; Richardson 1999) and significantly lower than TEB (OR 0.28, P = 0.007) (Davies 2006). The complications reported include inadvertent vascular puncture (3.8% to 6.8%); hypotension (4.0% to 4.6%); haematoma (2.4%); pain at site of skin puncture (1.3%); signs of epidural or intrathecal spread (1.0%); pleural puncture (0.8% to 1.1%); and pneumothorax (0.5%) (Lonnqvist 1995; Naja 2001). Recent evidence suggests that short-term side effects such as hypotension, urinary retention, nausea, and vomiting appear to be less frequent with PVB than with TEB (Daly 2009). The effect of paravertebral anaesthesia on blood pressure and heart rate is minimal, making this technique safe for patients with coexisting circulatory disease. PVB is thought to be associated with better pulmonary function and fewer pulmonary complications than TEB (Joshi 2008; Richardson 1999). Contraindications to thoracic epidural analgesia do not preclude PVB, which can also be safely performed in anaesthetized patients without an apparent increased risk of neurological injury.

How the intervention might work

The primary purpose of both these techniques is to achieve good postoperative analgesia. They employ the same pharmacological agents and both have been shown to produce important benefits in this clinical setting. This review is less concerned with the mode of action of PVB than with the ease of use, broad applicability, and relative safety of this technique. Technically, PVB is easier to perform than TEB, needle placement for paravertebral block is away from the midline and spinal cord (Richardson 1999), and some patients who are unsuitable for TEB may be suitable for PVB.

Why it is important to do this review

TEB using local anaesthetic and opioid has been widely regarded as the gold standard for analgesia and reduction of the associated complications after thoracotomy. A survey of Australian thoracic anaesthetists in 1997 revealed that 79% regarded TEB as the method of choice for analgesia in thoracotomy (Cook 1997). Similar results were found in the UK with 80% of anaesthetists considered TEB as the best mode of pain relief for upper abdominal surgery (Cook Eaton 1997). Recent evidence from two meta-analyses and systematic reviews comparing the analgesic efficacy and side effects of epidural versus paravertebral blockade for thoracotomy pain control concluded that although the analgesia was comparable, paravertebral blockade had a better short-term side effect profile, including urinary retention, hypotension, nausea and vomiting, and pulmonary complications (Davies 2006; Joshi 2008). The reviews suggest that paravertebral blockade may be superior to an epidural, but these reviews did not evaluate the more serious complications including mortality. A 2008 survey of all 38 thoracic units in the UK that was carried out by the Association of Cardiothoracic Anaesthetists (ACTA) reported that the majority of thoracic anaesthetists (2/3 units) prefer TEB to PVB, which suggests that most thoracic anaesthetists have yet to be convinced by the evidence available (Shelley 2008).

Compared to TEB, PVB may have several practical advantages. In patients on anti-coagulants or anti-platelet therapy, PVB can be placed with little concern about epidural haematoma, abscess, or neurological injury (Daly 2009; Luyet 2009). The catheter can be placed in the correct position under the direct guidance of the surgeon, ensuring accurate placement without damage to neurovascular structures or the pleura. Postoperative management of epidural infusion requires a specialized unit or ward whilst PVB can be managed on an ordinary ward (Daly 2009; Luyet 2009). PVB can be used in a higher proportion of patients and reduces their hospital stay, thereby reducing costs as well as improving the quality of patient care and satisfaction.

A large prospective multi-centre investigation into analgesic techniques and morbidity following elective pneumonectomy for cancer (Powell 2009) shows that TEB was associated with more major complications (including significant arrhythmias or pulmonary complications requiring treatment or ventilator support, unexpected intensive care unit (ICU) admissions, 30-day mortality, further surgery, inotrope usage) than PVB (odds ratio adjusted for patient and perioperative factors of 2.2, 95% confidence interval 1.1 to 3.8; P = 0.02) (Powell 2009). A comprehensive review of the existing evidence is needed to establish whether paravertebral block is associated with lower risk of major complications and to clarify whether further randomized trials are justified.

OBJECTIVES

To compare the two regional techniques of thoracic epidural blockade (TEB) and paravertebral block (PVB) in adults undergoing elective thoracotomy with respect to:

1. analgesic efficacy;
2. the incidence of major complications (including mortality);
3. the incidence of minor complications;
4. length of hospital stay;
5. cost effectiveness.

METHODS

Criteria for considering studies for this review

Types of studies

We will only include randomized controlled trials (RCTs). We will exclude quasi-randomized trials, for example where allocation was determined by days of the week or hospital number.

