Relias Media
From Relias

Vol. 28, Issue 11, February 2021
ReliasMedia.com

Critical Care [ALERT]

Authoritative, evidence-based summaries for the critical care clinician

SPECIAL FEATURE

Prone Positioning in Acute Respiratory Distress Syndrome

By Jane Guttendorf, DNP, CRNP, ACNP-BC, CCRN

Assistant Professor, Acute & Tertiary Care, University of Pittsburgh, School of Nursing

Managing acute respiratory distress syndrome (ARDS) with prone positioning has been identified as far back as 1976 with noted improvements in oxygenation but no associated mortality benefit.[1] In 2001, Gattinoni et al again demonstrated improved oxygenation in patients with acute lung injury or ARDS who were proned for an average of seven hours/day over 10 days.[2] There was improved PaO_2 and PaO_2/FiO_2 (P/F) ratio, but mortality was not significantly different: 21% in the prone group and 25% in the supine group.[2] However, this study enrolled subjects prior to the widespread adoption of the Berlin definition for ARDS and when the usual delivered tidal volume (TV) was 10 mL/kg ideal body weight (IBW). Continued advances in mechanical ventilation strategies for ARDS, including low TV ventilation (6 mL/kg based on IBW), use of neuromuscular blockade, and ARDSNet FiO_2 and positive end expiratory pressure (PEEP) titration tables, prompted a renewed interest in proning.

A 2013 study by Guerin et al (PROSEVA) documented improved outcomes in addition to improved oxygenation in patients with severe ARDS as identified by the American-European Consensus Conference criteria (P/F ratio < 150 mmHg on at least 60% FiO_2 and 5 cm H_2O of PEEP).[3] This was an unblinded, randomized controlled trial (RCT) that enrolled 466 subjects from 26 intensive care units (ICUs) in France and one in Spain, assigning patients to either a prone or supine group. Patients were ventilated with a low TV strategy (6 mL/kg IBW), FiO_2 of at least 60%, and PEEP ≥ 5 cm H_2O, targeting a plateau pressure of ≤ 30 cm H_2O, and pH of 7.20 to 7.45. Key points of this trial compared with earlier ones were that patients were enrolled early (within 36 hours of intubation and initiation of mechanical ventilation), had severe ARDS, and were proned for at least 16 hours daily until day 28. Mortality at day 28 was significantly lower in the prone group (16%) than in the supine group (32.8%) ($P < 0.001$), and this difference persisted out to 90 days.[3]

Financial Disclosure: None of the planners or authors of this educational activity have relevant financial relationships to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

[INSIDE]

Critical Care [ALERT]

Authoritative, evidence-based summaries for the critical care clinician

Critical Care Alert (ISSN 1067-9502) is published monthly by Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468. Periodicals postage paid at Morrisville, NC, and additional mailing offices. POSTMASTER: Send address changes to *Critical Care Alert*, Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468.

GST Registration Number: R128870672.

SUBSCRIBER INFORMATION
(800) 688-2421
customerservice@reliasmedia.com
ReliasMedia.com

Back issues: $42. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

ACCREDITATION

JOINTLY ACCREDITED PROVIDER™
INTERPROFESSIONAL CONTINUING EDUCATION

In support of improving patient care, Relias LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

The Relias LLC designates this enduring material for a maximum of 2 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

2 ANCC contact hours will be awarded to participants who meet the criteria for successful completion.

California Board ofRegistered Nursing, Provider CEP#13791.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2 MOC Medical Knowledge points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

This CME activity is intended for critical care physicians and nurses. It is in effect for 36 months from the date of the publication.

Since publication of the PROSEVA trial, there have been at least four systematic reviews of prone positioning in ARDS. In a 2015 Cochrane review including 2,165 participants in 10 studies, there was a trend toward improved (but not significantly different) mortality with proning.[4] However, in a subgroup analysis, three groups consistently saw favorable results with prone ventilation: those recruited within 48 hours of meeting entry criteria (relative risk [RR] 0.75; 95% confidence interval [CI], 0.59-94), those treated with proning for 16 or more hours per day (RR 0.77; 95% CI, 0.61-0.99), and patients with severe hypoxemia at enrollment (RR 0.77; 95% CI, 0.65-0.92).[4] Similarly, Munshi et al reviewed eight RCTs that included 2,129 patients.[5] There was no difference in mortality between prone and supine patients (RR 0.84; 95% CI, 0.68-1.04), but again, subgroup analyses found reduced mortality in patients with longer duration of proning (12 hours or more) (RR 0.74; 95% CI, 0.56-0.99) and for patients with moderate to severe ARDS (RR 0.74; 95% CI, 0.56-0.99). P/F ratio was significantly higher for all patients in the prone group at day 4.[5]

