Does Spontaneous Breathing Produce Harm in Patients With the Acute Respiratory Distress Syndrome?

In this issue of RESPIRATORY CARE, Leray et al[1] describe the case of a patient with acute respiratory distress syndrome (ARDS) who developed pneumomediastinum while receiving a tidal volume (V_T) of 14 mL/kg on pressure-support ventilation. This case raises several provocative questions. Can spontaneously breathing patients injure their own lungs? Should transpulmonary pressure be routinely assessed? Should spontaneous breathing modes be used in patients with ARDS?

SEE THE CASE REPORT ON PAGE 770

Nearly 25 years ago, some interesting studies related to ventilator-induced lung injury were conducted by Dreyfuss et al.[2] These investigators subjected rats to large or small V_T ventilation, using identical peak airway pressures (45 cm H_2O) in both groups. Low-V_T with high airway pressure was produced by thoracoabdominal strapping during positive airway pressure ventilation. The rats subjected to high-V_T and high airway pressure ventilation quickly developed permeability pulmonary edema (ventilator-induced lung injury). However, the animals that underwent thoracoabdominal strapping and were ventilated with high airway pressure but a normal V_T did not develop edema, and the ultrastructure of their lungs appeared normal. Relevant to the paper by Leray et al,[1] rats were also ventilated with a large V_T by means of an iron lung. Permeability edema developed in these animals, even when proximal airway pressure was atmospheric but V_T was high.

Exercise-induced pulmonary hemorrhage occurs commonly in thoroughbred race horses.[3] The mechanism for this injury is unclear, but perhaps it is related, in part, to parenchymal injury due to large V_T. Lung inflation may contribute to capillary wall tension and therefore to stress failure, resulting in damage to capillary endothelial cells.[4] Hopkins et al[5] performed bronchoalveolar lavage in 6 healthy athletes who had a history suggestive of pulmonary hemorrhage, 1 hour after a 7-min cycling race simulation, and in 4 normal sedentary control subjects who did not exercise before bronchoalveolar lavage. The athletes had higher concentrations of red blood cells and total protein in bronchoalveolar lavage fluid than did the control subjects. Could the pulmonary hemorrhage be related to high-V_T during exercise?

Since publication of the landmark ARDS Network study[6] more than 10 years ago, V_T and alveolar pressure limitation have become standard of care. However, studies such as those by Talmor et al[7] and Chiumello et al[8] have drawn attention to an important point of respiratory physiology. That is, transpulmonary pressure determines alveolar stretch and the potential for lung injury. Transpulmonary pressure is determined by the difference between alveolar pressure (measured as plateau pressure) and pleural pressure (measured as esophageal pressure). The study by Chimello et al[8] suggests that transpulmonary pressures over 27 cm H_2O may cause harm. Talmor et al[7] have suggested that, in patients with ARDS, PEEP should be titrated to transpulmonary pressure using an esophageal balloon. Indeed, those authors[7] have demonstrated that this approach is safe and may improve oxygenation.

These studies suggest that, in passive ventilated patients, a higher pleural pressure may be protective. Can we therefore conclude that a lower pleural pressure resulting from spontaneous breathing could be harmful? This has not been well studied, and the answer to this question is speculative. However, imagine a patient who is being ventilated with a pressure-targeted mode such as pressure control, pressure support, or airway pressure-release ventilation. The ventilator will provide flow to maintain airway pressure constant, and the spontaneous breathing efforts of the patient will lower the pleural pressure, thus increasing transpulmonary pressure. The pressure support settings used by Laray et al[1] probably resulted in greater transpulmonary pressure than that achieved during volume-controlled ventilation. As illustrated in Figure 1, a potentially injurious transpulmonary pressure could be generated using an airway pressure that might otherwise be considered safe. This is theoretical, however, and the extent to which this occurs clinically is unknown. This is an area of much-needed research. It is worth noting, however, that Neumann et al[9] have reported large pleural pressure swings with airway pressure-release ventilation.

