Prone-Positioning Therapy in ARDS

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The prone position has been used to improve oxygenation in patients with severe hypoxemia and acute respiratory failure since 1974. The prone position has been documented to induce an increase in both end-expiratory lung volume and alveolar recruitment. All studies with the prone position document an improvement in systemic oxygenation in 70% to 80% of patients with acute respiratory distress syndrome (ARDS), and the maximal improvements are seen in the most hypoxemic patients.

This article reviews the data regarding efficacy for use of the prone position in patients with ARDS. The authors also describe the simple, safe, quick, and inexpensive procedure that they use to prone a patient with severe ARDS on a standard bed in the intensive care unit (ICU) at the University of Michigan.

PHYSIOLOGIC EFFECTS OF PRONE POSITION IN ARDS

When the ARDS patient is prone, the mass of the dorsal lung, which reinflates (i.e., dorsal becomes the nondependent lung regions), is greater than the potential mass of the ventral (now dependent) lung regions, which may collapse (Fig. 1). When lung perfusion is substantially unmodified, the overall ventilation/perfusion (V/Q) matching improves as new pulmonary units are recruited for more effective gas exchange.

This mechanism is probably the primary one for the improvement in oxygenation in the prone ARDS patient, although other mechanisms (including a different shape of the diaphragm, changes of hypoxic pulmonary vasoconstriction, and a differential production of nitric oxide in different lung regions) may play a role. Both prone and semirecumbent positions facilitate the reaeration of dependent and caudal lung regions by partially relieving cardiac and abdominal compression, with resultant improvement in gas exchange.

Conflicts of Interest: None.

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Additional data confirm that the prone position may also limit ventilator-induced lung injury.\textsuperscript{5} It has been postulated that the prone position leads to more homogeneous lung inflation and more homogeneous alveolar ventilation, suggesting that the strain applied to the lung parenchyma and its associated stress are more homogeneously distributed than in the supine position; this may decrease ventilator-induced lung injury.\textsuperscript{6}

**PRONE POSITION IN ARDS: EVIDENCE FOR EFFICACY**

Changes in patient positioning can have a dramatic effect on oxygenation and ventilation in severe ARDS. Changing the patient position to prone or a steep lateral decubitus position can improve the distribution of perfusion to ventilated lung regions, decreasing intrapulmonary shunt and improving oxygenation.\textsuperscript{7} The use of intermittent prone positioning has been documented to significantly improve oxygenation in 60% to 70% of acute lung injury (ALI) and ARDS patients.\textsuperscript{1,8}

The Prone-Supine I Study\textsuperscript{9} was a multicenter, randomized trial, in patients aged 16 years or older with ALI or ARDS, of conventional treatment compared with placing patients (n = 295) in a prone position for 6 or more hours daily for 10 days. No differences in mortality or complications were identified for the prone versus conventional positioning group at any time point during the study, with up to 6 months of follow-up. The mean increase in the partial pressure of oxygen/fraction of inspired oxygen (PaO\textsubscript{2}/FiO\textsubscript{2}) ratio was greater in the prone than in the supine group (63 ± 67 vs 45 ± 68, P = .02). Of note is that the mean PaO\textsubscript{2} of 85 to 88 mm Hg and mean PaO\textsubscript{2}/FiO\textsubscript{2} ratio of 125 to 129 are quite high, that is, these patients did not have severe hypoxemia or severe ARDS (PaO\textsubscript{2}/FiO\textsubscript{2} ratio <100) and therefore these patients may not have been likely to benefit from the prone intervention as regards mortality. A retrospective analysis of patients in the prone-position arm of this study revealed that ALI/ARDS patients who responded to prone positioning with a reduction in their partial pressure of carbon dioxide (PaCO\textsubscript{2}) of 1 mm Hg or more showed an increase in survival at 28 days with a decrease in the mortality rate from 52% to 35%.\textsuperscript{10}

A multicenter, randomized, controlled clinical trial\textsuperscript{11} of supine versus prone positioning in 102 pediatric patients failed to demonstrate a significant difference in the main outcome measure, which was ventilator-free days to day 28. There were also no differences in the secondary end points study that included proportion alive and ventilator-free on day 28, mortality, time to recovery from lung injury, organ-failure free days, and functional health.