Dalmedico et al reviewed seven studies published between 2014 and 2016.[6] Combined use of a protective ventilation strategy and proning between 16-20 hours/day in patients with severe ARDS (P/F ratio < 150 mmHg) was associated with a significant reduction in mortality in at least four of the seven trials.[6] In another systematic review of therapeutic strategies in association with lung protective ventilation in moderate to severe ARDS patients, the addition of prone positioning was associated with significantly lower 28-day mortality (RR 0.69; 95% CI, 0.48-0.99).[7]

PHYSIOLOGIC BENEFITS OF PRONING IN IMPROVING GAS EXCHANGE

Pulmonary blood flow is preferentially distributed to the dependent lung fields (dorsal and basal lung segments), and perfusion remains relatively constant in these areas during both supine and prone ventilation. Prone ventilation is more sensitive to changes in pressure gradients and is affected by lung and chest wall compliance, intra-abdominal pressure, and displacement from the heart and lungs within the chest cavity.[8] ARDS is known to heterogeneously affect alveoli, producing severe capillary leak, and often affecting dependent alveoli to a greater extent than more ventral ones. Mechanical ventilation in the supine position often promotes better ventilation of the more ventral alveoli since the anterior chest is more readily able to expand (i.e., is more compliant). Subsequently, these alveoli can overinflate, leading to ventilator-induced lung injury (VILI).[8,9] Prone positioning in ARDS allows for better ventilation of the more dependent alveoli, while improving ventilation-perfusion matching as the dependent portions continue to receive a preferential amount of blood flow.[8-10] In some patients, clearance of carbon dioxide (CO_2) may improve with proning, and some patients experience improvement in cardiac output.[10] Right ventricular function may improve as well because of a decrease in pulmonary vascular resistance associated with improved alveolar recruitment.[10]

WHO BENEFITS FROM PRONING?

As noted earlier, the ARDS patients most likely to benefit from trials of prone positioning include those who have severe ARDS (P/F ratio < 100 mmHg to 150 mmHg), are early in the course of disease, and are on at least a moderate amount of PEEP (5 cmH_2O to 10 cmH_2O). Adding proning to high PEEP strategies can help mitigate the adverse effects of PEEP in that ventilation is better directed to the dependent alveoli, thus lessening VILI.[11] The proning trial should continue for at least 16 hours/day, and patients often benefit from repeated days of prone therapy.

A recent prevalence study that included 735 ARDS patients from 141 ICUs in 20 countries evaluating the use of prone positioning in ARDS patients demonstrated that proning likely still is under-utilized.[12] The prevalence of ARDS was between 8.9% and 13.3%. At least one proning session was completed in 13.7% of patients, and the rate of proning significantly differed among mild, moderate, and severe ARDS patients (5.9%, 10.3%, and 32.9%, respectively).[12,13]

More recently, data are emerging to support the use of prone positioning for patients with ARDS due to COVID-19. In one small single-center report, prolonged trials of proning (up to 36 hours) were useful in improving P/F ratio in patients failing a traditional 16-hour prone trial.[14]

