Meta-analysis: ventilation strategies and outcomes of the acute respiratory distress syndrome and acute lung injury

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CRD summary
This review evaluated different strategies for mechanical ventilation of critically ill patients with acute respiratory distress syndrome or acute lung injury. The authors concluded that evidence from a limited number of trials showed better outcomes with routine use of low tidal volume, but not high positive end-expiratory pressure ventilation. The conclusions reflected the evidence presented and appear reliable.

Authors' objectives
To determine whether ventilation with low tidal volume and limited airway pressure or higher positive end-expiratory pressure (PEEP) improved outcomes for patients with acute respiratory distress syndrome (ARDS) or acute lung injury.

Searching
The authors searched Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE to March 2009 without language restrictions. Search terms were reported. Reference lists of relevant articles and reviews were checked.

Study selection
Randomised controlled trials (RCTs) that compared lower versus higher tidal volume ventilation, lower versus higher PEEP application or a combination of these strategies in critically ill adults with acute lung injury or ARDS were eligible for the review. Acute lung injury and ARDS had to be defined by American-European Consensus Conference criteria or by Lung Injury Severity Score. Trials had to report mortality at hospital discharge. Secondary outcomes were listed. Trials published only as abstracts were excluded.

Most included trials recruited patients with either acute lung injury or ARDS; some involved patients with ARDS only. Various different strategies were compared. Trials differed with respect to pH threshold and management of acidosis, use of recruitment manoeuvres, use of rescue therapies, weaning procedures and termination of the trial. Trial duration ranged from 15 to 68 months. Several of the included trials were terminated early.

Two pairs of independent reviewers selected studies for the review.

Assessment of study quality
Validity was assessed based on randomisation, allocation concealment, blinding, adequate selection and description of study population, similarity of groups at baseline, use of a predefined treatment protocol, absence of confounders and co-interventions, a priori definition of outcomes, use of intention-to-treat analysis, extent of follow-up, sample size calculation and other criteria (listed). Two reviewers independently assessed validity; any disagreements were resolved by consensus and consultation with a third reviewer if necessary.

Data extraction
Data on numbers of patients with an outcome in each group were used to calculate the odds ratio (OR) and associated 95% confidence interval (CI) for dichotomous outcomes. For continuous outcomes, data on group means and standard deviations were used to calculate the mean difference between groups.

Two pairs of reviewers independently extracted data using a standardised form. Extracted data were checked for accuracy by a third reviewer.

Methods of synthesis
Trials were pooled by meta-analysis using a fixed-effect model. Heterogeneity was assessed using the Cochran Q
statistic and I² test. Random-effects meta-analysis was used if I² was greater than 25%. Clinical heterogeneity was discussed in the text and presented in tables. The authors did not state that they assessed publication bias.

**Results of the review**

Nine RCTs (3,596 participants) were included. All the trials reported random allocation and allocation concealment; none used blinding.

**Lower versus higher tidal volume ventilation using similar PEEP values (four RCTs):** Lower tidal volume ventilation significantly reduced hospital mortality (OR 0.75, 95% CI 0.58 to 0.96), but not mortality at follow-up or barotrauma.

**Lower versus higher PEEP at low tidal volume ventilation (three RCTs):** Hospital mortality and barotrauma did not differ significantly between groups. Based on two RCTs, higher PEEP reduced requirement for rescue therapy to prevent hypoxaemia (OR 0.51, 95% CI 0.36 to 0.71) and reduced mortality in patients who received rescue therapy (OR 0.51, 95% CI 0.36 to 0.71). Numbers of events presented in the paper for the lower PEEP strategy appeared to refer to the higher PEEP strategy and vice versa.

**Combination of higher tidal volume and lower PEEP versus lower tidal volume and higher PEEP (two RCTs, n = 148):** The combination of lower tidal volume and higher PEEP significantly reduced hospital mortality (OR 0.38, 95% CI 0.20 to 0.75) and barotrauma (OR 0.20, 95% CI 0.06 to 0.63).

Heterogeneity was not significant for the outcomes listed. Other outcomes and analyses were reported.

**Authors' conclusions**

Evidence from a limited number of RCTs showed better outcomes with routine use of low tidal volume but not high PEEP ventilation in unselected patients. Higher PEEP may help prevent life-threatening hypoxaemia in selected patients.

**CRD commentary**

The research question and inclusion criteria were clear. The authors searched a range of relevant sources without language restrictions. Attempts to locate unpublished trials were not reported and risk of publication bias was not evaluated. Study validity was assessed using a large number of criteria, although no overall summary was provided. Measures were taken to minimise reviewer errors and bias in study selection, validity assessment and data extraction. Extensive details of included studies were provided. Studies were pooled by meta-analysis. Statistical heterogeneity was assessed and clinical heterogeneity between trials was discussed. The authors noted limitations of the evidence, including that the benefit of low tidal volume ventilation was derived from only one RCT and the small number of participants in RCTs that compared combined strategies. This was a generally well-conducted systematic review. The authors' cautious conclusions reflected the evidence presented and appear reliable.

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

The authors did not state any implications for practice or research.

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