Indian Journal of Basic and Applied Medical Research; December 2019: Vol.-9, Issue- 1, P. 522 - 530

Original research article

PRONE POSITIONING IN ARDS A STUDY OF 79 CASES, CHALENGES AND OUT COMES

[1]DR.R. RAJENDRA BABU , [2]DR.DEVI PADMAKUMAR* , [3]DR.ARJUN.R.BABU

[4]DR. SANJEEV , [5]DR.T.RAVIKUMAR , [6]DR.ABRAHAM ITTACHAN

[1]ASSISTANT PROFESSOR OF ANAESTHESIOLOGY MALABAR MEDICAL COLLEGE ,CALICUT,KERALA

[2]JR IN ANAETHESIOLOGY,AMRITA INSTITUTE OF MEDICAL SCIENCE, KOCHI,KERALA

[3]ASSISTANT PROFESSOR OF COMMUNITY MEDICINE , MALABAR MEDICAL COLLEGE,CALICUT, KERALA

[4]ASSOCIATE PROFESSOR OF PAEDIATRICS, MALABAR MEDICAL COLLEGE ,CALICUT,KERALA

[5]PROFESSORAND MEDICAL SUPERINTENDENT, GMC ESI CBE

[6]PROFESSOR , CRITICAL CARE UNIT ,MOSC MEDICAL COLLEGE,KOLENCHERY

*CORRESPONDING AUTHOR

ABSTRACT

Background: Internationally, observations of critical care clinicians treating patients in critical care have reported that patients with moderate to severe ARDS (acute respiratory distress syndrome) appear to have responding well to ventilation in the prone position, leading to prone position ventilation being recommended in international guidelines for the management of ARDS

Materials and Methods: : Between January 2018- and December 2019, 79 patients were admitted with ARDS,in various tertiary care hospitals are taken for study. After eliminating patients not fit for prone position, patients with ARDS (Pao_2/FIo_2 ratio $\leq$ 200 mm Hg) were put in prone position to study the improvement. The primary end points were safety and complications of PP; the secondary end points were the effect on oxygenation (Pao_2/FIo_2 ratio at the end of PP), length of mechanical ventilation and ICU stay, nosocomial infections, and mortality.

Results: 79 patients were admitted for ARDS. twenty two- patients were diagnosed as leptospirosis, eight as dengue. others 49. The most common cause of ARDS is sepsis. Next vomiting leads to aspiration , near-drowning episodes, ICU stay, and nosocomial infections did not differ significantly, but mortality at 28 days was significantly lower in patients put on prone position(22% vs 40%,)when compared to conventional positions.

Conclusions: Prone position ventilation is safe and improves oxygenation in patients with ARDS .Early use of prone ventilation in patients with moderate to severe ARDS improves oxygenation and reduce mortality, Prone positioning is a simple intervention that can be done in most circumstances, is compatible with all forms of basic respiratory support and requires little or no equipment in the conscious patient.

INTRODUCTION

ARDS is a syndrome with multiple risk factors that trigger the acute onset of respiratory insufficiency. common pathological pulmonary features, such as increased permeability as reflected by alveolar edema due to epithelial and endothelial cell damage, and neutrophil infiltration in the early phase of ARDS. Until recently, the most accepted definition of ARDS was the American-European Consensus Conference (AECC) definition, published in 1994

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

ARDS was defined as: the acute onset of respiratory failure, bilateral infiltrates on chest radiograph, hypoxemia as defined by a PaO_2/FiO_2 ratio ≤200 mmHg, and no evidence of left atrial hypertension or a pulmonary capillary pressure <18 mmHg (if measured) to rule out cardiogenic edema. In addition, Acute Lung Injury (ALI), the less severe form of acute respiratory failure, was different from ARDS only for the degree of hypoxemia, in fact it was defined by a 200 < PaO_2/FiO_2 ≤300 mmHg.

ARDS Berlin definition.