Table 1: Procedure for Proning the Intensive Care Unit Patient

Preparation for Proning	• Evaluate need for additional sedation and/or neuromuscular blocker. • Prevent pressure injuries: pad the face (forehead, cheeks, chin, and endotracheal tube holder). • Pad bony prominences (shoulders, hips, knees, feet) and chest, sternum, abdomen, genitalia. • Secure invasive lines, endotracheal tube, ECMO cannulas, chest tubes. • Keep emergency drugs at bedside. • Assign one nurse to monitor hemodynamics, with ready access to infusion pumps for titration of pressors or fluid bolus as needed.
Supine to Prone Turn	• Cocoon or sandwich the patient in a sheet. • Pull patient to the edge of the bed with lateral/horizontal movement. • Tuck the dependent arm down next to the body. • Roll patient up on one side onto the tucked arm (lateral or side-lying position). • Place new electrodes for ECG monitoring on patient's back and remove old ones from the anterior chest and limbs (place new electrodes for each turn). • Complete the turn from side-lying to prone. • Position the head, neck, limbs once in prone position. • Position arms in swimmer's position. • Place pillows, wedges, rolls, and pressure-relief devices as needed. • Verify that tubes are patent and not kinked, particularly the endotracheal tube, chest tubes, ECMO cannulas, dialysis catheter.
Prone to Supine Turn	• Secure the airway, invasive lines, and all tubes. • Lift to remove pillows, rolls, wedges. • Cocoon or sandwich the patient in a sheet. • Pull patient to the edge of the bed with lateral/horizontal movement. • Tuck the dependent arm down next to body. • Roll patient up on one side (lateral or side-lying position). • Place new electrodes for ECG monitoring on anterior chest and limbs and remove old ones from the back and posterior limbs. • Complete the turn from side-lying to supine. • Position head, neck, and limbs properly.

ECMO = extracorporeal membrane oxygenation; ECG = electrocardiogram

Oxygenation improved significantly during ventilation in the prone position, and the P/F ratio in the supine position after a prolonged prone trial was significantly higher than before proning ($P = 0.034$).[14]

Another area of current study is the use of proning in awake, spontaneously breathing COVID-19 patients with respiratory failure outside of the ICU in an attempt to prevent escalation to intubation and mechanical ventilation.[15-19] In one study, 50 patients with mild to moderate ARDS from COVID-19 requiring oxygen therapy outside of the ICU were treated with a protocol of prone positioning three times per day for 30-60 minutes alternating with supine positioning. Prone positioning was associated with significant increases in oxygenation during proning and after returning to the supine position as well. At 45-day follow-up, there were two deaths, seven patients required ICU admission, and 41 patients had been discharged from the hospital.[18] Case reports also are beginning to appear, documenting the use of awake proning in conjunction with standard supplemental oxygen and as an adjunct to high-flow nasal cannula and even noninvasive ventilation.[20-23]

CONTRAINDICATIONS TO PRONE POSITIONING

There are few absolute contraindications to proning, but patients with facial fractures, unstable spinal or pelvic fractures, or increased intracranial pressure should avoid proning. An open chest or abdomen can be a contraindication, although if the open abdomen is well supported with the use of an abdominal binder, these patients may be successfully proned after consultation with the surgical team. Women in the third trimester of pregnancy may not tolerate proning and should be evaluated on a case-by-case basis. Obesity is not a contraindication to proning; in fact, morbidly obese patients may experience significant benefit from proning. However, obese patients may have increasing intra-abdominal hypertension in the prone position, which may lead to renal or hepatic dysfunction.[11] Veno-venous extracorporeal membrane oxygenation (ECMO) patients can be successfully proned with careful attention to adequate drainage and cannula positioning (offloading pressure on the cannula itself).

PRONING PRIMER: PLAN, PREPARE, PRACTICE

It is important for clinical teams to develop a protocol for proning patients, review procedures, prepare equipment/supplies, and have a coordinated effort. (*See Table 1.*) Educating patients and family members about expectations is important. Most centers are doing manual proning of patients in the standard ICU bed, but there are lift devices and proning beds available. Coordinate care such that activities like bathing, dressing changes, diagnostic testing, and off-unit travel for scans and procedures are provided while the patient is supine. If there are many patients to prone (e.g., in the setting of a COVID surge), consider a "unit schedule" since each patient will require about four to five staff members to assist with the turn. For planned (non-emergent) proning, we try to time the turn to prone in late afternoon to early evening so that the patient will remain proned for the remainder of the night; the patients then will be returned to the supine position in the early to mid-morning.

A coordinated team effort is critically important. The leader is at the head of the bed and is responsible for managing the airway, securing the endotracheal tube during the turn, and coordinating the team's actions. Participants may include nurses, respiratory therapists, perfusionists, physicians, advanced practice providers, and patient care technicians. Some centers have established dedicated proning teams and may include assistance from physical therapists and rehabilitation personnel.