Does one need to insert an esophageal balloon catheter to estimate transpulmonary pressure during spontaneous breathing? It is probably not needed in most cases. Use of esophageal pressure to estimate pleural pressure is not without technical problems and problems of interpretation.[10] The use of esophageal pressure to estimate pleural

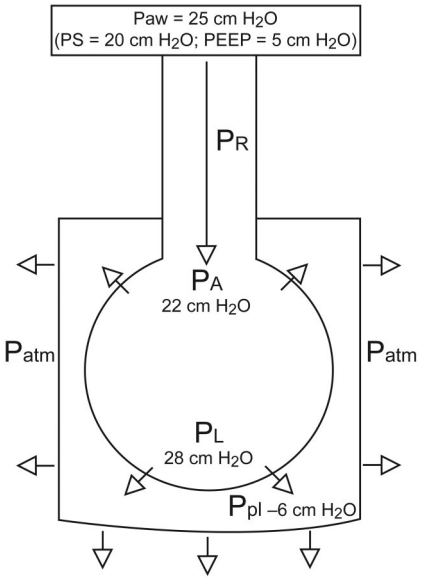

Fig. 1. Estimate of transpulmonary pressure using settings similar to that in the report by Leray et al.[1] P_{aw} = proximal airway pressure. PS = pressure support. PEEP = positive end-expiratory pressure. P_R = pressure drop due to airways resistance. P_A = alveolar pressure. P_L = transpulmonary pressure. P_{atm} = atmospheric pressure. P_{pl} = pleural pressure.

pressure is confounded due to the pleural pressure gradient that is normally present, the weight of the mediastinum on the esophagus in supine patients, and the inhomogeneous disease process in patients with ARDS. Respiratory variation in central venous pressure, which is commonly available in mechanically ventilated patients, may provide information about pleural pressure changes during the respiratory cycle. However, this approach does not provide the absolute pleural pressure.[11] Perhaps most important, and easiest to monitor at the bedside, is the V_T that results from the patient's inspiratory effort. If the V_T is not excessive, in most cases the transpulmonary pressure will be acceptable. Regardless of the ventilator mode, in critically ill patients the V_T target should be 6 mL/kg ideal body weight for patients with ARDS, and should be < 10 mL/kg for others.[12,13] For severe ARDS, recent evidence suggests that the V_T target should be even lower than 6 mL/kg.[14]

A proposed benefit of pressure-targeted modes is better patient-ventilator interaction and the potential for less sedation.[15] Less sedation is associated with decreased time on the ventilator[16,17] and improved ability to participate in care, including mobilization and ambulation.[18-20] Spontaneous breathing also offers the advantage of better ventilation of dorsal lung units, resulting in improved alveolar recruitment and arterial oxygenation. Whether the potential benefits of spontaneous breathing translate into improved patient outcomes is unknown. The peer-reviewed literature does not give us clear guidance on whether a patient with ARDS should be deeply sedated or allowed to breathe spontaneously. As recently reviewed by Forel et al,[21] there is evidence that paralysis might be beneficial early in the course of severe ARDS. In one study, paralysis for the first 48 hours following intubation in patients with ARDS led to a lower mortality.[22] In a patient with ARDS who is generating a high V_T due to spontaneous breathing, which is the greatest harm? Is it lung injury due to the high V_T or complications related to sedation and paralysis that may be required to allow a lower V_T? Based on available evidence, the answer remains elusive.

The case reported by Leray et al[1] shines light on a common clinical conundrum. Are spontaneous modes of ventilation harmful in ARDS? Mindful that a case report is the lowest level of evidence, practice should not be dictated by a single anecdote. But this case does draw attention to the potential for lung injury when high V_T is delivered, regardless of the ventilator mode.