The Berlin definition of acute respiratory distress syndrome

Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging	Bilateral opacities — not fully explained by effusions, lobar/lung collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation	
Mild	200 mmHg < PaO_2/FIO_2 ≤300 mmHg with PEEP or CPAP ≥5 cmH_2O[c]
Moderate	100 mmHg < PaO_2/FIO_2 ≤200 mmHg with PEEP ≥5 cmH_2O
Severe	PaO_2/FIO_2 ≤100 mmHg with PEEP ≥5 cmH_2O

ARDS is considered the most common cause of non-cardiogenic pulmonary edema. It is clinically defined by the presence of pulmonary infiltrates due to alveolar fluid accumulation, without evidence suggestive of a cardiogenic etiology

Therefore, the main cause of pulmonary edema in ARDS is the damage to the alveolar-capillary membrane, which becomes leaky, allowing fluid rich in protein to exit into the interstitial and alveolar spaces. This leads to reduced diffusing capacity, shortness of breath, and hypoxemia.

ARDS can be caused by a variety of etiologies, but the clinical manifestations are the same once the alveolar-capillary membrane has been damaged.

Common causes of ARDS

- **Sepsis.** The most common cause of ARDS is sepsis, a serious and widespread infection of the bloodstream. **like leptospirossis, dengue, swineflu,sars**
- **Inhalation of harmful substances.** Breathing high concentrations of smoke or chemical fumes can result in ARDS, as can inhaling (aspirating) vomit or near-drowning episodes.

Severe pneumonia. Community acquired pneumonia is probably the most common cause of ARDS that develops outside of the hospital . Common pathogens include Streptococcus pneumoniae , Legionella pneumophila,

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Pneumocystis jirovecii (formerly called Pneumocystis carinii), Staphylococcus aureus, enteric gram negative organisms, and a variety of respiratory viruses

- **Head, chest or other major injury.** Accidents, such as falls or car crashes, can directly damage the lungs or the portion of the brain that controls breathing.
- **Others.** Pancreatitis (inflammation of the pancreas), massive blood transfusions and burns.

Within intensive care units, approximately 10 to 15 percent of admitted patients and up to 23 percent of mechanically ventilated patients meet criteria for ARDS . As an example, in a multicenter, international study of nearly 30,000 intensive care unit (ICU) patients, 10 percent of admissions to the ICU were due to ARDS . The majority of patients with ARDS (80 percent) required mechanical ventilation. Among those with ARDS, the majority (47 percent) had moderate ARDS while the remainder had mild (30 percent) or severe disease (23 percent). ARDS was responsible for 23 percent of patients mechanically ventilated in the ICU.

Current therapies

Numerous clinical studies have been conducted in patients with ARDS, but great advances in the care of the patients are still lacking and supportive therapies remain the mainstay in the ARDS management.

Protective mechanical ventilation

There is a large body of evidence from experimental and clinical studies demonstrating that mechanical ventilation, particularly in the setting of lung injury, can exacerbate functional and structural alterations in the lung . It is noteworthy that mechanical ventilation not only perpetuates lung injury, but also contributes to both the morbidity and mortality of ARDS. The concept that the limitation of end inspiratory lung stretch may reduce mortality in ARDS patients, culminated in the NIH-sponsored multicenter study of patients with ARDS. In this trial, patients randomized to receive a lower tidal volume (Vt) [4-6 mL/kg predict body weight (PBW), and maintenance of plateau pressure between 25 and 30 cmH_2O] had a survival benefit. Mortality was reduced from 40% in the conventional arm to 31% in the low Vt arm The benefit in terms of mortality and ventilation free days did not appear to be related to the value of the lung compliance at baseline or to the underlying risk factor for ARDS. Of note, the survival benefit was associated with a reduction of plasma IL-6 concentration, supporting the hypothesis that a lung protective strategy limits the spill over into the systemic circulation of inflammatory mediators, which in turn may induce multiple system organ failure .