Plan ahead for potential emergency complications that may occur during the prone trial, such as hemodynamic instability, desaturation, agitation/moving, bleeding, tracheal secretions, or arrest. Have emergency medications, such as intravenous fluids and vasopressors, available, particularly for the first proning session until it is clear how each patient will respond. Consider developing a procedure for early return to the supine position in the event of an emergency. Cardiopulmonary resuscitation can be provided in the prone position, as can cardioversion and defibrillation, until enough people have assembled to safely return the patient to a supine position.[24-26]

Resources for education and training exist. The *New England Journal of Medicine* website (nejm.org) has "how to" videos associated with the PROSEVA trial publication (https://www.nejm.org/doi/full/10.1056/NEJMoa1214103).[3] Consider developing a checklist for proning to ensure patient safety.[27,28]

COMPLICATIONS OF PRONING

Immediate complications of proning include hemodynamic instability, arrhythmias, cardiac arrest, worsened hypoxemia, accidental extubation, or unintentional line removal. It is helpful to have a supraglottic device readily available in the event the airway needs to be secured immediately. A videolaryngoscope can be very helpful if the patient must be intubated while proned. There are case reports of ultrasound-guided IJ line insertions in the prone position if a line needs to be placed emergently.[29]

More delayed complications nearly all relate to pressure injury. The most common complication is facial pressure injury from the endotracheal tube stabilizing device as well as pressure on bony parts of the forehead, cheeks, and chin, and over the bridge of the nose.[30] Proper positioning of the arm and shoulder (*see Table 1*) will help avoid brachial plexus injury or peripheral nerve root compression.[31,32] There is a case report of lower cranial nerve (CN) dysfunction (CN IX-XII) associated with significant dysphagia in the recovery period, along with tongue deviation, trapezius and sternocleidomastoid weakness that was thought to be the result of pressure on the face and possible neck hyperextension during prone positioning.[33] Other serious pressure complications can involve the eye and include increased intraocular pressure, edema of sclera, and corneal injury. An increase in intraocular pressure can be sight-threatening and needs close surveillance.[34] Lubrication of the eye can help to reduce the risks of corneal ulceration and exposure keratopathy.

Edematous scrotum and genitalia may predispose to pressure injury, breakdown, and, in one case report, was thought to be responsible for the development of Fournier's gangrene, which required surgical debridement.[35] Other complications may include vomiting or reflux of gastric contents while in the prone position. This may be lessened by placing the bed in reverse Trendelenburg position. Increased intra-abdominal pressure may make it difficult for patients to tolerate gastric feedings, so smaller volume feedings may be indicated.

SUMMARY

The benefits of prone positioning as an adjunctive therapy for severe ARDS patients are clearly outlined with regard to improved oxygenation, with more recent reports demonstrating a survival benefit. However, there are risks associated with the process of turning as well as with known pressure-related injuries. Careful assessment for complications is an important component of daily care. Meticulous attention to positioning of limbs, padding of pressure points, and the use of pillows, wedges, and foams to offload pressure are useful mitigation strategies. ■

REFERENCES

1. Douglas WW, et al. Improved oxygenation in patients with acute respiratory failure: The prone position. *Am Rev Respir Dis* 1977;115:559-566.
2. Gattinoni L, et al. Effect of prone positioning on the survival of patients with acute respiratory failure. *N Engl J Med* 2001;345:568-573.
3. Guérin C, et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 2013;368:2159-2168.
4. Bloomfield R, et al. Prone position for acute respiratory failure in adults. *Cochrane Database Syst Rev* 2015;11:CD008095.
5. Munshi L, et al. Prone position for acute respiratory distress syndrome. A systematic review and meta-analysis. *Ann Am Thorac Soc* 2017;14(Suppl 4):S280-S288.
6. Dalmedico MM, et al. Efficacy of prone position in acute respiratory distress syndrome: Overview of systematic reviews. *Rev Esc Enferm USP* 2017;51:e03251.

