

## JOURNAL CLUB CRITIQUE

# The esophagus ... not just for food anymore?

Matthew Zaccheo<sup>1</sup>, Eric B Milbrandt<sup>2</sup>, and Arthur Boujoukos<sup>\*3</sup>

University of Pittsburgh Department of Critical Care Medicine: Evidence-Based Medicine Journal Club, edited by Sachin Yende

### Expanded Abstract

#### Citation

Talmor D, Sarge T, Malhotra A, O'Donnell CR, Ritz R, Lisbon A, Novack V, Loring SH: Mechanical ventilation guided by esophageal pressure in acute lung injury. *N Engl J Med* 2008, 359:2095-2104 [1].

#### Background

Survival of patients with acute lung injury or the acute respiratory distress syndrome (ARDS) has been improved by ventilation with small tidal volumes and the use of positive end-expiratory pressure (PEEP); the optimal level of PEEP has been difficult to determine. In this pilot study, we estimated transpulmonary pressure with the use of esophageal balloon catheters. We reasoned that the use of pleural-pressure measurements, despite the technical limitations to the accuracy of such measurements, would enable us to find a PEEP value that could maintain oxygenation while preventing lung injury due to repeated alveolar collapse or overdistention.

#### Methods

**Objective:** To evaluate the effectiveness of using an esophageal balloon catheter to measure pleural pressure and guide PEEP titration to achieve normal physiologic parameters in individual patients.

**Design:** Single center, randomized-controlled pilot trial.

**Setting:** Medical and surgical ICUs at Beth Israel Deaconess Medical Center.

**Subjects:** 61 patients with acute lung injury or ARDS as defined by the American-European Consensus Conference definition.

**Intervention:** Patients with acute lung injury or ARDS were randomly assigned to undergo mechanical ventilation with PEEP adjusted according to measurements of esophageal pressure (the esophageal-pressure-guided group) or according to the Acute Respiratory Distress

Syndrome Network standard-of-care recommendations (the control group).

**Outcomes:** The primary end point was improvement in oxygenation at 72 hours after randomization. Secondary end points included indexes of lung mechanics and gas exchange, number of ventilator free days, length of ICU stay, and death at 28 days and 180 days.

#### Results

The study reached its stopping criterion and was terminated after 61 patients had been enrolled. The ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen at 72 hours was 88 mmHg higher in the esophageal-pressure-guided group than in the control group (95% confidence interval, 78.1 to 98.3;  $P = 0.002$ ). This effect was persistent over the entire follow-up time (at 24, 48, and 72 hours;  $P = 0.001$  by repeated-measures analysis of variance). Respiratory-system compliance was also significantly better at 24, 48, and 72 hours in the esophageal-pressure-guided group ( $P = 0.01$  by repeated-measures analysis of variance).

#### Conclusions

As compared with the current standard of care, a ventilator strategy using esophageal pressures to estimate the transpulmonary pressure significantly improves oxygenation and compliance. Multicenter clinical trials are needed to determine whether this approach should be widely adopted. (ClinicalTrials.gov number, NCT00127491.)

#### Commentary

In 2000, the landmark ARDS Network Trial was published [2]. It concluded that low tidal volume ventilation led to a significant decrease in mortality [2]. In this trial, positive end expiratory pressure (PEEP) was adjusted according to a scale based on fraction of inspired oxygen ( $\text{FiO}_2$ ) requirements. This did not allow for the appreciation of individual patient physiology with regard to chest wall or lung mechanics. The actual levels of PEEP used were relatively low (5 to 13  $\text{cmH}_2\text{O}$ ). Following the publication of the ARDS Network Trial, three additional large randomized controlled trials were concluded comparing the effects of higher PEEP and recruitment strategies on clinical outcomes and mortality. The

\*Correspondence: boujoukosaj@upmc.edu

<sup>3</sup>Associate Professor, Department of Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA

Full list of author information is available at the end of the article

ALVEOLI study [3], LOVS study [4], and the EXPRESS study [5] utilized the universally accepted low tidal volume strategy, but implemented higher levels of PEEP (10 to 20 cmH<sub>2</sub>O) to increase alveolar recruitment and improve oxygenation. These studies concluded that better arterial oxygenation and lung compliance were achieved with higher levels of PEEP. However, better arterial oxygenation and lung mechanics did not translate into any significant mortality benefit.

The disappointing results of the previous three studies may have been due in part to the fact that patients with ARDS have a non-homogenous lung injury pattern and a 'one size fits all' PEEP titration strategy may be not be adequate for all patients. For a given level of PEEP, transpulmonary pressures may vary widely from patient to patient. If the clinician could measure transpulmonary pressure at the bedside he/she may be able to find the 'best' individual PEEP to maintain oxygenation while minimizing atelectrauma and volutrauma.

In the critiqued pilot trial, Talmor, et al. evaluated a ventilator strategy using esophageal pressures to estimate actual transpulmonary pressures in individual patients, thus allowing for determination of 'best' individual PEEP. Critically-ill patients (80% ARDS/20% Acute Lung Injury) were randomized to either ARDS Network protocol ventilation or a ventilation strategy utilizing esophageal pressures to estimate individual patients' transpulmonary pressures and guide application of PEEP to maintain normal physiologic parameters. All patients had an esophageal balloon catheter placed allowing for the measurement of esophageal pressures during mechanical ventilation. Each patient underwent mechanical ventilation according to the treatment assignment. In the study arm, PEEP was titrated to maintain normal physiologic transpulmonary pressure (0 to 10 cmH<sub>2</sub>O at end expiration).