In addition to lung over-distention, cyclic opening and closing of small airways and alveolar units (so called atelectrauma) can also lead to lung injury . Several clinical trials have been conducted in ARDS patients to examine the effects of an “open lung” approach in which the application of recruitment maneuvers and higher levels of PEEP may limit atelectrauma. In two randomized studies, Amato and colleagues, and Villar and colleagues examined the effect of a composite strategy that minimized tidal volume, adopted lung recruitment maneuvers, and applied a level of PEEP above the closing pressure of the lung . Although the intervention arms decreased mortality, the studies were criticized due to relatively small sample sizes and relatively high mortality in the control arms. The ARDS Network performed a second large clinical trial comparing lower *vs.* higher levels of PEEP (the ALVEOLI study). The trial was stopped early for futility, showing a trend to worse outcome in the higher PEEP arm, although there

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

was an imbalance in patient characteristics at baseline favoring the control arm; the mean age of the higher PEEP arm was higher (54±17 *vs.* 49±17, P<0.05), the mean PaO_2/FiO_2 was lower (151±67 *vs.* 165±77, P<0.05), and there was a trend to higher APACHE III scores, at baseline.

Historically prone positioning, high frequency oscillatory ventilation and extracorporeal membrane oxygenation have been proposed as non-conventional therapies for life-threatening refractory hypoxemia in severe ARDS patients. Although all these strategies have demonstrated to improve oxygenation, their impact on mortality is controversial. In fact, two recent RCT have questioned the safety of HFOV , where promising results come from a French study in which mortality was significantly lower in patients treated with extended period of prone position .

The prone positioning exploits gravity and re-positioning of the heart in the thorax to recruit the lung and to improve ventilation perfusion matching. Despite improving arterial oxygenation ,prone position failed to show a significant improvement in mortality in one study. In a subsequent study, prone ventilation was associated with a decrease in (37.8% *vs.* 46.1%) 28-day mortality in the subgroup of patients with severe hypoxemia, but given the small numbers, definitive conclusions cannot be drawn regarding the effect on mortality in this subgroup . However, pending results from a recent French study seem to clearly demonstrate a lower mortality in patients with severe ARDS who were treated with longer period of prone position.

In theory, high frequency oscillatory ventilation (HFOV) encapsulates the main principles of lung protection: it delivers extremely small tidal volumes around a relatively high mean airway pressure, at high respiratory frequencies (3-15 Hz), with the goal of avoiding tidal overstretch and recruitment/derecruitment . Despite the strong physiological rationale and preliminary human studies showing improvement in oxygenation two recent large clinical trials of HFOV in patients with moderate/severe ARDS failed to show any improvement in survival and have questioned safety of HFOV.

Prone positioning has been used for many years to improve oxygenation in patients who require mechanical ventilatory support for management of the acute respiratory distress syndrome … Furthermore, several lines of evidence have shown that prone positioning could prevent ventilator-induced lung injury."

alternating between supine and prone positioning appeared to improve lung recruitability in a small cohort of mechanically ventilated patients with severe DENGUE,LEPTOSPIRA,SWINEFLU infection who developed acute respiratory distress syndrome."

The acute respiratory distress syndrome (ARDS) previously had a mortality rate greater than 50 percent Mortality has since declined but the precise mortality rate is uncertain because estimates tend to be higher in observational studies than randomized trials No single change in the management of ARDS can explain the decrease in mortality, which is likely due to multiple factors (improved approaches to mechanical ventilation and supportive care)Management.

