Journal of Critical Care xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

# Gas exchange and lung mechanics in patients with acute respiratory distress syndrome: Comparison of three different strategies of positive end expiratory pressure selection☆,☆☆

Ricardo Valentini, MD *, José Aquino-Esperanza, MD, Ignacio Bonelli, MD, Patricio Maskin, MD, Mariano Setten, RT, Florencia Danze, MD, Shiry Attie, MD, Pablo O. Rodriguez, MD

*Intensive Care Unit, Department of Medicine Instituto Universitario "Centro de Educación Médica e Investigaciones Clínicas" (CEMIC), Buenos Aires, Argentina*

ARTICLE INFO

*Keywords:*
ARDS
Lung mechanics
Mechanical ventilation
PEEP selection
Transpulmonary pressure

ABSTRACT

*Purpose:* The purpose of the study was to compare gas exchange and lung mechanics between different strategies to select positive end-expiratory pressure (PEEP) in acute respiratory distress syndrome (ARDS).
*Methods:* In 20 consecutive ARDS patients, 3 PEEP selection strategies were evaluated. One strategy was based on oxygenation using the ARDS network PEEP/fraction of inspired oxygen ($F_{IO_2}$) table; and two were based on lung mechanics, either PEEP titrated to reach a plateau pressure of 28 to 30 cm $H_2O$ as in the ExPress trial or best respiratory compliance method during a derecruitment maneuver. Gas exchange, airway pressures, stress index (SI), and end-expiratory transpulmonary pressure ($P_{tpe}$) and end-inspiratory transpulmonary pressure ($P_{tpi}$) values were assessed. Data are expressed as median (interquartile range [IQR]).
*Results:* Lower total PEEP levels were observed with the use of the PEEP/$F_{IO_2}$ table (8.7 [6-10] cm $H_2O$); intermediate PEEP levels, with the Best Compliance approach (13.0 [10.2-13.8] cm $H_2O$); and higher PEEP levels, with the ExPress strategy (16.5 [15.0-18.5] cm $H_2O$) ($P < .01$). $Pa_{O_2}$/$F_{IO_2}$ ratio was lower with the PEEP/$F_{IO_2}$ table. Oxygenation with Best Compliance approach and ExPress strategy was not different with lower plateau pressure in the former (23 [20-25] vs 30 [29-30] cm $H_2O$; $P < .01$). $Pa_{CO_2}$ was slightly higher with the ExPress method than the others 2 strategies. Negative $P_{tpe}$ was observed in 35% of the patients with the PEEP/$F_{IO_2}$ table, in 15% applying the Best Compliance, and in only 1 case with the ExPress method. Higher SI and $P_{tpi}$, with lower lung compliance, were obtained with ExPress strategy.
*Conclusions:* Using a best respiratory compliance approach resulted in better oxygenation levels without risk of overdistension according to SI and $P_{tpi}$, achieving a mild risk of lung collapse according to $P_{tpe}$.


## 1. Introduction

A lung-protective ventilation strategy based on low tidal volume ($V_T$) reduces mortality in acute respiratory distress syndrome (ARDS) [1]. The use of adequate positive end-expiratory pressure (PEEP) levels may improve gas exchange; and because of the reduction of the proportion of nonaerated lung and the repeated opening and closing of small airways, it may decrease ventilator-induced lung injury [2,3]. Therefore, it could be important to optimize the PEEP level in each patient. The best way to select PEEP remains unestablished. In several clinical trials, PEEP was adjusted to reach an oxygenation target [1,4,5], whereas in others, the goal was based on lung mechanics [6,7]. The impact of different strategies of PEEP selection on some specific aspects of the lung mechanics like transpulmonary pressure ($P_{tp}$) and stress index (SI) is not extensively described in clinical practice. It has been reported that the end-expiratory transpulmonary pressure ($P_{tpe}$) became negative at variable levels of PEEP in patients with pulmonary ARDS [8]. This negative $P_{tpe}$ could potentially indicate an increased risk of alveolar collapse and lung injury because of cyclic opening and closing of alveolar units alveolar units [9]. In turn, end-inspiratory transpulmonary pressure ($P_{tpi}$) instead of plateau pressure could be a better expression of lung distension and as a consequence of the risk of stress injury. Meanwhile, the SI, which is a dimensionless number, describes the shape of the airway pressure-time curve during constant flow inflation, suggesting tidal recruitment when the slope of the SI is less than 1 (progressive increase in slope) and hyperinflation when SI is greater than 1 (progressive decrease in slope) [10].

