

# Prone positioning for acute respiratory failure improved short-term oxygenation but not survival

Gattinoni L, Tognoni G, Pesenti A, et al., for the Prone-Supine Study Group. Effect of prone positioning on the survival of patients with acute respiratory failure. *N Engl J Med*. 2001 Aug 23;345:568-73.

## QUESTION

Does prone positioning for  $\geq 6$  hours/d for 10 days improve survival in patients with acute lung injury or the acute respiratory distress syndrome (ARDS)?

## DESIGN

Randomized (allocation concealed\*), unblinded, controlled trial with follow-up to 6 months.

## SETTING

28 intensive care units (ICUs) in Italy and 2 in Switzerland.

## PATIENTS

304 patients (mean age 58 y, 68% men) who were receiving mechanical ventilation and met the following modified criteria for acute lung injury or ARDS: ratio of partial pressure of arterial oxygen ( $\text{PaO}_2$ ) to fraction of inspired oxygen ( $\text{FiO}_2$ )  $\leq 200$  with a positive end-expiratory pressure (PEEP)  $\geq 5$  cm of water or a  $\text{PaO}_2$ - $\text{FiO}_2$  ratio  $\leq 300$  with a PEEP  $\geq 10$  cm of water; radiographic evidence of bilateral pulmonary infiltrates; and if measured, pulmonary-capillary wedge pressure  $\leq 18$  mm Hg or absence of clinical evidence of left atrial hypertension. Exclusion criteria were age  $< 16$  years, cardiogenic pulmonary edema, cerebral edema, intracranial hypertension, or clinical conditions contraindicating the use of prone positioning. Follow-up at 6 months was 98%.

## INTERVENTION

152 patients were allocated to prone positioning and were kept prone continuously for  $\geq 6$  hours per day for 10 days. Patients were assessed in the supine position each morning. A change to the prone position was triggered by a  $\text{PaO}_2$ - $\text{FiO}_2$  ratio  $\leq 200$  with a PEEP  $\geq 5$  cm of water or a  $\text{PaO}_2$ - $\text{FiO}_2$  ratio  $\leq 300$  with a PEEP  $\geq 10$  cm of water. 152 patients were allocated to conventional (supine) positioning.

## MAIN OUTCOME MEASURES

Main outcomes were death at 10 days (end of intervention), during ICU stay, and at 6 months. Other outcomes included improvement in respiratory failure and organ dysfunction; presence, site, and severity of pressure sores; and accidental displacement of tracheal or thoracotomy tubes or loss of venous access.

## MAIN RESULTS

Analysis was by intention to treat. The prone and supine groups had similar 10-day, ICU,

and 6-month mortality (Table); incidence of organ dysfunction; percentage of patients with new or worsening pressure sores; number of days with pressure sores; accidental displacement of tubes; and loss of venous access. Patients in the prone group had slightly greater increases in the  $\text{PaO}_2$ - $\text{FiO}_2$  ratio on morning assessments (average change 63.0 vs 44.6,  $P = 0.02$ ) and more new or worsening pressure sores (2.7 vs 1.9 per patient,  $P = 0.004$ ).

## CONCLUSION

Prone positioning of patients with acute lung injury or the acute respiratory distress syndrome improved short-term oxygenation more than did supine positioning but did not improve survival.

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\*See Glossary.

## Prone vs supine positioning for acute respiratory failure†

Mortality	Prone	Supine	RRR (95% CI)	NNT (CI)
At 10 d	21%	25%	16% (-27 to 44)	Not significant
			NNH	RRI (CI)
At ICU discharge	51%	48%	5% (-16 to 32)	Not significant
At 6 mo	63%	59%	6% (-12 to 28)	Not significant

†ICU = intensive care unit. Other abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

## COMMENTARY

The trial by Gattinoni and colleagues is an important part of an international effort to determine the effect of prone ventilation on survival in patients with acute lung injury. Prone positioning makes good sense physiologically; preclinical and clinical investigations have provided mechanistic information, and observational studies including  $> 260$  patients with severe acute lung injury suggest that 60% to 70% of patients have immediate improvement in oxygenation. On the other hand, intensive care clinicians are increasingly faced with the frustrating reality that physiologic improvement does not always lead to a survival benefit. More important, the potential for such serious complications of prone ventilation as inadvertent extubation, loss of venous access and chest tubes, delayed cardiopulmonary resuscitation, and blindness is clear. As a result, the intensive care world has awaited the completion of this study with great anticipation.

The results are disappointing; they fail to show a survival benefit in patients cared for in the prone position for  $\geq 6$  consecutive hours each day. However, the true effect of prone ventilation remains unclear.

Examination of the confidence intervals reveals that prone positioning for  $\geq 6$  consecutive hours per day may reduce ICU mortality by as much as 16% (in which case, we would use it routinely) or may increase ICU mortality by as much as 32% (in which case, we would not). Therefore, more randomized trials are necessary to clarify the role of prone positioning in patients with acute lung injury. In addition, many clinicians believe that 6 hours per day is insufficient to achieve the full potential of prone ventilation. Two randomized trials of prone ventilation are currently under way in Europe, with protocols for longer daily periods of prone ventilation. For now, as the best available evidence suggests no survival benefit and a potential for serious complications, prone positioning should be reserved for patients who are profoundly hypoxemic (as indicated by an intriguing post hoc analysis of these data) or for those enrolled in further clinical research.

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