Key components of supportive care include appropriate use of sedatives, careful hemodynamic management, nutritional support, control of blood glucose, expeditious evaluation and treatment of nosocomial pneumonia, and prophylaxis against deep vein thrombosis (DVT) and gastrointestinal (GI) bleeding. When ARDS has been precipitated by a steroid-responsive process (eg, acute eosinophilic pneumonia), systemic glucocorticoid therapy

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

should be administered. Similarly, glucocorticoids may also be administered to patients with ARDS who have refractory sepsis or community-acquired pneumonia if they meet indications

In addition, for most patients who are relatively early in the disease course (within 14 days of onset) who have persistent or refractory moderate to severe ARDS (partial arterial pressure of oxygen/fraction of inspired oxygen [PaO_2/FiO_2] ratio <200) despite initial management with standard therapies, including low tidal volume ventilation, we recommend glucocorticoid therapy A typical regimen is methylprednisolone 1 mg/kg per day for 21 to 28 days followed by a taper or dexamethasone 20 mg IV once daily for five days followed by 10 mg once daily for five days. We do not routinely use glucocorticoids in patients who have less severe ARDS and we avoid their use in patients who have persistent ARDS beyond 14 days based upon limited data suggesting glucocorticoids may be harmful in this setting .

Petersson *et al.* provides us with a physiologic study describing, in anesthetized human volunteers, the effects of prone positioning and the application of 10 cm H^2O positive end-expiratory pressure (PEEP) on the regional distribution of pulmonary ventilation and perfusion.1This article creates a complete formulation of the pulmonary ventilation and perfusion in the prone position.

In the supine position, at 0 cm H^2O PEEP, the size of the alveolar units decreases exponentially from ventral (nondependent) to dorsal (dependent) lung regions.2This indicates that the distending forces of the lung (*i.e.* , the difference between the alveolar and the pleural pressure) decreases along the ventral-to-dorsal axis. The increase of pleural pressure close to the dependent lung regions is commonly considered the result of the push of the abdominal organs towards the lungs, which increases from the ventral to the dorsal regions.

In spontaneously breathing subjects, the engine of ventilation is the diaphragm, which displaces a huge amount in its dorsal (dependent) portion. This action is associated with a more favorable position of the dependent alveolar units along their pressure-volume curves and accounts for the greater ventilation observed in the most dependent lung regions. During anesthesia and paralysis, however, the diaphragm acts as a passive flaccid membrane. The insufflated gas is then preferentially distributed towards the ventral and nondependent lung areas.Because the regional distribution of lung perfusion is greater in the dependent lung regions, the final result is that mechanical ventilation, at 0 cm H^2O PEEP, is associated with some degree of ventilation-to-perfusion (V^A/Q) mismatch. This result is consistent with both the gravitational or fractal distribution theories of lung ventilation/perfusion. The addition of PEEP partially corrects this mismatch because it progressively moves ventilation towards the dependent lung regions whereas perfusion is further increased in the dependent lung regions.

In the prone position, at 0 cm H^2O PEEP, the size of alveolar units decreases with an exponential decay from dorsal (now nondependent) to ventral (now dependent) lung regions. This occurs to a much lower extent than that observed in the supine position. As a result, alveolar ventilation is more homogeneously distributed in the prone than in the supine position.Because lung perfusion redistributes towards the dependent regions, this results in a more homogenous V^A/Q matching at 0 cm H^2O PEEP, Surprisingly, after the addition of PEEP. found that perfusion increased in the ventral lung regions (now dependent), whereas the distribution of alveolar ventilation remained unchanged. Consequently, the authors claimed that V^A/Q matching was decreased by the addition of PEEP in the

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

prone position and suggested that lower PEEP levels might be preferred in the prone position compared with the levels of PEEP used in the supine position.

This conclusion may be incorrect when a patient has underlying acute lung injury. Because patients with acute lung injury often have severe hypoxemia resistant to typical therapies, Bryan suggested that prone positioning might lead to improved oxygenation. His prediction was fully confirmed in most of the studies subsequently published, which undoubtedly showed that in approximately 70% of patients with acute respiratory distress syndrome (ARDS), prone position–always applied in association with some degree of PEEP–improves oxygenation. Therefore, there is clearly a difference between normal lungs; for example, a deterioration of V^A/Q was observed by the current authors after 10 cm H^2O PEEP was added to the patients in the prone position.

