Air Medical Journal 35 (2016) 59–62

Contents lists available at ScienceDirect

Air Medical Journal

journal homepage: http://www.airmedicaljournal.com/

Critical Care Update

Acute Respiratory Distress Syndrome and Lung Protection

David J. Dries, MSE, MD

Hypoxemic respiratory failure, frequently termed acute respiratory distress syndrome (ARDS), is 1 of the classic problems confronting the clinician using mechanical ventilation. Multiple trials over recent decades have identified the manipulation of mean airway pressure as the essential intervention to improve oxygenation. The easiest method to increase mean airway pressure (that the clinician can titrate) is increasing the positive end-expiratory pressure (PEEP). We have also learned that alveolar pressure rises with a consistent tidal volume and increasing PEEP. Key studies reviewed in the last column identify the value of reducing tidal volume and maintaining static alveolar pressure, measured as plateau pressure less than 30 cm H_2O. If tidal volume is reduced, patients may develop a degree of hypercarbia because of reduced minute ventilation (defined as respiratory rate $\times$ tidal volume). In general, reduced minute ventilation will cause the pH to decrease. Most critical care providers would accept a pH as low as 7.20 reflecting reduced minute ventilation and respiratory acidosis. Clinician must strike a balance between adequate ventilation and acid/base protection for the patient and the need to increase mean airway pressure while avoiding excessive airway pressure through the increase in PEEP with a reduction in the tidal volume.

The articles discussed in this column describe current definitions for ARDS, review important comanagement strategies, and present physiologic causes for injury to the lungs by mechanical ventilation as reflected in the failure of recent trials involving high-frequency oscillatory ventilation (HFOV).

Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. *Lancet*. 1967;2:319-323.

Bernard GR, Artigas A, Brigham KL, et al. The American-European Consensus Conference on ARDS: definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med*. 1994;149:818-824.

ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307:2526-2533.

Angus DC. The acute respiratory distress syndrome: what's in a name? *JAMA*. 2012;307:2542-2544.

ARDS was first described in 1967. The 1967 report includes a series of 12 patients who were cared for in a single intensive care unit. The patients had been admitted for a variety of problems but all shared common features of persistent tachypnea and hypoxemia accompanied by infiltrates on chest x-rays. Lung stiffness compromised mechanical ventilation, and survival was poor. Soon other centers were reporting similar patients, and attempts began to define this syndrome.

In 1994, an American-European Consensus Conference developed criteria for acute respiratory distress and related syndromes. There were 4 key components. First, the syndrome must present acutely. Second, hypoxemia must be present measured as an arterial partial pressure of oxygen to fraction of inspired oxygen ratio (PaO_2/FiO_2) less than 200 mm Hg (the ratio is greater than 450 mm Hg in healthy persons). Third, bilateral infiltrates must be present on a chest x-ray. Fourth, findings cannot be caused by cardiac failure as reflected by elevated filling pressures (pulmonary capillary wedge pressure greater than 18 mm Hg). An additional concept introduced at this time was that of acute lung injury, which shared a similar pathogenesis. Acute lung injury patients had a higher PaO_2/FiO_2 ratio (200-300 mm Hg).

These criteria had limited effectiveness when applied in practice. Definitions were unclear. Oxygenation criteria could be easily manipulated by the use of PEEP. Chest radiograph interpretation was highly subjective. Cardiac exclusion criteria were unreliable in part because the pulmonary artery catheter fell from favor. Finally, the term acute lung injury was used inconsistently, and there were no criteria for patients with a greater severity of illness.

In 2011, the European Society of Intensive Care Medicine convened an international expert panel to revisit the definition of ARDS. The group met in Berlin; thus, the name “Berlin Criteria.” More rigorous statistical analysis was applied to a data set of over 4,000 patients with presumed ARDS recruited from clinical trials and observational cohorts in North America, Europe, and Australia. Therefore, the clinical data driving the definition process was more rigorous than in 1994. The new criteria attempted to be more specific in the definition of ARDS. First, “acute” was defined as 1 week or less. Second, the term “acute lung injury” was abandoned. Third, measurement of the PaO_2/FiO_2 ratio was changed to require a specific minimum amount of PEEP. Fourth, 3 categories of ARDS were proposed (mild, moderate, and severe) based on the PaO_2/FiO_2 ratio. Fifth, chest radiograph criteria were clarified to improve reading consistency. Sixth, the pulmonary capillary wedge pressure criterion was removed, and clarity was added to improve the ability to exclude cardiac causes of bilateral infiltrates on chest x-rays (Table 1).

When the Berlin criteria were compared with the original 1994 definition of ARDS, neither approach was a particularly good

1067-991X/$36.00

http://dx.doi.org/10.1016/j.amj.2015.12.011

Table 1
Berlin Definition of Acute Respiratory Distress Syndrome

- Within 1 week of inciting insult
- Bilateral chest x-ray infiltrates not *fully* explained by fluid overload or heart failure
- Grades of severity:
  Mild: 200 mm Hg < $PaO_2/FiO_2 \leq$ 300 mm Hg with PEEP $\geq$ 5 cm H_2O
  Moderate: 100 mm Hg $PaO_2/FiO_2 \leq$ 200 mm Hg with PEEP $\geq$ 5 cm H_2O
  Severe: PaO_2/FiO_2 < 100 mm Hg with PEEP $\geq$ 5 cm H_2O

PaO_2 = arterial partial pressure of oxygen; FiO_2 = fraction of inspired oxygen; PEEP = positive end-expiratory pressure.

predictor of death (area under the receiver operating curve of 0.57 for the final Berlin definition vs. 0.536 for the 1994 definition) because the goal was to define ARDS not predict mortality, which may be driven by factors other than lung injury. However, having 3 categories of severity for ARDS may facilitate clinical research, resource allocation, and triage.