Ulrich H Schmidt MD PhD
Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts

Dean R Hess PhD RRT FAARC
Respiratory Care
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts

REFERENCES

1. Leray V, Bourdin G, Flandreau G, Bayle F, Wallet F, Richard JC, Guérin C. A case of pneumomediastinum in a patient with acute respiratory distress syndrome on pressure support ventilation. Respir Care 2010;55(6):770-773.
2. Dreyfuss D, Soler P, Basset G, Saumon G. High inflation pressure pulmonary edema: respective effects of high airway pressure, high tidal volume, and positive end-expiratory pressure. Am Rev Respir Dis 1988;137(5):1159-1164.
3. Birks EK, Durando MM, McBride S. Exercise-induced pulmonary hemorrhage. Vet Clin North Am Equine Pract 2003;19(1):87-100.
4. West JB, Tsukimoto K, Mathieu-Costello O, Prediletto R. Stress failure in pulmonary capillaries. J Appl Physiol 1991;70(4):1731-1742.
5. Hopkins SR, Schoene RB, Henderson WR, Spragg RG, Martin TR, West JB. Intense exercise impairs the integrity of the pulmonary blood-gas barrier in elite athletes. Am J Respir Crit Care Med 1997; 155(3):1090-1094.
6. NHLBI Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute respiratory distress syndrome. N Engl J Med 2000; 342(18): 1301-1308.

7. Talmor D, Sarge T, Malhotra A, O'Donnell CR, Ritz R, Lisbon A, et al. Mechanical ventilation guided by esophageal pressure in acute lung injury. N Engl J Med 2008;359(20):2095-2104.
8. Chiumello D, Carlesso E, Cadringher P, Caironi P, Valenza F, Polli F, et al. Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med 2008;178(4):346-355.
9. Neumann P, Golisch W, Strohmeyer A, Buscher H, Burchardi H, Sydow M. Influence of different release times on spontaneous breathing pattern during airway pressure release ventilation. Intensive Care Med 2002;28(12):1742-1749.
10. Talmor DS, Fessler HE. Are esophageal pressure measurements important in clinical decision-making in mechanically ventilated patients? Respir Care 2010;55(2):162-174.
11. Hess DR, Bigatello LM. The chest wall in acute lung injury/acute respiratory distress syndrome. Curr Opin Crit Care 2008;14(1):94-102.
12. Yilmaz M, Keegan MT, Iscimen R, Afessa B, Buck CF, Hubmayr RD, Gajic O. Toward the prevention of acute lung injury: protocol-guided limitation of large tidal volume ventilation and inappropriate transfusion. Crit Care Med 2007;35(7):1660-1667.
13. Schultz MJ, Haitsma JJ, Slutsky AS, Gajic O. What tidal volumes should be used in patients without acute lung injury? Anesthesiology 2007;106(6):1226-1231.
14. Terragni PP, Rosboch G, Tealdi A, Corno E, Menaldo E, Davini O, et al. Tidal hyperinflation during low tidal volume ventilation in acute respiratory distress syndrome. Am J Respir Crit Care Med 2007;175(2):160-166.
15. MacIntyre NR, Sessler CN. Are there benefits or harm from pressure targeting during lung-protective ventilation? Respir Care 2010;55(2):175-183.
16. Girard TD, Kress JP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. Lancet 2008;371(9607):126-134.
17. Strøm T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. Lancet 2010;375(9713):475-480.
18. Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet 2009;373(9678):1874-1882.
19. Bourdin G, Barbier J, Burle JF, Durante G, Passant S, Vincent B, et al. The feasibility of early physical activity in intensive care unit patients: a prospective observational one-center study. Respir Care 2010;55(4):400-407.
20. Hopkins RO. Early activity in the ICU: beyond safety and feasibility. Respir Care 2010;55(4):481-484.
21. Forel JM, Roch A, Papazian L. Paralytics in critical care: not always the bad guy. Curr Opin Crit Care 2009;15(1):59-66.
22. Papazian L, Forel J, Gacouin A, et al. Systematic two-day muscle relaxants course in the early phase of severe acute respiratory distress syndrome. A multicenter randomized controlled trial. Intensive Care Medicine 2009;35(Suppl 1):S6.

Dr Hess has disclosed relationships with Respironics, Pari, Impact, and Novartis. Dr Schmidt has disclosed no conflicts of interest.

Correspondence: Ulrich H Schmidt MD PhD, Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, 55 Fruit Street, Gray 4, Boston MA 02114. E-mail: uschmidt@partners.org.