The explanation for the improvement of V^A/Q in patients with ARDS in the prone position involves understanding the distribution of edema in the diseased lungs. In patients with ARDS, the mass of the lung with the edema may be increased to 300% of that of normal lungs.Therefore, the dependent lung regions in ARDS patients are compressed from the abnormal weight of the lung tissue above (nondependent) in the supine position. 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.When lung perfusion is substantially unmodified, the overall V^A/Q matching improves as new pulmonary units are recruited for more effective gas exchange.

This is probably the primary mechanism 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. Sadly, there can be negative consequences to prone positioning, including a possible increase in chest wall stiffness. The reduced chest wall compliance leads, in the case of pressure-controlled ventilation, to an initial reduction in transpulmonary pressure (*i.e.* , decreased tidal volume) or, in the case of volume-controlled ventilation, to an increase in plateau airway pressure. The overall balance of the positive and negative effects of the prone position can be observed by looking at the variation in arterial carbon dioxide. Independent of oxygenation changes, a decrease in arterial carbon dioxide indicates a recruitment of lung parenchyma, whereas an increase in arterial carbon dioxide may indicate a large increase in chest wall stiffness.

We believe that the most recent clinical trial of prone ARDS patients may provide some insights about the relationship between PEEP and the prone position.In that study, the patients that had been randomized to the prone-arm were allowed to undergo a variation in the ventilator settings aimed towards a less dangerous ventilation, if the oxygenation improved. Two maneuvers were allowed: first, a reduction of inspired oxygen fraction, and second, a reduction of PEEP, with a target arterial partial pressure of oxygen between 70–90 mmHg. The results clearly showed an identical level of PEEP between the two arms, suggesting that a decrease in PEEP was not possible in the prone ARDS patients.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

These data from prone ARDS patients, contrast with the findings observed by Petersson *et al.* in normal patients.The comparison of the results suggest that in ARDS patients, reductions of PEEP are inappropriate, at least when V^A/Q matching and systemic oxygenation are being evaluated.

Finally, although the article by Petersson *et al.* , , have focused on gas exchange, there may be an effect from prone positioning in ARDS patients on their survival. The survival benefit of prone positioning during ARDS is probably a result of a decrease in the harmful effects of mechanical ventilation. 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 should decrease ventilator-induced lung injury. As a matter of fact, all the meta-analyses performed on prone positioning of ARDS patients, so far, agree with two major points: (1) In all patients, a systemic oxygenation improvement is observed, and this is obviously greater in the most hypoxemic patients; and (2) in the most severe ARDS patients, when lung dishomogeneity is the greatest, prone positioning appears to provide about a 10% more survival benefit.

RESULTS

out of 260 patients with ARDS, only 79 patients were eligible and taken for prone position study . twenty two-patients were diagnosed as leptospirosis, eight as dengue. others 49. The most common cause of ARDS is **sepsis**. Next vomiting leads to aspiration , near-drowning episodes, ICU stay, and nosocomial infections did not differ significantly, but mortality at 28 days was significantly lower in patients put on prone position(22% vs 40%,)when compared to conventional positions. study bias cannot be ruled out because the comparative arm have more severe and contra indication cases for prone position. second, large scale studies are required to confirm and recommend the prone position mechanical ventilation as first line of management

cause	mildARDS	moderateARDS	TOTAL
DENGUE	03	05	08
LEPTOSPIROSIS	10	04	14
SEPSIS	11	08	19
ASPIRATION	05	16	21
NEAR DROWNING	05	12	17
	34	45	79

DISCUSSION

Prone positioning was first proposed in the 1970s as a method to improve gas exchange in ARDS. Subsequent observations of dramatic improvement in oxygenation with simple patient rotation motivated the next several decades of research. This work elucidated the physiological mechanisms underlying changes in gas exchange and respiratory mechanics with prone ventilation. However, translating physiological improvements into a clinical benefit has proved challenging; several contemporary trials showed no major clinical benefits with prone

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

positioning. By optimizing patient selection and treatment protocols, the recent Proning Severe ARDS Patients (PROSEVA) trial demonstrated a significant mortality benefit with prone ventilation.