7. Aoyama H, et al. Assessment of therapeutic interventions and lung protective ventilation in patients with moderate to severe Acute Respiratory Distress Syndrome: A systematic review and network meta-analysis. *JAMA Netw Open* 2019;2:e198116.
8. Gordon A, et al. Prone positioning in ARDS. *Crit Care Nurs Q* 2019;42:371-375.
9. Guérin C. Prone position. *Curr Opin Crit Care* 2014;20:92-97.
10. Johnson NJ, et al. Gas exchange in the prone posture. *Respir Care* 2017;62:1097-1110.
11. Scholten EL, et al. Treatment of ARDS with prone positioning. *Chest* 2017;151:215-224.
12. Guérin C, et al. A prospective international observational prevalence study on prone positioning ARDS patients: The APRONET (ARDS Prone Position Network) study. *Intensive Care Med* 2018;44:22-37.
13. Chiumello D, et al. Prone position in ARDS: A simple maneuver still underused. *Intensive Care Med* 2018;44:241-243.
14. Carsetti A, et al. Prolonged prone position ventilation for SARS-CoV-2 patients is feasible and effective. *Crit Care* 2020;24: 225-227.
15. Bower G, He H. Protocol for awake prone positioning in COVID-19 patients: To do it earlier, easier, and longer. *Crit Care* 2020;24:371.
16. Elharrar X, et al. Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. *JAMA* 2020;323:2336-2338.
17. Koeckerling D, et al. Awake prone positioning in COVID-19. *Thorax* 2020;75:833-834.
18. Taboada M, et al. Short-term outcomes of 50 patients with acute respiratory distress by COVID-19 where prone positioning was used outside the ICU. *J Clin Anesth* 2020;67:110028.
19. Telias I, et al. Is the prone position helpful during spontaneous breathing in patients with COVID-19? *JAMA* 2020;323: 2265-2267.
20. Despres C, et al. Prone positioning combined with high-flow nasal or conventional oxygen therapy in severe Covid-19 patients. *Crit Care* 2020;24:256.
21. Ding L, et al. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: A multi-center prospective cohort study. *Crit Care* 2020;24:28.
22. Raoof S, et al. High-flow, noninvasive ventilation and awake (nonintubation) proning in patients with coronavirus disease 2019 with respiratory failure. *Chest* 2020;158:1992-2002.
23. Winearls S, et al. Early conscious prone positioning in patients with COVID-19 receiving continuous positive airway pressure: A retrospective analysis. *BMJ Open Respir Res* 2020;7:e000711.
24. Douma MJ, et al. Prone cardiopulmonary resuscitation: A scoping and expanded grey literature review for the COVID-19 pandemic. *Resuscitation* 2020;155:103-111.
25. Ludwin K, et al. Cardiopulmonary resuscitation in the prone position: A good option for patients with COVID-19. *Anesth Analg* 2020;131:e172-e173.
26. Moscarelli A, et al. Cardiopulmonary resuscitation in prone position: A scoping review. *Am J Emerg Med* 2020;38:2416-2424.
27. Oliveira VM, et al. Safe prone checklist: Construction and implementation of a tool for performing the prone maneuver. *Rev Bras Ter Intensiva* 2017;29:131-141.
28. Cotton S, et al. Proning during covid-19: Challenges and solutions. *Heart Lung* 2020;49:686-687.
29. Chen GY, et al. Ultrasound-guided central venous catheterization in the prone position. *Br J Anaesth* 2017;119:337-338.
30. Lucchini A, et al. Prone position in acute respiratory distress syndrome patients: A retrospective analysis of complications. *Dimens Crit Care Nurs* 2020;39:39-46.
31. Simpson AI, et al. Reducing the risk and impact of brachial plexus injury sustained from prone positioning — A clinical commentary. *J Intensive Care Med* 2020;35:1576-1582.
32. Malik GR, et al. Injury-prone: Peripheral nerve injuries associated with prone positioning for COVID-19-related acute respiratory distress syndrome. *Br J Anaesth* 2020;125:e478-e480.
33. Trejo-Gabriel-Galan JM, et al. Lower cranial nerves paralysis following prone-position mechanical ventilation. *Crit Care Med* 2017;45:e865-e866.
34. Saran S, et al. Effect of prone positioning on intraocular pressure in patients with acute respiratory distress syndrome. *Crit Care Med* 2019;47:e761-e766.
35. Kappel C, et al. A case of possible Fournier's gangrene associated with proning in COVID-19 ARDS. *Can J Anaesth* 2020;67:1697-1698.

ABSTRACT & COMMENTARY

In the Setting of Non-COVID ARDS, Improvement in Oxygenation with Proning Predicts Survival

By Vibhu Sharma, MD, MS

Assistant Professor of Medicine, University of Colorado, Denver

SYNOPSIS: In this retrospective cohort study, improvement in the PaO_2/FiO_2 (P/F) ratio by 54% was the optimal cutoff to predict those more likely to be alive at 28 days.