Lee JM, Bae W, Lee YJ, Cho YJ. The efficacy and safety of prone positional ventilation in acute respiratory distress syndrome: updated study-level meta-analysis of 11 randomized controlled trials. *Crit Care Med*. 2014;42:1252-1262.

Prone positioning during mechanical ventilation for ARDS can be supported by physiologic studies. Prone positioning redirects blood flow away from collapsed, dependent lung regions and, by changing chest wall mechanics, improves global pulmonary expansion. Therefore, alternating prone and supine positioning improves ventilation perfusion matching and increases the volume of each lung available for gas exchange. However, this intervention is likely most successful when used early in the course of ARDS and appears to be more efficacious when periods of prone ventilation are longer (probably in excess of 10 hours at a time).

A major concern in proning patients for respiratory failure is complications associated with this procedure. Prone positioning increases the risk of pressure ulcers and major airway problems. Among the airway issues described are unplanned extubation, selective intubation into a main stem bronchus, and endotracheal tube obstruction. Endotracheal tube obstruction is typically caused by secretions because secretion mobilization is enhanced in the setting of prone ventilation. In this meta-analysis, the authors found no significant association between prone positioning and the prevalence of ventilator-associated pneumonia, loss of venous or arterial access, thoracostomy tube problems, pneumothorax, cardiac arrest, or clinically significant cardiac rhythm changes. Major airway problems increased with prone positioning, but none of the included trials reported fatal consequences from a major airway problem.

The positive effects of prone positioning are clearer in patients with more severe lung injury. The use of lung protective ventilation including small tidal volumes also appeared to increase the effectiveness of prone ventilation. In general, patients selected for prone positioning are most likely to show benefit when the PaO_2/FiO_2 ratio is less than 150 to 200 mmHg. Despite the inclusion of patients with varying underlying disease problems, these authors did not identify a particular patient group that should not be considered for prone ventilation.

Grissom CK, Hirshberg EL, Dickerson JB, et al. Fluid management with a simplified conservative protocol for the acute respiratory distress syndrome. *Crit Care Med*. 2015;43:288-295.

National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Wiedemann HP, Wheeler AP, et al. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med*. 2006;354:2564-2575.

Conservative fluid management improves ventilator-free days and oxygenation in patients with ARDS. In the Fluid and Catheter Treatment Trial (FACTT) of the ARDSNet investigators, patients were randomized and managed with either a conservative fluid management protocol or a liberal fluid administration protocol. Both liberal and conservative fluid protocols provided instructions for the management of subjects with a mean arterial pressure greater than 60 mm Hg who had not received vasopressors for at least 12 hours. The conservative fluid protocol targeted a central venous pressure (CVP) of less than 4 mm Hg or a pulmonary artery occlusion pressure of less than 8 mm Hg, whereas the liberal protocol targeted a CVP of 10 to 14 mm Hg or a pulmonary artery occlusion pressure of 14 to 18 mm Hg. Management with the conservative fluid protocol resulted in significantly lower cumulative fluid balance over the 7-day study period. There was no difference in 60-day mortality between conservative and liberal fluid administration, but the conservative fluid administration group had more ventilator-free days and improved oxygenation and lung injury scores.

Next, the ARDSNet investigators developed a simplified conservative fluid management protocol. The simplified conservative fluid protocol excluded many of the alternative pathways in the previous conservative fluid protocol based on ineffective circulation because the clinical examination findings of ineffective circulation did not correspond with filling pressure parameters. The simplified conservative fluid protocol included 3 pathways determined by CVP and urine output: furosemide administration, fluid bolus, or observation without the use of furosemide or fluid. The simplified conservative fluid protocol (FACTT Lite) contained instructions to hold interventions until the subject had achieved at least 12 hours of mean arterial pressure greater than 60 mm Hg off vasopressors. Fluid management of subjects in shock was left to the discretion of the clinical team (Table 2).

FACTT Lite was designed as an easier protocol to implement in the intensive care unit than the original FACTT conservative strategy. Eliminating categories of ineffective circulation as defined by clinical examination findings and condensing target CVP ranges from 4 to 3, the FACCT Lite protocol required less training and was readily implemented.

Overall, the FACTT Lite protocol had greater cumulative fluid balance than the stricter original conservative fluid protocol. When patients who did not meet criteria for shock at the initiation of the 7-day fluid management study were analyzed, the FACTT Lite patients had a cumulative positive fluid balance of approximately 50 mL, whereas the FACTT conservative patients had a negative cumulative fluid balance of approximately 1,250 mL. The FACTT liberal fluid group had a positive cumulative fluid balance of approximately 5,250 mL over the 7 days of the protocol. However, the results of this review indicate that the FACTT Lite protocol was safe and had equivalent ventilator-free days, intensive care unit–free days, incidence of acute kidney injury, and adjusted 60-day mortality when compared with the more complex conservative fluid protocol. FACTT Lite, as summarized in this article, can be used as a simplified and safe alternative to a traditional conservative fluid management strategy in patients with ARDS. It is still best to try to keep the ARDS patient “dry.”

Young D, Lamb SE, Shah S, et al. High-frequency oscillation for acute respiratory distress syndrome. *N Engl J Med*. 2013;368:806-813.