In this study, we compared gas exchange and respiratory mechanics (mainly transpulmonary pressure and SI) between 3 frequently used strategies of PEEP selection in clinical practice for ARDS patients: 1 method based on oxygenation goal (ARDS network PEEP/$F_{IO_2}$ table) [1] and 2 methods based on lung mechanics: the ExPress strategy [6] and PEEP selection based on best compliance of the respiratory system obtained during a derecruitment maneuver [11]. Preliminary results have been previously presented in an international meeting [12].

☆ Neither of the authors has conflict of interest to disclose.
☆☆ Funding: none.
* Corresponding author at: Av Las Heras 2900 (1425) Buenos Aires, Argentina. Tel.: +54 11 4808 8141; fax: +54 11 4808 8156.
*E-mail address:* rvalentini@cemic.edu.ar (R. Valentini).

http://dx.doi.org/10.1016/j.jcrc.2014.11.019
0883-9441/© 2014 Elsevier Inc. All rights reserved.

## 2. Materials and methods

### 2.1. Patients

This prospective study was conducted in a 19-bed mixed medical and surgical intensive care unit of a university hospital. The study protocol was approved by our institutional review board, and an informed consent was obtained from the next of kin. Patients were studied within 48 hours of intensive care unit admission for ARDS, as defined by the American-European consensus conference [13]. The subjects were included if they had a $Pa_{O_2}/F_{IO_2}$ not greater than 200 mm Hg with PEEP greater than 5 cm $H_2O$ and a Lung Injury Score of at least 2.5 [14] at some moment within the first 48 hours of mechanical ventilation. This criterion corresponds to moderate and severe ARDS according to the new Berlin definition that was published after our study was designed [15]. Exclusion criteria were as follows: pneumothorax, bronchopleural fistula, contraindications to place an esophageal catheter such as nasal lesions, hemodynamic instability (mean arterial pressure [MAP] $\leq$65 mm Hg with norepinephrine $\geq$1 $\mu$g/[kg min]), severe hypoxemia ($Pa_{O_2}/F_{IO_2} \leq 70$ mm Hg with PEEP $\geq$ 10 cm $H_2O$), or elevated intracranial pressure. Patients were ventilated with volume-controlled ventilation (Puritan Bennett 840, Pleasanton, CA); ventilator parameters before inclusion were chosen by the attending physician.

Esophageal pressure ($P_{es}$) was measured with a thin latex balloon-tipped catheter connected to a pressure transducer. The esophageal balloon was filled with 5 mL of air and then deflated to a residual volume of 1 mL. It was positioned between the middle and the distal third of the esophagus to minimize cardiac artifacts and verified with a chest radiograph before measurements. We also analyzed the ratio of change in $P_{es}$ and airway pressure ($P_{aw}$) by simultaneous airway occlusion and manual chest compressions [8]. Values of $P_{aw}$, $P_{es}$, and flow at the Y piece of the respirator circuit were recorded with a FluxMed respiratory monitor (MBMed System, Buenos Aires, Argentina). Tidal volume values were obtained by integrating the flow overtime signal. In addition, we calculated the SI using the Levenberg-Marquardt algorithm, as was previously described [10]. When SI equals 1, the tracing of the pressure vs time curve is a straight line, indicating that $V_T$ insufflations occur in a low-risk ventilatory zone. The threshold value that identifies best tidal recruitment ranges between 0.9 and 1.1. Possibility of derecruitment is considered with values of SI less than 0.9, corresponding to a downward concavity of the pressure curve; and on the other hand, upward concavity (SI > 1.1) means that compliance is decreasing over time with insufflation, reflecting overinflation.