SOURCE: Lee HY, Cho J, Kwak N, et al. Improved oxygenation after prone positioning may be a predictor of survival in patients with acute respiratory distress syndrome. *Crit Care Med* 2020;48:1729-1736.

This was a retrospective cohort study of patients admitted to a single center in Seoul, South Korea. The cohort included was admitted to the intensive care unit (ICU) between 2014 and 2020, prior to the onset of the COVID-19 pandemic. The authors reviewed charts of patients who were proned for at least 12 hours. Patients were proned if their PaO_2/FiO_2 (P/F) ratio was < 150 with a positive end expiratory pressure (PEEP) ≥ 5 and $FiO_2 \geq 0.6$, consistent with inclusion criteria in the PROSEVA trial.[1] The authors reviewed the charts of 223 patients with moderate to severe acute respiratory distress syndrome (ARDS) by the Berlin criteria. Of these, 142 were proned; 26 of these were excluded because they were proned for less than 12 hours. Thus, 116 patients formed the study cohort. Almost all (96%) received neuromuscular blockade.

The primary outcomes were ICU and 28-day mortality. Arterial blood gases (ABGs) were collected prior to proning (time 0), at 4 hours (time P1), at 4-8 hours (time P2), at 8-12 hours (time P3), and at some point between 12 hours and the end of prone positioning (time P4). The P/F ratio also was calculated within four hours of supination (time S1) and at 4-12 hours after supination (time S2). The authors assessed the predictive utility of percent change in P/F ratio and the change in minute ventilation (Ve) to $PaCO_2$ ratio (Ve:$PaCO_2$) at the specified times after the first prone positioning session during the ICU stay. The latter variable allows for an indirect measurement of improvement in dead space. Since (almost) all of the patients were paralyzed, assuming Ve remained constant with controlled mechanical ventilation, $PaCO_2$ would be expected to decrease ("$PaCO_2$ responders") and the ratio to increase as ventilation perfusion (VQ) mismatch improved.

The median duration of the first prone session was 17.8 hours. ICU survivors were more likely to be proned early (1.2 vs. 2.7 days, $P < 0.006$). Patients who survived were more likely to have a larger change in their P/F ratio at all time points after proning. A change in P/F ratio of 53.5% from time 0 to time P3 optimally predicted improved mortality. Patients with at least this percent change in P/F ratio were deemed "prone responders." The optimal cutoff for the percent change in the P/F ratio from time 0 to time S2 (> 4 hours after supination) was 10.4%. A change of > 41.7% in the Ve:$PaCO_2$ ratio from time 0 to time P3 (8-12 hours from time proned) also predicted survival at 28 days.

■ COMMENTARY

The authors of this study concluded that among patients with moderate to severe ARDS, prone responders were more likely to survive their ICU stay. The PROSEVA trial demonstrated that prone positioning of patients with ARDS for at least 16 hours a day reduced 28- and 90-day mortality when adjusted for Sequential Organ Failure Assessment (SOFA) scores, vasopressor use, and use of neuromuscular blockade. In the PROSEVA trial, responders were defined as those with an increase in P/F ratio of at least 20 mmHg. Changes in the P/F ratio by this amount did not predict mortality. ABGs were not assessed at fixed time points in the PROSEVA trial; however, a retrospective analysis of the PROSEVA cohort found that ABGs at any time did not predict mortality.[2] In addition, there were no differences in survival when ABGs were assessed at the completion of the first session of prone ventilation.

Other studies have also shown that the P/F ratio is not an independent predictor of mortality in multivariate analyses that control for other severity of illness variables.[3-4] With respect to $PaCO_2$, the large LUNG-SAFE study showed that sustained hypercapnia (over days 1-2) was not harmful, using a 28-day mortality endpoint, and was seen mostly in patients with severe ARDS.[5] However, hypocapnia was harmful in mild to moderate ARDS. The LUNG-SAFE study did not assess changes in $PaCO_2$ over time; however, there is some literature to suggest that improvements in $PaCO_2$ with proning may predict a better prognosis.[6]