The Prone-Supine II Study\textsuperscript{12} is the largest clinical trial (N = 342) in adult ARDS patients, conducted in 23 centers in Italy and 2 in Spain. Patients underwent supine...
or prone (20 hours per day) positioning during mechanical ventilation. Prone and supine patients from the entire study population had similar 28-day (31.0% vs 32.8%; relative risk [RR], 0.97; 95% confidence interval [CI], 0.84–1.13; \( P = .72 \)) and 6-month (47.0% vs 52.3%; RR, 0.90; 95% CI, 0.73–1.11; \( P = .33 \)) mortality rates, despite significantly higher complication rates in the prone group. Outcomes were also similar for patients with moderate hypoxemia in the prone and supine groups at 28 days (25.5% vs 22.5%; RR, 1.04; 95% CI, 0.89–1.22; \( P = .62 \)) and at 6 months (42.6% vs 43.9%; RR, 0.98; 95% CI, 0.76–1.25; \( P = .85 \)). Of importance, the 28-day mortality of patients with severe hypoxemia was decreased in the prone group (37.8% in the prone group and 46.1% in the supine group [RR, 0.87; 95% CI, 0.66–1.14; \( P = .31 \)], while their 6-month mortality was 52.7% and 63.2%, respectively (RR, 0.78; 95% CI, 0.53–1.14; \( P = .19 \)).

A recent systematic review of the effect of mechanical ventilation in the prone position on clinical outcomes in patients with acute hypoxemic respiratory failure reported that it does not reduce mortality or duration of ventilation despite improved oxygenation and a decreased risk of pneumonia (Figs. 2 and 3). However, despite there being no significant effect on mortality reduction, these data do confirm a significant improvement in oxygenation, and support the use of prone-position ventilation as a rescue strategy in patients with severe hypoxemia. Additional systematic reviews

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**Fig. 2.** Effect of prone position ventilation on oxygenation. Effect of ventilation in the prone position on daily ratio of partial pressure of oxygen to inspired fraction of oxygen. A random-effects model was used in the analysis. Values were recorded at the end of the period of prone positioning (prone group) and simultaneously in the supine group. Ratio of means = mean ratio of partial pressure of oxygen to inspired fraction of oxygen in the prone group divided by that in the supine group. \( I^2 \) = percentage of total variation across studies owing to between-study heterogeneity rather than chance. CI, confidence interval. Reference citations apply to references as listed in the source article. (From Sud S, Sud M, Friedrich JO, et al. Effect of mechanical ventilation in the prone position on clinical outcomes in patients with acute hypoxemic respiratory failure: a systematic review and meta-analysis. CMAJ 2008;178(8):1153–61; with permission.)
and meta-analyses have confirmed similar findings. Furthermore, the pooled OR for ICU mortality in the selected group of the more severely ill patients favored prone positioning (OR, 0.29; 95% CI, 0.12–0.70).14–18

Of interest, prone position was used in 42% of patients in the conventional management group (control arm) of the CESAR trial, the multicenter randomized trial of extracorporeal membrane oxygenation (ECMO) versus conventional therapy for treating severe ARDS in adults, compared with only 4% in the ECMO group.19 The authors also use prone position for posterior dependent lung recruitment in patients on ECMO when they are beginning to recruit the native lung and progressing toward trialing off ECMO.