Types of participants

We will include all adults undergoing elective thoracotomy including for upper gastrointestinal surgery.

Types of interventions

We will include continuous thoracic epidural infusions using local anaesthetics, opioids, and any adjuvant therapies. The comparator will be continuous paravertebral blockade using local anaesthetics and adjuvant therapies.

Types of outcome measures

Primary outcomes

1. Mortality to 30 days (we will seek data from the authors and accept mortality measured at the closest time to 30 days that is available from each study).
2. Major complications including any of: cardiovascular complications (systemic hypotension requiring inotropic support, significant arrhythmias requiring anti-arrhythmic or cardioversion treatment, myocardial infarction, pulmonary oedema); pulmonary complications requiring treatment (postoperative ventilatory support, reintubation for respiratory failure, acute carbon dioxide retention (CO_2> 45 mm Hg), pneumonia, atelectasis); neurological complications (delirium); unexpected admission to intensive care; any complications that lead to further surgery.

Secondary outcomes

3. Analgesic efficacy including pain scores (visual analogue scores), acute pain, failure of technique, supplemental analgesia, morphine consumption.
4. Minor complications including hypotension (not requiring inotropes), postoperative ileus, excessive sedation, nausea and vomiting, pruritis, and urinary retention.
5. Chronic pain at six months and one year.
6. Duration of hospital stay and cost.

Search methods for identification of studies

Electronic searches

We will search for studies on thoracic epidural and paravertebral blocks in adult patients undergoing thoracotomy in the current issue of the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*); MEDLINE via Ovid (1966 to date); EMBASE via Ovid (1980 to date); and CINAHL via EBSCOhost (1982 to date); trial reference lists; and in conference abstracts. Our MEDLINE search strategy will be found in Appendix 1.

We will limit the results to randomized controlled clinical trials (RCTs) using the Cochrane highly sensitive search strategy (Higgins 2011). We will not impose a language restriction.

We will combine a free text search with a controlled vocabulary search, from the inception of a database to the present.

Searching other resources

We will search conference proceedings and abstracts of important meetings in cardiothoracic surgery and anaesthesia and all efforts will be made to contact authors and experts in order to identify unpublished research and trials still underway.

We will handsearch the *Journal of Cardiothoracic Surgery* and *Journal of Cardiothoracic and Vascular Anesthesia (*from 1996 to 2010).

We will also search the databases of on-going trials such as:
http://www.controlled-trials.com/; or
http://clinicaltrials.gov/.

Data collection and analysis

Selection of studies

Two review authors (JY and SG) will screen the abstracts of all publications obtained by the search strategies. We will note any reasons for study exclusion in RevMan 5.1. For trials that appear to be eligible RCTs, we will obtain the full articles to assess their relevance based on the predefined criteria for inclusion. We will resolve any disagreement through discussion or, if required, we will consult FG.

Data extraction and management

We will use a data collection form to extract data (see Appendix 2). For eligible studies, the two review authors (JY and SG) will extract data independently from original publications onto the agreed form. We will resolve any disagreement through discussion or, if required, we will consult FG. As far as possible, we will contact study authors for important information that is missing or unclear. We will enter data into RevMan 5.1 and check it for accuracy.

Assessment of risk of bias in included studies

Two review authors (JY and SG) will independently assess risk of bias for each study using the criteria outlined in the Cochrane risk of bias assessment tool (Higgins 2011). We will resolve any disagreement through discussion or, if required, we will consult FG. We will construct a risk of bias table for all included studies in the review.

(1) Random sequence generation

We will describe for each included study the method used to generate the random sequence in sufficient detail to allow assessment of whether it should produce comparable groups.
We will assess the method as:
§ low risk of bias (any truly random process e.g. random number table, computerized random number sequence)
§ high risk of bias (inadequate generation of randomization sequence e.g. consecutive)
§ unclear risk of bias

(2) Allocation concealment (checking for possible selection bias)

We will describe for each included study the method used to conceal the allocation sequence in sufficient detail and determine whether intervention allocation could have been foreseen in advance of or during recruitment, or changed after assignment.
We will assess the methods as:
§ low risk of bias (e.g. telephone or central randomization; consecutively numbered sealed opaque envelopes);
§ high risk of bias (e.g. open random allocation; unsealed or non-opaque envelopes; alternation; date of birth);
§ unclear.

(3) Blinding (checking for possible performance bias)

We will describe for each included study the methods used, if any, to blind the study participants personnel and outcome assessment from knowledge of which intervention a participant received. We will judge studies to be at low risk of bias if they were blinded, or if we judge that the lack of blinding could not have affected the results. We recognize that it may not be possible to blind clinicians or patients.
We will assess the methods as:
§ low risk of bias, high risk of bias, or unclear risk of bias for participants;
§ low risk of bias, high risk of bias, or unclear risk of bias for personnel;
§ low risk of bias, high risk of bias, or unclear risk of bias for outcome assessors.