Another notable critique of this study was that delivery of mechanical ventilation in the pressure-controlled mode resulted in a mean tidal volume of 7 ± 1.3 mL/kg ideal body weight, with some patients therefore receiving more than the upper limit of recommended tidal volume per ARDSNet criteria. Second, this was a single-center study, and the majority of the patients were immunosuppressed related to a malignant process and therapeutics, with 90% in each group receiving corticosteroids, thereby limiting generalizability. It is unclear what, if anything, clinicians should take to the bedside with respect to the results of this retrospective single-center study given the disappointing associations of oxygenation with mortality. A recent study assessed the predictive value of the oxygen saturation index (OSI).[7] This index incorporates the stiffness of the lung and is calculated as follows:

$$(FiO_2 \times \text{mean airway pressure} \times 100)/SpO_2.$$

In a cohort of 326 adult patients with ARDS in diverse clinical settings (trauma/medical/surgical ICUs), the OSI was found to predict mortality when measured on the first day of diagnosis of ARDS, with the worst value for SpO_2 and the highest values for FiO_2 and mean airway pressure incorporated.[7] When available, measurement of the OSI on day 1 of diagnosis of ARDS predicts mortality, and if available, the percent change in P/F ratio and, in my opinion, more importantly, the Ve:$PaCO_2$ ratio may provide supportive evidence for a better prognosis in the narrow spectrum of patients described by Lee et al. ■

REFERENCES

1. Guérin C, et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 2013;368:2159-2168.
2. Albert RK, et al; Proseva Investigators. Prone position-induced improvement in gas exchange does not predict improved survival in the acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2014;189:494-496.
3. Ware LB. Prognostic determinants of acute respiratory distress syndrome in adults: Impact on clinical trial design. *Crit Care Med* 2005;33:S217-S222.
4. Seeley E, et al. Predictors of mortality in acute lung injury during the era of lung protective ventilation. *Thorax* 2008;63:994-998.
5. Madotto F, et al. Patterns and impact of arterial CO(2) management in patients with acute respiratory distress syndrome: Insights from the LUNG SAFE study. *Chest* 2020;158:1967-1982.
6. Gattinoni L, et al. Decrease in $PaCO_2$ with prone position is predictive of improved outcome in acute respiratory distress syndrome. *Crit Care Med* 2003;31:2727-2733.
7. DesPrez K, et al. Oxygenation saturation index predicts clinical outcomes in ARDS. *Chest* 2017;152:1151-1158.

ABSTRACT & COMMENTARY

COVID-19 Patients Can Be Managed Safely with Noninvasive Respiratory Strategies

By Betty Tran, MD, MSc

Associate Professor of Medicine, Division of Pulmonary and Critical Care Medicine, Northwestern University Feinberg School of Medicine, Chicago

SYNOPSIS: In this retrospective chart review of adult patients hospitalized with COVID-19 over a one-month period, the implementation of a noninvasive respiratory protocol that encouraged high-flow nasal cannula, noninvasive mechanical ventilation, and self-proning did not result in any significant increase in mortality.

SOURCE: Soares WE 3rd, Schoenfeld EM, Visintainer P, et al. Safety assessment of a noninvasive respiratory protocol for adults with COVID-19. *J Hosp Med* 2020;15:734-738.

This was a retrospective chart review of 469 consecutive adult patients admitted to any of four hospitals in the Baystate Health system with a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test for SARS-CoV-2 between March 15, 2020, and April 15, 2020. A noninvasive COVID-19 respiratory protocol (NCRP) encouraging early use of high-flow nasal cannula (HFNC), noninvasive ventilation (NIV), and self-proning was developed and implemented on April 3, 2020. The primary outcome was mortality during the post-NCRP implementation period compared to the preimplementation period. Rates of proning, HFNC, NIV, and intubation before and after protocol implementation were analyzed. Secondary outcomes included unexpected cardiac arrests, intensive care unit (ICU) transfers and consultations, and rapid response team (RRT) activations in the pre-implementation vs. postimplementation period.