**UPDATED META-ANALYSES OF RANDOMIZED TRIALS IN SEVERE ARDS**

In patients with ALI or ARDS, more recent randomized controlled trials (RCTs) showed a consistent trend of mortality reduction with prone ventilation. An updated meta-analysis included 2 subgroups of studies: those that included all ALI or hypoxicemic patients, and those that restricted inclusion to only ARDS patients. In the overall meta-analysis that included 7 RCTs with 1675 adult patients (862 in prone position), prone position was not associated with a mortality reduction (OR 0.91, 95% CI 0.75–1.08; \( P = .39 \)). However, in the 4 most recent RCTs that enrolled only patients with ARDS, and that also applied the longest prone position durations and used lung-protective ventilation, prone position was associated with significantly reduced mortality (OR 0.71, 95% CI 0.5–0.99; \( P = .048 \); number needed to treat = 11)

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**Fig. 3.** Effect of prone position ventilation on mortality. A random-effects model was used for analysis. The duration of prone positioning was up to 24 hours for 1 to 2 days in the short-term trials and up to 24 hours daily for more than 2 days in the prolonged-duration trials. The trial by Gattinoni and colleagues included data only for patients with acute hypoxicemic respiratory failure. Including all patients from this trial (7/25 deaths in the prone group and 14/28 deaths in the supine group) did not change the result (RR 0.95, 95% CI 0.83–1.08; \( P = .41 \)). \( I^2 \) = percentage of total variation across studies owing to between-study heterogeneity rather than chance. CI, confidence interval; RR, relative risk. Reference citations apply to references as listed in the source article. (From Sud S, Sud M, Friedrich JO, et al. Effect of mechanical ventilation in the prone position on clinical outcomes in patients with acute hypoxicemic respiratory failure: a systematic review and meta-analysis. CMAJ 2008;178(8):1153–61; with permission.)
Prone position was not associated with any increase in major airway complications in this meta-analysis.\(^{20}\)

Gattinoni and colleagues\(^{21}\) performed an individual patient meta-analysis of the 4 major clinical trials,\(^{9,12,22,23}\) which documented that with prone positioning, the absolute mortality of severely hypoxemic ARDS patients may be reduced by approximately 10\% (Fig. 5). This study also suggested that long-term prone positioning may expose patients with less severe ARDS to unnecessary complications. A recent review of all published meta-analyses on the efficacy of prone position in ALI and ARDS concluded that prone ventilation was associated with reduced mortality in patients with severe hypoxemic respiratory failure.\(^{24}\)

EXTENDED PRONE POSITION VENTILATION

Extended prone position ventilation (extended PPV) in severe ARDS has been confirmed in a recent pilot feasibility study. Extended PPV was defined as PPV for 48 hours or until the oxygenation index was 10 or less. A prospective interventional study\(^{25}\) in 15 patients confirmed that there was a statistically significant improvement in oxygenation ($\text{PaO}_2/\text{FiO}_2 \ 92 \pm 12 \text{ vs } 227 \pm 43, P<.0001$) and oxygenation index ($22 \pm 5 \text{ vs } 8 \pm 2, P<.0001$), reduction of $\text{PaCO}_2$ ($54 \pm 9 \text{ vs } 39 \pm 4, P<.0001$) and plateau pressure ($32 \pm 2 \text{ vs } 27 \pm 3, P<.0001$), and improved static compliance ($21 \pm 3 \text{ vs } 37 \pm 6, P<.0001$) with extended PPV. All the parameters continued to improve significantly while the patients remained in prone position and did not change on the patients’ return to the supine position. The results obtained suggest that extended PPV is safe and effective in patients with severe ARDS when it is performed by trained staff and within an established protocol. Extended PPV is emerging as an effective rescue therapy for patients with severe ARDS and severe hypoxemia.

A prospective randomized study ($n = 136$),\(^{23}\) with guidelines established for ventilator settings and weaning, examined the efficacy of the prolonged prone position

![Fig. 4. Effect of prone position on ICU mortality. Point estimates (by random-effects model) are reported separately for the groups of studies that included both ALI and ARDS, those that included only ARDS patients, and the pooled overall effects of all patients included in the meta-analysis. (From Abroug F, Ouanes-Besbes L, Dachraoui F, et al. An updated study-level meta-analysis of randomised controlled trials on proning in ARDS and acute lung injury. Crit Care 2011;15(1):R6; with permission.)](#)
(continuous prone position for 20 hours daily) in severe ARDS patients with 48 hours of tracheal intubation. Multivariate analysis documented that randomization to the supine position was an independent risk factor for mortality (OR 2.53, \( P = .03 \)). These investigators concluded that prone ventilation is feasible and safe, and may reduce mortality in patients with severe ARDS when it is initiated early and applied for most of the day.