(4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)

We will describe for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We will state whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total number of randomized participants), the reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information is reported, or can be supplied by trial authors, we will re-include missing data in the analyses which we undertake.
We will assess the methods as:
§ low risk of bias (where numbers and reasons for attrition, exclusion or re-inclusion have been reported);
§ high-risk of bias (where there are high number of dropouts and protocol deviations leading to loss of followup);
§ unclear.

(5) Selective reporting bias

Where the original protocol of a study is available (for example as a separate publication), we will assess whether all of the prespecified outcomes and analyses were presented.
We will assess the methods as:
§ low risk of bias (where it is clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported);
§ high-risk of bias (where not all the study's prespecified outcomes have been reported, one or more of the reported primary outcomes were not prespecified, outcomes of interest were reported incompletely and so cannot be used, the study fails to include results of a key outcome that would have been expected to have been reported);
§ unclear.

(6) Other bias

We will describe for each included study any important concerns we have about other possible sources of bias.
We will assess whether each study was free of other problems that could put it at risk of bias:
§ low risk of bias
§ high risk of bias;
§ unclear.

(7) Overall risk of bias

We will make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the Handbook for Systematic Reviews of Interventions (Higgins 2011). With reference to (1) to (6) above, we will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact

on the findings. We will explore the impact of the level of bias through undertaking sensitivity analyses, *see* Sensitivity analysis.

Measures of treatment effect

Dichotomous data

For dichotomous data, we will present results as summary risk ratio with 95% confidence interval.

Continuous data

For continuous data, we will use the mean difference if outcomes are measured in the same way between trials. We will use the standardized mean difference to combine trials that measure the same outcome but use different methods.

Unit of analysis issues

Cluster-randomized trials

We will include cluster-randomized trials in the analyses along with individually randomized trials. Their sample sizes or standard errors will be adjusted using the methods described in the Handbook, Section 16.3.4 or 16.3.6 (Higgins 2011) using an estimate of the intracluster correlation coefficient (ICC) derived from the trial if possible, or from a similar trial or from a study of a similar population. If ICCs from other sources are used, this will be reported and sensitivity analyses conducted to investigate the effect of variation in the ICC. If we identify both cluster-randomized trials and individually-randomized trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomization unit is considered to be unlikely.

We will also acknowledge heterogeneity in the randomization unit and perform a subgroup analyses to investigate the effects of the different types of randomization.

Dealing with missing data

For included studies, levels of attrition will be noted. The impact of including studies with high levels of missing data in the overall assessment of treatment effect will be explored by using sensitivity analysis.

For all outcomes, analyses will be carried out, as far as possible, on an intention-to-treat basis. That is, we will attempt to include all participants randomized in the analyses and all participants will be analysed in the group to which they were allocated, regardless of whether or not they received the allocated intervention.

Assessment of heterogeneity

If substantial heterogeneity is detected we will consider whether a pooled result would be meaningful and, if it is, we will use a random-effects model analysis to produce it. We will present the results of random-effects analyses as the estimated average treatment effect with its 95% confidence interval, and the 95% prediction interval for the underlying treatment effect. We will assess statistical heterogeneity in each meta-analysis using the I^2 and τ^2 statistics. Heterogeneity will be regarded as substantial if the I^2 statistic exceeds 30% and either τ^2 is greater than zero, there is a low P value (< 0.10) in the Chi^2 test for heterogeneity, or there is clearly substantial inconsistency between trials in the direction or magnitude of effects as judged by visual inspection.

Assessment of reporting biases

If there are 10 or more studies in a meta-analysis we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually and by formal tests. For continuous outcomes we will use the test proposed by Egger 1997, and for dichotomous outcomes the tests proposed by Harbord 2006 or Peters 2006 will be used. If asymmetry is detected by any of these tests or is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We will carry out statistical analysis using the Review Manager software (RevMan 5.1). We will use a fixed-effect model meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect. That is, where trials are examining the same intervention and the trials' populations and methods are judged to be sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, a random-effects model analysis will be used to produce an overall summary, if this is considered clinically meaningful. If an average treatment effect across trials is not clinically meaningful we will not combine heterogeneous trials. If random-effects analyses are used, the results will present the average treatment effect and its 95% confidence interval, the 95% prediction interval for the underlying treatment effect, and the estimates of τ^2 and I^2 statistic.