The study concluded that arterial oxygenation and respiratory system compliance improved in the esophageal-pressure guided group as compared with the control group. Consistent with all prior studies to date, there was no statistically significant difference in mortality between the treatment groups at 180 days. Additionally, there was no significant difference between groups with regard to ventilator-free days or length of ICU stay.

This study has several limitations. It was a single-center study utilizing physiologic expert staff. The sample size was small. The findings cannot be generalized until confirmed in a larger trial powered to detect changes in clinical end points. This study does have significant appeal. Few clinicians question the physiologic effect of PEEP as it relates to arterial oxygenation, but optimal PEEP titration for individual patients remains elusive. Adjusting PEEP to maintain normal physiologic

transpulmonary pressure is a reasonable premise. However, measurement of true pleural pressure is not readily attainable at the bedside. In this sense, utilizing esophageal pressure to estimate pleural pressure seems reasonable. However, many assumptions must be made in order to accept that the pressure at one locus of the esophagus reliably reflects actual pleural pressure over the entire physiologic system. One must assume that the transmural pressure in the esophagus is 0 cmH<sub>2</sub>O and that actual pleural pressure is uniform throughout the entire thorax (unlikely in the setting of a non-homogenous lung injury pattern). In addition, a correction of 5 cmH<sub>2</sub>O was subtracted from the measured esophageal pressure in an attempt to account for the weight of mediastinal structures overlying the balloon in the esophagus. This correction is subject to much debate, as the exact correction factor for this artifact may be highly variable among supine, critically-ill patients. Prior research yielding the stated correction factor of 5 cmH<sub>2</sub>O was conducted in healthy subjects, maintained in an upright posture [6,7].

This study, using an invasive balloon catheter to guide PEEP titration, ultimately led to the same conclusion as all prior studies to date: increased levels of PEEP improve arterial oxygenation and lung compliance. However, better oxygenation does not convey a significant mortality benefit. When comparing the conclusions of the ALVEOLI, LOVS, and EXPRESS studies to the Talmor and colleagues study, it is realized that all use similarly higher levels of PEEP (10 to 20 cmH<sub>2</sub>O). This is in contrast to the PEEP used in the ARDS Network Trial (5 to 12 cmH<sub>2</sub>O). The question that remains unanswered is whether the improvement in oxygenation found in the Talmor, et al. study is a true reflection of a unique response to PEEP titration based on esophageal pressures or just a generic response to the utilization of higher PEEP overall.

## Recommendation

In conclusion, as compared with standard ARDS Network ventilation, a ventilation strategy using esophageal pressures to titrate PEEP improves arterial oxygenation and lung compliance. However, since improved oxygenation is not a surrogate end point for mortality, this study is not sufficient to recommend a change in current clinical practice. It seems reasonable to conduct further, larger, randomized trials to assess the clinical viability of utilizing this invasive technique.

## Competing interests

The authors declare no competing interests

## Author Details

<sup>1</sup>Clinical Fellow, Department of Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA. <sup>2</sup>Assistant Professor, Department of Critical Care Medicine, University of Pittsburgh School of

Medicine, Pittsburgh, Pennsylvania, USA. <sup>3</sup>Associate Professor, Department of Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA.

#### Competing interests

The authors declare that they have no competing interests.

Published: 5 November 2010

#### References

1. Talmor D, Sarge T, Malhotra A, O'Donnell CR, Ritz R, Lisbon A, Novack V, Loring SH: **Mechanical ventilation guided by esophageal pressure in acute lung injury.** *N Engl J Med* 2008, **359**:2095-2104.
2. The Acute Respiratory Distress Syndrome Network: **Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome.** *N Engl J Med* 2000, **342**:1301-1308.
3. The National Heart, Lung, and Blood Institute ARDS Clinical Trials Network: **Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome.** *N Engl J Med* 2004, **351**:327-336.
4. Meade MO, Cook DJ, Guyatt, GH, Slutsky AS, Arabi YM, Cooper DJ, Davies, AR, Hand LE, Zhou Q, Thabane L, Austin P, Lapinsky S, Baxter A, Russell J, Skrobik Y, Ronco JJ, Stewart TE: **Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: A randomized controlled trial.** *JAMA* 2008, **299**:637-645.
5. Mercat A, Richard JCM, Vielle B, Jaber S, Osman D, Diehl JL, Lefrant JY, Prat G, Richecoeur J, Nieszkowska A, Gervais C, Baudot J, Bouadma L, Brochard L: **Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: A randomized controlled trial.** *JAMA* 2008, **299**:646-655.
6. Washko GR, O'Donnell CR, Loring SH: **Volume-related and volume-independent effects of posture on esophageal and transpulmonary pressures in healthy subjects.** *J Appl Physiol* 2006, **100**:753-758.
7. Talmor D, Sarge T, O'Donnell CR, Ritz R, Malhotra A, Lisbon A, Loring SH: **Esophageal and transpulmonary pressures in acute respiratory failure.** *Crit Care Med* 2006, **34**:1389-1394.

doi:10.1186/cc9314

**Cite this article as:** Zaccheo M, et al.: The esophagus ... not just for food anymore? *Critical Care* 2010, **14**:326.