An open randomized controlled trial\(^{26}\) in 17 medical-surgical ICUs enrolled 40 mechanically ventilated patients with early and refractory ARDS despite protective ventilation in the supine position. Patients were randomized to remain supine or be moved to early (within 48 hours) and continuous (\( \geq 20 \) hours per day) prone position until recovery or death. The trial was prematurely stopped, due to a low patient recruitment rate. \( \text{PaO}_2/\text{FiO}_2 \) tended to be higher in prone than in supine patients after 6 hours (202 ± 78 vs 165 ± 70 mm Hg); this difference reached statistical significance on day 3 (234 ± 85 vs 159 ± 78). Prone-related side effects were minimal and reversible. Sixty-day survival reached the targeted 15% absolute increase in prone patients (62% vs 47%), but failed to reach significance because of the small sample. This study adds data to reinforce the potential beneficial effect of early continuous prone positioning on survival in ARDS patients.

**COMPLICATIONS ASSOCIATED WITH PRONE POSITION**

Prone positioning has associated risks to both the patient and the health care worker. One hindrance to use of the prone position in ARDS patients has been the difficulty of safely moving a patient with severe hypoxemia due to ARDS. Complications can arise...
in the process and include unplanned extubation, lines being pulled, and tubes becoming kinked. In addition, proning obese patients can be labor intensive and can result in staff injuries. However, the technique can be performed safely by trained and dedicated critical care staff who are aware of its potential benefits in critically ill patients with ARDS and severe hypoxemia.

Complications that have been reported with prone positioning include inadvertent extubation, airway complications, pressure sores, and brachial plexus injuries.27 Some of these complications are fully preventable with proper technique and careful attention to detail. Avoidance of pressure ulceration requires the use of appropriate cushioning of the dependent portions of the body.

In the Prone-Supine I Study, Gattinoni and colleagues9 reported complications related to pressure in 36% of patients and cannula loss in 1.2% of patients. In a comprehensive review conducted by Curley and colleagues,11 displacement of venous lines and indwelling catheters was found to be the most common complication, occurring in 0.6% of turning cycles (supine to prone and back to supine). In the more recent Prone-Supine II Study,12 a significantly greater proportion of patients in the prone group experienced at least one complication (94.6% vs 76.4%) and the incidence of most of the complications was significantly higher in the prone group (Table 1). However, other reports have confirmed the safety of prone positioning with open abdomen28 and with high-flow venous access.29

<p>| Table 1 |</p>
<table>
<thead>
<tr>
<th>Incidence of complications during the 28-day Prone-Supine II Study</th>
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<tbody>
<tr>
<td>Complication</td>
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<tr>
<td>Entire Population</td>
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<tr>
<td>Need for increased sedation/muscle relaxants</td>
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<tr>
<td>Airway obstruction</td>
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<tr>
<td>Transient desaturation</td>
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<tr>
<td>Vomiting</td>
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<tr>
<td>Hypotension, arrhythmias, increased vasopressors</td>
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<tr>
<td>Loss of venous access</td>
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<tr>
<td>Displacement of endotracheal tube</td>
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<td>Displacement of thoracotomy tube</td>
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<sup>a</sup> Percentage of patients who experienced at least 1 episode of the complication considered during the 28-day study period.

<sup>b</sup> Number of days with at least 1 event, divided by 100 patient-days (2760 patient-days for the prone group and 2764 patient-days for the supine group).

<sup>c</sup> For comparison between prone and supine groups.

<sup>d</sup> Percentage of events in the prone group that occurred during the positional changes.