After protocol implementation, there was an increase in HFNC use (5.5% to 24.7%) and self-proning (7.5% to 22.8%), while intubation rates decreased from 25.2% to 10.7% ($P < 0.01$). The median time to mechanical ventilation increased from 0.66 days (interquartile range [IQR] 0.23-1.69 days) to 1.4 days (IQR 0.21-2.9 days) in the pre-implementation vs. postimplementation period. Overall mortality was 26.2% during the study period. During the pre-implementation period, 24% (61 of 254) of patients died compared to 28.8% (62 of 215) in the postimplementation period ($P = 0.14$). After excluding patients with established (prior to admission) do not resuscitate/do not intubate (DNR/DNI) orders, the mortality rate was comparable pre-implementation vs. postimplementation (21.8% vs. 21.9%, respectively). In terms of secondary outcomes, there was no increase in RRT activations or ICU consults in the postimplementation period. ICU transfers decreased in the postimplementation period. There was one unexpected cardiac arrest in the postimplementation period compared to none before the protocol.

■ COMMENTARY

Since the first positive case of COVID-19 was confirmed in the United States on Jan. 21, 2020, our management of COVID-19 patients has evolved rapidly. In the early months of the pandemic, patients with COVID-19 were intubated and placed on mechanical ventilation early in their course, often after failing up to 6 L/min of nasal cannula. This strategy was based on perceptions and reports of rapid clinical decline, ineffectiveness of noninvasive methods, and incomplete knowledge of viral transmissibility with a focus on healthcare provider safety.

In their review, the investigators reported that 24% of patients died in the pre-implementation period compared to 28.8% in the postimplementation period (P = 0.14), although this finding was not statistically significant. The comparison became more equal after excluding patients with an established DNR/DNI order prior to admission.

Given the study's retrospective nature, we are unable to evaluate the effectiveness of the noninvasive respiratory protocol itself because of the potential for selection bias and unadjusted confounders. In other words, if more patients died while on an early noninvasive respiratory strategy, does it mean that this strategy was truly harmful (in terms of delaying the need for invasive mechanical ventilation) or just that sicker patients ultimately will require invasive mechanical ventilation and be more likely to die regardless of the interventions they received?

Overall, the findings suggest that an early noninvasive respiratory approach can reduce the rate of mechanical ventilation while not significantly affecting overall mortality, although the latter conclusion is limited by retrospective data. The authors noted that the failure to find a reduced mortality post-protocol implementation could be related to other factors, namely because of an increased proportion of established DNR/DNI patients, many coming from skilled nursing facilities and nursing homes, admitted after the protocol was implemented compared to prior. Given the one-month time span of this chart review, there were no novel medications, and it was unlikely that providers changed their interventions or treatment plans significantly during this time frame, with the exception of perhaps encouraging more patient self-proning.

Even if there is no significant reduction in mortality with an early noninvasive approach, the reduction in rates of invasive mechanical ventilation may have other benefits that were not explored in this study, such as reduced length of stay, lower hospital-related comorbidities, decreased rates of post-traumatic stress disorder and functional impairment, and lower healthcare costs, while freeing up resources, such as ventilators and ICU beds. ■

CME/CE QUESTIONS

1. **A notable outcome of the PROSEVA trial was:**
   a. improved carbon dioxide removal while in the prone position.
   b. less ventilator-induced lung injury due to use of low tidal volume ventilation.
   c. improved mortality in patients undergoing prone positioning.
   d. improved oxygenation in the supine patient group but not in the prone patient group.
2. **Which of the following patients will likely benefit from a trial of prone positioning?**
   a. A woman with mild to moderate acute respiratory distress syndrome (ARDS) (PaO_2/FiO_2 ratio of 300 mmHg)
   b. A young man with closed head injury following motor vehicle accident
   c. A man with moderate to severe ARDS (PaO_2/FiO_2 ratio of < 150 mmHg)
   d. A multi-trauma patient with unstable pelvic fracture and tension pneumothorax
3. **What percentage change in P/F ratio from baseline was found to predict 28-day mortality in the setting of ARDS?**
   a. 7% at eight hours after proning
   b. 10% at eight hours after proning
   c. 41.7% at eight hours after proning
   d. 54% at eight hours after proning
4. **In patients admitted to the hospital with COVID-19 after implementation of a noninvasive respiratory protocol, which of the following statements is true, based on the study by Soares et al?**
   a. There was an increase in rapid response team activations.
   b. There was an increase in intensive care unit consultations.
   c. There was no change in rates of intubation.
   d. There was no change in mortality.

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- identify relevant topics in the practice of critical care medicine;
- utilize recommendations from current clinical guidelines; and
- manage common critically ill patient and ICU administration scenarios.