Pressure and volume limited ventilation for the ventilatory management of patients with acute lung injury: a systematic review and meta-analysis
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CRD summary
This review found that pressure and volume limited ventilation strategies were associated with reductions in mortality and associated with increased use of paralytic agents in patients with acute lung injury or acute respiratory distress syndrome. The review was generally well conducted and the authors conclusions are likely to be reliable.

Authors' objectives
To compare pressure and volume-limited ventilation strategies with traditional mechanical ventilation in acute lung injury and acute respiratory distress syndrome.

Searching
MEDLINE, EMBASE, HealthStar and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to July 2010 for relevant studies. Abstracts from American Journal of Respiratory and Critical Care Medicine, Chest, Intensive Care Medicine and Critical Care Medicine from 1995 to 2006 were searched. The reviewers checked the reference lists of retrieved articles and used the related articles feature on PubMed to identify additional studies. There were no language restrictions.

Study selection
Randomised controlled trials of critically ill patients where at least 80% were adults who received mechanical ventilation and had acute lung injury were eligible for inclusion where ventilation strategies differed in relation to tidal volumes and/or airway pressures. Trials were included if they reported on mortality, barotrauma, duration of mechanical ventilation, use of sedation or paralytic agents, requirement for acute dialysis or non-pulmonary organ dysfunction. Also eligible were trials that observed incidental gradients in tidal volume (at least 3mL/kg) of at least 5cm H₂O during the first seven days of the study. Trials that evaluated high-frequency ventilation or oscillation, extracorporeal circulation or implantable devices to augment gas exchange were excluded from the review.

The mean age of the patients ranged from 34.4 to 58.5 years. Patients in the included trials had illness severity rated as APACHE II to III. Some trials included patients with organ failure. Where reported, the baseline arterial partial pressure of oxygen/fractional concentration of inspired oxygen ratio (PaO₂/FiO₂) ranged from 122.0 ± 58.8 to 149.5 ± 64.6 and lung injury scores ranged from 2.8 to 3.0 points. Sepsis was similar between groups in most trials. Sedation and weaning were performed at the clinician's discretion with the use of suggested guidelines in a few trials. The reported mean tidal volumes in the pressure and volume limited groups ranged from 9.8 to 12mL/kg and from 6.1 to 9.0mL/kg in the control groups.

Three reviewers performed the study selection; any disagreements were resolved by consensus.

Assessment of study quality
Methodological quality was assessed by two reviewers using GRADE criteria. Randomised trials were regarded as high quality evidence but rated down for apparent risk of bias, imprecision, inconsistency, indirectness and suspicion of publication bias. Particular quality components were randomisation, concealment of allocation and completeness of follow-up. Any disagreements between the reviewers were resolved by a third reviewer.

Data extraction
Two reviewers independently abstracted data to calculate relative risk (RR) and 95% confidence intervals for the outcomes. The reviewers contacted the authors of the included trials for additional information.

Methods of synthesis
Pooled relative risks and 95% CIs were calculated using a random-effects model. Statistical heterogeneity was evaluated using the Cochran's Q and I². Potential sources of heterogeneity (use of open-lung techniques, varied...
thresholds for correcting respiratory acidosis, between-group gradients and case mix) were explored using meta-regression analyses. Sensitivity analyses were performed for open lung strategies. Subgroup analyses were performed for different approaches to acidosis management. The reviewers tested for publication bias using visual appraisal of funnel plots.

**Results of the review**

Ten trials (1,749 participants) were included in the review. Seven trials were randomised. Allocation concealment was unclear in two trials. Five trials did not completely report potentially relevant cointerventions. Six trials ceased prematurely because of benefit (three trials) and futility (three trials). Two trials were not designed to compare ventilation strategies but noted incidental differences in mean tidal volume and plateau airway pressures between groups and were included in the review.

There was a borderline significant reduction in hospital mortality with pressure and volume limited strategies (RR 0.84, 95% CI 0.70 to 1.00; 10 RCTs, 1,749 participants) with moderate heterogeneity ($I^2=43.1\%$). The results of sensitivity analyses that removed two trials that used open lung techniques and a trial where randomisation was not outlined showed a non-significant attenuated result. Magnitude of within-study gradients in assigned or achieved tidal volumes or airway pressures between treatment groups were not found to be modifiers of the effect. There were no relationships between mean age and mean baseline ($\text{PaO}_2/\text{FiO}_2$) and mortality; meta-regression analyses were underpowered and limited by the small numbers of included studies.

There was a significant increase in use of paralytic agents with the use of pressure and volume limited ventilation strategies compared to conventional methods of ventilation (RR 1.37, 95% CI 1.04 to 1.82; five trials, 1,202 participants).

There were no significant differences observed between pressure and volume limited ventilation strategies and conventional strategies in barotrauma (seven trials, 1,497 participants) and initiation of dialysis (two trials, 173 participants).

**Authors’ conclusions**

The results of the review suggested that pressure and volume limited ventilation strategies were associated with reductions in mortality and increased use of paralytic agents in patients with acute lung injury or acute respiratory distress syndrome. There was no dose response effect and this borderline significant finding was not supported in sensitivity analyses so some uncertainty remained for the effect of pressure and volume limited ventilation.

**CRD commentary**

The review addressed a clear question. Criteria for inclusion of studies in the review were stipulated. Appropriate databases were searched for relevant studies. There were no language restrictions. The reviewers attempted to identify unpublished studies. Steps were taken by the reviewers to minimise errors and bias at each stage of the review process. Study quality appeared to be assessed with criteria that were appropriate for the study designs. The reviewers also used appropriate methods of pooling the results of the studies and explored potential sources of heterogeneity using meta-regression analyses.

The authors' cautious conclusions are likely to be reliable.

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

**Practice:** The authors stated that the results of the review supported current practice in ventilating patients with acute lung injury and acute respiratory distress syndrome with low tidal volumes.

**Research:** The authors stated uncertainty over the effect of pressure and volume limited ventilation and noted that further research was being conducted to assess the effect of paralytic agents to mortality in acute respiratory distress syndrome.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.