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Conceptual Paper

Prone Positioning for ARDS Patients, Still a Debate?

Tsimogianni Angeliki*

Department of ICU, "Saint Savvas" Oncology Hospital, Athens, Greece

***Corresponding Author**: Tsimogianni Angeliki, Department of ICU, "Saint Savvas" Oncology Hospital, Athens, Greece.

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Acute respiratory distress syndrome (ARDS) is one of the most common admission diagnoses in Intensive Care Unit with considerable morbidity and mortality. There exist no targeted treatments strategies and every supportive measure is welcoming. Low target volume has become the standard of care, with neuromuscular blockade and prone position being used as rescue therapies in more severe cases. In surviving sepsis campaign 2016 guidelines it is recommended to use prone position in patients with sepsis-induced ARDS and PaO_2/FiO_2 ratio < 150, which is a strong recommendation, with moderate level of evidence. Prone positioning has been used in ARDS for more than 40 years, with significant improvement in oxygenation in more than 70% of patients, but without clear survival benefit [1,2].

Potential benefits of proning may include [1,2]:

- Improved lung ventilation perfusion matching as redistribution of ventilation towards dorsal well perfused areas occurs.
- Improved right ventricular dysfunction and cardiac index in patients who were preload dependent [3,4].
- Recruitment of lower lobe atelectatic lung units perhaps due to reduced compression of lower lobe lung units, mainly in patients with high recruitability and high peep in the supine position.
- Decreased intrapulmonary shunting.
- It may also homogenize tidal volume distribution and reduce tissue stress/strain, thus limiting ventilation induced lung injury.
- Possibly improves clearance secretion in some patients reducing the incidence of ventilator associated pneumonia [2].

Three of the beneficial effects of proning are expected to improve patients' survival: first the reduced extent and duration of hypoxaemia, second the reduced propensity to ventilator-induced lung injury and last the reduced incidence of nosocomial or ventilator associated pneumonia.

Early randomized controlled trials (RCTS) by Gattinoni and Guerin failed to show reduction in mortality. These trials included patients with mild ARDS, with short duration of prone positioning and protective lung ventilation was not used [5,6].

One of the first trials that showed survival benefit with prone position was Proseva trial [7]. This trial had a strict protocol: included 466 patients with severe ARDS with PaO_2/FiO_2 < 150 mmHg, peep > 5 cmH_2O, and FiO_2 of at least 60% who were ventilated with low tidal volumes, neuromuscular blockade was used and the proning sessions lasted at least 16 consecutive hours. With this protocol a significant reduction in mortality was obtained form 32.8% in the supine group to 16% in the prone group at day 28 after randomization, which was confirmed at day 90 (41% vs 23.6% respectively).

A recent systematic review and meta-analysis [5] identified six trials with 1016 patients with moderate to severe ARDS, with median PaO_2/FiO_2 118 mmHg (range 100 - 221 mmHg) that used protective ventilation with reduced tidal volumes, in which prone positioning significantly reduced mortality (risk ratio 0.74, 95% confidence interval (CI) 0.59 - 0.95). Prone positioning was used a median of 17 hours per day in these studies.

A later systematic review [2] with data from six trials demonstrated an RR 0.84 - 0.86 in favor of the prone position, but the findings were not statistically significant. In the short term (10 - 30 days post ICU admission) mortality for those ventilated prone was 33.4% versus 38.3% for those ventilated supine. This resulted in a RR of 0.84 (95% CI 0.69 - 1.02). For long term mortality (> 30 days) results showed 41.7% for prone and 47.1% for supine position, with an RR of 0.86 (95% CI 0.69 - 1.02). Subgroup analysis for mortality identified three groups of patients that showed survival benefit with prone position: those included within 48 hours of meeting entry criteria; five trials with 1024 participants showed an RR of 0.75 (95% CI 0.65 - 0.92), those treated in the prone position for 16 hours or more/day; five trials with 1005 participants showed an RR of 0.77 (95% CI 0.61 - 0.99) and participants with more severe hypoxaemia at study entry; six trials with 1108 participants showed an RR of 0.77 (95% CI 0.65 - 0.92).

A recent review [8] including Proseva trial concludes that significant improvement in survival has been demonstrated in the most severe ARDS patients at a threshold of 100 -150 mmHg PaO_2/FiO_2 ratio. The effect of proning on survival cannot be predicted and seems unrelated with both severity of oxygenation impairment and oxygenation response to proning.

A very recent trial [9] with 98 patients who underwent abdominal surgery and developed ARDS showed that the rate of surgical complications was not higher in prone position and that the oxygenation of these patients significantly improved after prone positioning, PaO_2/FiO_2 increased from 95 ± 47 to 189 ± 92 mmHg, $p < 0.001$.

Absolute contraindications to prone positioning are spinal instability and unmonitored increased intracranial pressure. For other relative contraindications like open abdominal wounds, pregnancy and trauma with unstable fractures, the risks and benefits of prone position should be balanced [10]. Prone positioning has some significant adverse effects: tracheal tube obstruction or dislodgement with potentially catastrophic hypoxaemia, pressure sores, ocular complications and intracranial hypertension which can compromise cerebral circulation. The rate of complications is declining with the increase in centers expertise.

Prone positioning improves oxygenation, prevents ventilator induced lung injury and in selected patients with severe ARDS managed with protective ventilation improves survival.

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