Effect of mechanical ventilation in the prone position on clinical outcomes in patients with acute hypoxemic respiratory failure: a systematic review and meta-analysis

Sud S, Sud M, Friedrich J O, Adhikari N K

CRD summary
This review assessed the efficacy and safety of prone positioning for mechanical ventilation in patients with acute hypoxemic respiratory failure. The authors concluded that there is no reduction in mortality or duration of ventilation, although oxygenation is improved and the incidence of pneumonia decreased. This was a clearly reported and well-conducted review, and the conclusions are likely to be reliable.

Authors' objectives
To evaluate the effect of prone positioning compared with supine positioning for mechanical ventilation on clinical outcomes in patients with acute hypoxemic respiratory failure.

Searching
MEDLINE, EMBASE, the Cochrane CENTRAL Register and the Science Citation Index were searched from inception to February 2008, without any language restrictions; the search terms were reported. Conference proceedings (1994 to 2007) of four relevant societies and two clinical trials registries were also searched. Related articles were searched, the references of included studies and review articles were checked, and clinical experts and the authors of included studies were contacted.

Study selection
Studies of patients with acute hypoxemic respiratory failure, defined as a ratio of partial pressure of oxygen to inspired fraction of oxygen of 300 mmHg or lower, receiving mechanical ventilation, were eligible for inclusion; studies of patients with acute lung injury or respiratory distress syndrome were included provided this criterion was met. Studies of both adults and children were eligible for inclusion. Two of the included studies enrolled only children. The majority of trials enrolled patients within 48 hours of diagnosis. Parallel-design randomised controlled trials (RCTs) and quasi-randomised trials, which compared treatment at least once in the prone position with treatment in the supine position, were eligible for inclusion; crossover RCTs were excluded from the review. The median length of ventilation was 12 hours per day (range: 4 to 24 hours). The majority of included studies employed at least one cointervention such as sedation, paralysis or ventilator weaning. Studies were required to report one of the following outcomes: all-cause mortality (the primary outcome), the ratio of partial pressure of oxygen to inspired fraction of oxygen, ventilator-associated pneumonia, duration of ventilation, number of ventilator-free days from randomisation to day 28 or 30, or a range of adverse events including pneumothoraces and cardiac arrests.

Four reviewers independently assessed studies for inclusion in the review, and any disagreements were resolved through consensus.

Assessment of study quality
The validity of the studies was assessed using the following criteria; allocation concealment, post-allocation withdrawals, losses to follow-up, crossover between groups, intention-to-treat analysis, blinding of the outcome assessors, cointerventions and early stopping of trials.

Four reviewers independently performed the validity assessment, and any disagreements were resolved through consensus.

Data extraction
The authors of all included studies were contacted for clarification of methodology and missing data. Relative risks (RRs) with 95% confidence intervals (CIs) were calculated for dichotomous data, while mean differences with 95% CIs were calculated for continuous data.
Four reviewers independently carried out the data extraction, and any disagreements were resolved through consensus.

**Methods of synthesis**
The studies were combined in a meta-analysis using a random-effects model to calculate the pooled RRs with 95% CIs for dichotomous outcomes and weighted mean differences (WMDs) with 95% CIs for continuous outcomes. A priori subgroup analyses were carried out based on patient population (acute lung injury or respiratory distress syndrome versus other) and duration of prone positioning (prolonged versus short-term). Subgroup analyses were also conducted on the effect of blinded outcome assessment for analyses of ventilator-assisted pneumonia. Statistical heterogeneity between the studies was investigated using the $I^2$ statistic. Publication bias was investigated using a funnel plot analysis and the Begg and modified Macaskill tests.

**Results of the review**
Thirteen trials ($n=1,559$) were included in the review: 11 RCTs and 2 quasi-randomised trials.

The quality of the included studies was generally high. Nine studies had adequate allocation concealment, nine standardised or described cointerventions, and all used an intention-to-treat analysis.

Mortality (10 trials): no overall statistically significant difference was found between prone and supine positioning (RR 0.96, 95% CI: 0.46, 1.28, $p=0.52$). The subgroup analysis revealed no difference in either trials using short-term prone positioning or in those using prolonged prone positioning; there was also no difference between patients with acute lung injury or respiratory failure and others.

Oxygenation (9 trials): prone ventilation resulted in an increased ratio of partial pressure of oxygen to inspired fraction of oxygen of between 23 and 34% on post-randomisation days 1 to 3, measured at the end of the prone manoeuvre. This ratio remained elevated by between 6 and 9% after return to a supine position.

Ventilator-associated pneumonia (6 trials): there was a significantly lower rate of pneumonia in patients in the prone position groups compared with the supine groups (RR 0.81, 95% CI: 0.66, 0.99, $p=0.04$).

Duration of ventilation (6 trials): there was a trend towards shorter duration of ventilation for patients in the prone position groups (WMD -0.9 days, 95% CI: -1.9, 0.1, $p=0.06$).

Number of ventilator-free days (4 trials): there was no significant difference between the groups in the number of ventilator-free days.

Adverse events (8 trials): there was a higher incidence of pressure ulcers in patients in the prone position groups (RR 1.36, 95% CI: 1.07, 1.71, $p=0.01$; 6 trials). There were no significant differences in any of the following adverse events: endotracheal tube obstruction, accidental extubation, loss of central venous or arterial access, thoracostomy tube dislodgement, pneumothorax, cardiac arrest. However, an alternative analysis using data from an additional trial reporting adverse event data in a different format did produce a statistically significantly higher risk of endotracheal tube obstruction in the prone position groups (RR 2.46, 95% CI: 1.33, 4.55, $p=0.004$).

There was no evidence of statistical heterogeneity in any of the analyses.

There was some evidence of publication bias from the funnel plot analysis, which was not confirmed by statistical tests.

Further results were reported on the CMAJ website. See Web address at end of abstract.

**Authors’ conclusions**
Use of the prone position for mechanical ventilation does not reduce mortality or duration of ventilation, despite improved oxygenation and a decreased risk of pneumonia.

**CRD commentary**
The review question and the inclusion criteria were clear. The authors searched a number of relevant databases, used no
language restrictions, and made reasonable attempts to identify unpublished studies, thereby reducing the possibility that some relevant studies were not included in the review. Publication bias was assessed, with conflicting results. The authors used appropriate methods to minimise reviewer bias and error in all aspects of the review process. An appropriate assessment of study validity was performed and this informed the synthesis. The use of meta-analysis was appropriate and subgroup analyses were pre-planned, while heterogeneity was formally assessed and found to be low. The authors’ conclusions are clearly based on the results of this well-conducted review and are likely to be reliable.

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

Practice: The authors stated that prone positioning for mechanical ventilation should not be used routinely for acute hypoxemic respiratory failure, although there may be some benefit in patients with very severe hypoxemia.

Research: The authors stated that trials of prone positioning for mechanical ventilation for life-threatening hypoxemia are desirable, though likely to face recruitment difficulties.

**Funding**

Canadian Institutes of Health Research.

**Bibliographic details**


**Original Paper URL**

http://www.cmaj.ca

**Indexing Status**

Subject indexing assigned by CRD

**MeSH**

Acute Disease; Prone Position; Respiration, Artificial /adverse effects /mortality; Respiratory Distress Syndrome, Adult /complications /mortality /therapy; Respiratory Insufficiency /complications /mortality /therapy

**AccessionNumber**

12008102660

**Date bibliographic record published**

09/08/2008

**Date abstract record published**

03/11/2008

**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.