Letters

Invited Commentary

Prone Positioning in Awake, Nonintubated Patients With COVID-19: Necessity Is the Mother of Invention

In this issue of *JAMA Internal Medicine*, Thompson and colleagues report the association of prone positioning with pulse oximetry in 25 awake, nonintubated patients with hypoxemic respiratory failure due to coronavirus disease 2019 (COVID-19).[1] This study included patients who were hypoxemic (oxyhemoglobin saturation [Spo_2] ≤ 93%) despite receiving 15 L/min oxygen by face mask and 6 L/min oxygen by nasal cannula and excluded patients who were unable to turn in bed without assistance and those determined to be in respiratory distress and requiring immediate intubation. The median (SE) improvement in oxygen saturation was 7% (1.2%) (95% CI, 4.6%-9.4%) after 1 hour of prone positioning. This study adds to a growing body of literature suggesting that prone positioning may improve oxygenation in patients with early acute respiratory distress syndrome (ARDS) prior to intubation.

Related article

Prone positioning has several beneficial effects on pulmonary physiology in patients with ARDS.[2] In the supine position, pulmonary edema accumulates in basilar regions, and the heart and abdominal contents further compress these dependent lung regions. This leads to heterogenous ventilation, with increased volume delivered to apical and anterior lung units, which are also the regions that receive less of the pulmonary circulation. Together, these factors lead to perfusion of poorly ventilated lung units and hypoxemia. Prone positioning of the patient leads to a more homogeneous distribution of ventilation, thus decreasing the shunt fraction and improving matching of ventilation and perfusion. Moreover, homogeneous ventilation may decrease lung injury by more evenly distributing mechanical force from the ventilator across the lung during inhalation.[2]

Despite compelling experimental evidence of these physiologic changes, most of the early randomized clinical trials of the prone position in mechanically ventilated patients with ARDS did not demonstrate a benefit compared with standard care. These trials, however, may have been limited by the late initiation and short duration of the use of the prone position. To address these limitations, the Proning Severe ARDS Patients (PROSEVA) trial,[3] published in 2013, randomized patients with a ratio of arterial oxygen tension (Pao_2) to fraction of inspired oxygen (Fio_2) less than 150 mm Hg within 36 hours of intubation to be placed in the prone position for long durations—on average, 17 hours a day. The comparison group was patients ventilated in the supine position. The trial found a hazard ratio for death of 0.39 (95% CI, 0.25-0.63) in the study arm with prone positioning compared with standard care (mortality at 28 days, 16.0% vs 32.8%). The findings have led to increased adoption of prone positioning for mechanically ventilated patients with moderate to severe ARDS.

Before COVID-19, there was limited published research on prone positioning in nonintubated patients.[4] The COVID-19 pandemic, however, has led to a sudden and dramatic increase in the number of patients requiring respiratory support for ARDS, straining critical care resources at many hospitals and forcing clinicians to use innovative approaches to limit the need for mechanical ventilation, including so-called awake proning. In a report on 50 nonintubated hypoxemic patients with suspected COVID-19 who presented to an emergency department in New York City, Caputo and colleagues[5] found a significant increase in Spo_2 5 minutes after proning (preproning: 84%; interquartile range [IQR], 75%-85%; postproning: 94%; IQR, 90%-95%; $P = .001$). Elharrar et al[6] conducted an observational study of prone positioning in patients with confirmed COVID-19 and posterior lung opacities on chest computed tomography who were admitted to a single center in France, most of whom were on 4 L or less of oxygen delivered via nasal cannula. Among 24 eligible patients, the majority (15 [63%]) were able to tolerate being prone for at least 3 hours, but oxygenation increased with the prone position in only 6 patients (25%). Finally, Sartini et al[7] tested prone positioning in 15 patients admitted to a single center in Milan, Italy, who were hypoxemic despite 10 cm H_2O continuous positive airway pressure and 0.6 Fio_2, and Spo_2 increased in all 15 patients. The report by Thompson et al adds to this body of observational evidence by demonstrating that many patients with severe acute hypoxemic respiratory failure yet not on positive pressure ventilation had improved oxygenation in the prone position.[1]

Although promising, these case series should be interpreted with caution because of the lack of randomization. Even in this selected group of patients, not all patients tolerated the prone position, and nearly half the patients in the case series from Thompson et al eventually required intubation. Although improved oxygen saturation with the prone position is important, hypoxemia has not been a reliable surrogate biomarker for mortality in clinical trials of ARDS. Notably, in the National Heart, Lung, and Blood Institute ARDS Network trial of low tidal volumes,[8] the Pao_2/Fio_2 ratio was higher in the high-tidal-volume arm than the low-tidal-volume arm on study days 1 and 3. Nonetheless, mortality was lower in the low-tidal-volume arm (31.0% vs 39.8%).[8]

One potential concern with the use of the prone position in spontaneously breathing patients is that it could delay intubation and mechanical ventilation. The optimal timing of intubation and mechanical ventilation for patients with ARDS is not known, but delayed intubation has been associated with increased mortality in patients with ARDS.[9] Spontaneously breathing patients with ARDS generate relatively large tidal volumes; the result could be inadvertent self-inflicted lung injury. Controlled modes of mechanical ventilation minimize

progression of lung injury owing to barotrauma. These benefits should be balanced with the risks of mechanical ventilation, including the need for prolonged sedation and the risk of ventilator-associated pneumonia. Ongoing clinical trials of prone positioning in non-mechanically ventilated patients (eg, NCT04383613, NCT04359797) should help clarify the role of this simple, low-cost approach for patients with acute hypoxemic respiratory failure.

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