METHODS FOR PRONE POSITIONING

Several methods for prone positioning have been developed. The authors use a simple, manual 3-step procedure (Figs. 6 and 7) that takes 4 staff members (2 on each side of the bed) to manage all lines and tubes. First, patients are moved to the edge of the bed with a full sheet. This sheet is then wrapped around the patient’s

Fig. 6. Simple steps to placing an ARDS patient in the prone position: University of Michigan method.
arm that is located toward the middle of the bed. A second flat sheet is tucked under the covered arm and then the patient is rolled further as far as possible to the side of the bed. Finally, the patient is carefully turned back over by pulling the first sheet from the side of the bed back toward the middle of the bed. The wrapped arm is gently pulled from under the patient while pulling the second sheet fully under the patient.

**Box 1**

**Requirements for safe prone positioning in ALI/ARDS patients**

- Preoxygenate the patient with FiO₂ 1.0
- Secure the endotracheal tube and arterial and central venous catheters
- Adequate number of staff to assist in the turn and to monitor the turn
- Supplies to turn (pads for bed, sheet, protection for the patient, or specialty bed)
- Knowledge of how to perform the turn or use the specialty bed
- Knowledge of how to supine the patient in the event of an emergency
This maneuver releases the first sheet that can be thrown away, and leaves the second sheet under the patient to reverse the patient to a supine position later. This technique is simple and easy to perform, but most importantly allows the ICU staff full access to the patient, particularly to provide posterior skin care.

In their ICU, the authors have standardized this process and prone patients frequently. This prone-position procedure is routinely completed in less than 5 minutes by the ICU staff with the patient on a standard ICU bed. After the patient is prone, appropriate padding of the chest, extremities, and face and neck is necessary. The bed is then placed in a slight reverse Trendelenburg position to minimize pressure in the head and neck area.

In response to perceived difficulties in placing ALI/ARDS patients in the prone position, several manufacturers have developed devices, frames, or complete bed systems to help staff efficiently and safely prone patients. These methods may require extensive staff training and are often quite expensive, limiting their availability at some hospitals; the authors do not use these methods in their ICU (Box 1).

Fig. 8. Use of the Vollman Prone Positioner. (© 2007 Hill-Rom Services, Inc. REPRINTED WITH PERMISSION-ALL RIGHTS RESERVED.)

Fig. 9. The use of the Rotoprone Therapy System (KCI USA, Inc, San Antonio, TX). This is an automated system that allows multiple intervals of prone therapy over an extended time. (Courtesy of Rotoprone Therapy System, KCI USA, Inc, San Antonio, TX; with permission.)
One method used to establish the prone position is via the use of the Vollman Prone Positioner (Hill-Rom Services Inc, Batesville, IN, USA) (Fig. 8). Others use the Rotoprone Therapy System (KCI USA Inc, San Antonio, TX, USA) (Fig. 9), which is an automated system that allows multiple intervals of prone therapy over an extended time. This technique has some advantages due to its automated use, but is somewhat limited because of the daily expense of bed rental. In the Prone-Supine II Study, prone positioning was applied using this rotational bed in 20 participating centers and applied manually in the remaining 5 centers. There is some concern, however, that easy access to the patient in the Rotoprone bed is limited. Others implement prone positioning with the use of a Stryker frame (Stryker, Kalamazoo, MI); however, care must be taken to appropriately pad all exposed areas to prevent ulcerations, because there is a metal frame.

SUMMARY

In the authors’ experience, the use of the prone position is an effective strategy for the treatment of severe hypoxemia in patient with ARDS. To establish the prone position, the authors favor a simple technique that uses 4 staff members and a regular ICU bed with no specialized equipment. More recent studies document the benefit of extended prone position therapy (>20 hours per day) in ARDS. A recent review of all published meta-analyses on the efficacy of prone position in ALI and ARDS concluded that prone ventilation was associated with reduced mortality in the cohort of patients with severe hypoxemia, defined as $\text{PaO}_2/\text{FiO}_2$ ratio less than 100 mm Hg. In addition, prone positioning serves a role as rescue therapy for patients with ARDS and refractory life-threatening hypoxemia.

REFERENCES