Subgroup analysis and investigation of heterogeneity

If substantial heterogeneity is identified, we will investigate it using subgroup and sensitivity analyses.

We will consider whether an overall summary is meaningful and, if it is, use a random-effects model analysis to produce it. We plan to carry out the following subgroup analyses.

1. Different types of epidurals (e.g. local anaesthetics with or without added opioid).
2. Different types of surgery (e.g. thoracic surgery, upper gastrointestinal surgery).
3. Timing of insertion (before skin incision, after operation).
4. Method of insertion (blind, under ultrasound guidance, under direct vision).

5. Other additives used in local anaesthetic mixture (beside local anaesthetics and opiates).
Only the primary outcome (major complications) will be used in subgroup analysis.
For fixed-effect inverse variance meta-analysis we will assess the differences between subgroups by interaction tests implemented in Revman. For other types of analysis we will conduct interaction tests using mixed effects meta-regression in external statistical software.

Sensitivity analysis

We will carry out sensitivity analysis to explore the effects of fixed-effect or random-effects analyses for outcomes with statistical heterogeneity and the effects of any assumptions made such as the value of the ICC used for cluster randomized trials. We will also use sensitivity analyses to explore the effects of inclusion of studies at high risk of bias (by assessing the effects of deletion of high risk studies), and the effects of missing outcome data (by assessing best case and worst case scenarios, and whether plausible values of missing data are likely to make a substantial difference to the results).

Summary of findings tables

We will use the principles of the GRADE system (Guyatt 2008) to assess the quality of the body of evidence associated with specific outcomes. We will include the following as outcomes: cardiovascular complications, pulmonary complications, critical care admission, further surgery, 30-day mortality, analgesia efficacy, minor complications in our review and construct a Summary of Findings (SoF) table using the GRADE software. The GRADE approach appraises the quality of a body of evidence based on the extent to which one can be confident that an estimate of effect or association reflects the item being assessed. The quality of a body of evidence considers within study risk of bias (methodologic quality), the directness of the evidence, heterogeneity of the data, precision of effect estimates, and risk of publication bias.

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. MEDLINE (via Ovid) search strategy

1. exp Analgesia, Epidural/ or exp Anesthesia, Epidural/ or epidural.mp. or exp Nerve Block/ or (block adj5 (paravertebral or extrapleural or subpleural or retropleural or intercostal)).mp. or "Length of Stay"/ or "Postoperative Nausea and Vomiting"/ or Arrhythmias, Cardiac/ or Postoperative Complications/ or Cost-Benefit Analysis/ or Pain, Postoperative/
2. Thoracotomy.af. or exp Thoracotomy/
3. 1 and 2
4. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti.) not (animals not (humans and animals)).sh.
5. 3 and 4

Appendix 2. Data extraction form

Cochrane Anaesthesia Review Group
Study Selection, Quality Assessment and Data Extraction Form

First author	Journal/Conference Proceedings etc	Year

Study eligibility

RCT	Relevant participants	Relevant interventions	Relevant outcomes
Yes / No / Unclear	Yes / No / Unclear	Yes / No / Unclear	Yes / No* / Unclear

Do not proceed if any of the above answers are 'No'. If study to be included in 'Excluded studies' section of the review, record below the information to be inserted into 'Table of excluded studies'.

Freehand space for comments on study design and treatment:

References to trial

Check other references identified in searches. If there are further references to this trial link the papers now & list below. All references to a trial should be linked under one *Study ID* in RevMan.

Code each paper	Author(s)	Journal/Conference Proceedings etc	Year
A			
B			

Participants and trial characteristics

Participant characteristics	
	Further details
Age (mean, median, range, etc)	
Sex of participants (numbers / %, etc)	
Disease status / type, etc (if applicable)	
Other	

Methodological quality

Allocation of intervention	
State here method used to generate allocation and reasons for grading	Grade (circle)
	Low risk of bias

(*Continued*)

	High risk of bias
	Unclear

Concealment of allocation **Process used to prevent foreknowledge of group assignment in a RCT, which should be seen as distinct from blinding**	
State here method used to conceal allocation and reasons for grading	Grade (circle)
	Low risk of bias
	High risk of bias
	Unclear

Blinding	
Person responsible for participants care	Low risk of bias/High risk of bias/Unclear
Participant	Low risk of bias/High risk of bias/Unclear
Outcome assessor	Low risk of bias/High risk of bias/Unclear
Other (please specify)	Low risk of bias/High risk of bias/Unclear
Intention-to-treat An intention-to-treat analysis is one in which all the participants in a trial are analysed according to the intervention to which they were allocated, whether they received it or not.	
All participants entering trial	
15% or fewer excluded	
More than 15% excluded	
Not analysed as 'intention-to-treat'	

(*Continued*)

Unclear	

Were withdrawals described? Yes ? No ? not clear ?