Recommendations for Prone Ventilation

Who to place in prone position? • Patients with severe ARDS (Pao_2/Fio_2 < 200 mm Hg) • Early in the course (ideally within 48 h) • Best outcomes reported when prone positioning is used in combination with *both* low tidal volume ventilation (6 cc/kg) and neuromuscular blockade	Who not to place in prone position? • Patients with facial/neck trauma or spinal instability • Patients with recent sternotomy or large ventral surface burn • Patients with elevated intracranial pressure • Patients with massive hemoptysis • Patients at high risk of requiring CPR or defibrillation
How to place patient in prone position? • Requires 3-5 people, close attention to endotracheal tube (ETT) and central lines • Preparation: preoxygenation, empty stomach, suction ETT/oral cavity, remove ECG leads and reattach to back, repeated zeroing of hemodynamic transducers • Support and frequently reposition pressure points: face, shoulder, anterior pelvis	Potential complications • Temporary increase in oral and tracheal secretions occluding airway • ETT migration or kinking • Vascular catheter kinking • Elevated intra abdominal pressure • Increased gastric residuals • Facial pressure ulcers, facial edema, lip trauma from ETT, brachial plexus injury (arm extension)
How long to have patient in prone position each day? • at least 16 hours of daily proning • Long prone positioning sessions likely avoid derecruitment	When to stop? • prone positioning was stopped when Pao_2/Fio_2 remained > 150 mm Hg 4 h after supinating (with PEEP < 10 cm H_2O and Fio_2 < 0.6) • continuing prone positioning until clear improvement in gas exchange, mechanics, and overall clinical course.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

CONCLUSION

PRONE POSITIONING IN ARDS should be done early, IN MILD , MODERATE ARDS with experienced staff to avoid logistical complications, and at extended durations (≥ 16 h/d). For patients who fall outside these relatively narrow criteria, the clinician must balance the appealing physiological rationale behind prone positioning against the equivocal evidence base for patients with less severe lung injury, late-stage ARDS, or non-ARDS conditions.

REFERENCES

1. Chambers J., Manley L., Nolen J.E., Pruitt K., Weaver T., Maple D. American Lung Association; New York, NY: 2008. American Lung Association: lung disease data]

2. Esteban A., Ferguson N.D., Meade M.O. Evolution of mechanical ventilation in response to clinical research. Am J Respir Crit Care Med. 2008;177(2):170–177.

3. Cheung A.M., Tansey C.M., Tomlinson G. Two-year outcomes, health care use, and costs of survivors of acute respiratory distress syndrome. Am J Respir Crit Care Med. 2006;174(5):538–5444. Ashbaugh D.G., Bigelow D.B., Petty T.L., Levine B.E. Acute respiratory distress in adults. Lancet. 1967;290(7511):319–323. 5. Bryan A.C. Comments of a devil's advocate. Am Rev Respir Dis. 1974;110(62):143–1446. Piehl M., Brown R. Use of extreme position changes in acute respiratory failure. Crit Care Med. 1976;4(1):13–14. 7. Mancebo J., Fernández R., Blanch L. A multicenter trial of prolonged prone ventilation in severe acute respiratory distress syndrome. Am J Respir Crit Care Med. 2006;173(11):1233–1239. 8. Guérin C., Gaillard S.A., Lemasson S. Effects of systematic prone positioning in hypoxemic acute respiratory failure: a randomized controlled trial. JAMA. 2004;292(19):2379–2387

9. Guérin C., Reignier J., Richard J.C. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med. 2013;368(23):2159–2168.