Discuss if appropriate

Data extraction

Outcomes relevant to your review • Denotes primary outcomes	
	Reported in paper (circle)
Significant arrhythmias*	Yes / No
Pulmonary complications including ventilatory support*	Yes / No
Unexpected critical care admissions*	Yes / No
Further surgery*	Yes / No
Inotropic support*	Yes / No
30 day mortality*	Yes / No
Analgesic efficacy (VAS, morphine, additional analgesia)	Yes / No
Nausea & vomiting	Yes / No
Failure of technique	Yes / No
Urinary retention	Yes / No
Duration of hospital stay	Yes / No
Cost effectiveness	Yes / No

For Continuous data

Code of paper	Outcomes	Unit of measurement	Intervention group		Control group		Details if outcome only described in text
			n	Mean (SD)	n	Mean (SD)	
	Significant arrhythmias*						
	Pulmonary complications/ Ventilator support*						
	Unexpected ICU admission*						
	Further surgery*						
	Inotropic support*						
	30 day mortality*						
	Analgesic efficacy						
	N&V						
	Failure of technique						
	Urinary retention						
	Duration of hospital stay						
	Cost effectiveness						

For Dichotomous data			
Code of paper	Outcomes (rename)	Intervention group (n) n = number of participants, not number of events	Control group (n) n = number of participants, not number of events
A	Significant arrhythmias*		
	Pulmonary complications/ Ventilator support*		
	Unexpected ICU admission*		
	Further surgery*		
	Inotropic support*		
	30 day mortality*		
	Analgesic efficacy		
	N&V		
	Failure of technique		
	Urinary retention		
	Duration of hospital stay		
	Cost effectiveness		

Other information which you feel is relevant to the results

Indicate if: any data were obtained from the primary author; if results were estimated from graphs etc; or calculated by you using a formula (this should be stated and the formula given). In general if results not reported in paper(s) are obtained this should be made clear here to be cited in review.

Freehand space for writing actions such as contact with study authors and changes

References to other trials

Did this report include any references to published reports of potentially eligible trials not already identified for this review?		
First author	Journal / Conference	Year of publication

Did this report include any references to unpublished data from potentially eligible trials not already identified for this review? If yes, give list contact name and details

Trial characteristics	
	Further details
Single centre / multicentre	
Country / Countries	
How was participant eligibility defined?	
How many people were randomized?	
Number of participants in each intervention group	
Number of participants who received intended treatment	
Number of participants who were analysed	
Drug treatment(s) used	
Dose / frequency of administration	

(*Continued*)

Duration of treatment (State weeks / months, etc, if cross-over trial give length of time in each arm)	
Median (range) length of follow-up reported in this paper (state weeks, months or years or if not stated)	
Time-points when measurements were taken during the study	
Time-points reported in the study	
Time-points you are using in RevMan	
Trial design (e.g. parallel / cross-over*)	
Other	

* If cross-over design, please refer to the Cochrane Editorial Office for further advice on how to analyse these data

HISTORY

Protocol first published: Issue 5, 2011

CONTRIBUTIONS OF AUTHORS

Conceiving the review: FG

Designing the review: FG, JY, SG

Co-ordinating the review: FG

Undertaking manual searches: JY, SG

Screening search results: JY, SG

Organizing retrieval of papers: JY, SG

Screening retrieved papers against inclusion criteria: JY,SG

Appraising quality of papers: JY, SG

Abstracting data from papers: JY, SG

Writing to authors of papers for additional information: FG

Providing additional data about papers: FG

Obtaining and screening data on unpublished studies: FG

Data management for the review: JY

Entering data into Review Manager (RevMan 5.1): JY, SG

RevMan statistical data: SG

Other statistical analysis not using RevMan: SG

Double entry of data: (data entered by person one: JY; data entered by person two: SG)

Interpretation of data: JY, SG, FG, ML

Statistical inferences: SG

Writing the review: JY, SG, FG, ML

Providing guidance on the review: FG, ML

Securing funding for the review: FG

Performing previous work that was the foundation of the present study: FG

Guarantor for the review (one author): FG

Person responsible for reading and checking review before submission: FG, ML

DECLARATIONS OF INTEREST

None declared

SOURCES OF SUPPORT

Internal sources

- New Source of support, Not specified.

External sources

- No sources of support supplied