End-inspiratory plateau pressure of the respiratory system ($P_{PLAT}$) and end-inspiratory $P_{es}$ were measured after an airway occlusion of 3 seconds at the end of inspiration. Total PEEP (PEEPt) was measured performing an occlusion of 3 seconds at the end of expiration. End-expiratory transpulmonary pressure was calculated as PEEPt − expiratory $P_{es}$; and $P_{tpi}$, as $P_{PLAT}$ − inspiratory $P_{es}$. Static respiratory system ($C_{RS}$), lung ($C_{LUNG}$) compliances, and elastance of the chest wall ($E_{CW}$) were calculated with standard formulae:

- $$C_{RS} = V_T/(P_{PLAT} - \text{PEEPt}),$$
- $$C_{LUNG} = V_T/\left(P_{tpi} - P_{tpe}\right),$$
- $$E_{CW} = (\text{inspiratory } P_{es} - \text{expiratory } P_{es})/V_T.$$

Before measurements, airway secretions were suctioned; and the pressure of the cuff and other potential leaks were ruled out.

Hemodynamic parameters, including MAP, cardiac index (CI), stroke volume (SV), and stroke volume variation (SVV) were obtained with a radial artery catheter connected to a hemodynamic monitor (Vigileo-FloTrac third-generation system; Edwards Lifesciences, Unterschleissheim, Germany).

### 2.2. PEEP selection strategies

Three PEEP selection strategies were evaluated in each patient.

1. PEEP according to the $Pa_{O_2}/F_{IO_2}$ table of the National Institutes of Health ARDS network trial [1] (PEEP/$F_{IO_2}$ table): PEEP and $F_{IO_2}$ were titrated to maintain $Pa_{O_2}$ between 55 and 80 mm Hg or pulse oxymetry between 88% and 95%.
2. Best $C_{RS}$ during a decremental PEEP maneuver (Best Compliance strategy): To obtain the PEEP level with this method, a recruitment maneuver was performed on pressure control ventilation with an inspiratory pressure of 20 cm $H_2O$ above PEEP, $F_{IO_2}$: 1.00, PEEP 25 cm $H_2O$, respiratory rate to achieve pH of at least 7.30, rise time 100%, inspiratory time 0.9 to 1 second. This setting was maintained for 2 minutes. Then PEEP was progressively reduced in steps of 2 cm $H_2O$ every 5 minutes up to a value of 5 cm $H_2O$. In each step, we ensure that the inspiratory flow reached zero. Positive end-expiratory pressure was chosen as the value at which the highest static compliance of the respiratory system was observed.
3. PEEP according to the increased recruitment arm of the ExPress trial [6]: PEEP was adjusted to reach a $P_{PLAT}$ between 28 and 30 cm $H_2O$.

### 2.3. Study protocol

Patients were initially ventilated on volume control ventilation, with a $V_T$ of 6 mL/kg predicted body weight, constant flow, PEEP 5 cm $H_2O$, inspiration to Expiration ratio (I.E.) ratio 1:2, a respiratory rate to achieve pH of at least 7.30, and $F_{IO_2}$ to obtain a arterial oxygen saturation ($Sa_{O_2}$) between 88% and 95%, for a period of 20 minutes (baseline ventilation). Then, the PEEP levels according to the PEEP/$F_{IO_2}$ table, Best Compliance, and ExPress strategy were established. Then, $F_{IO_2}$ was set to 1.00; and patients were sequentially ventilated for 20 minutes with the PEEP values selected for each of the 3 strategies in a random order, separated by periods of 20 minutes of baseline ventilation with 5 cm $H_2O$ of PEEP (Fig. 1). To standardize lung volume history, a recruitment maneuver was applied before each PEEP strategy, with 25 cm $H_2O$ of PEEP and an inspiratory pressure of 15 cm $H_2O$ for 40 seconds. Respiratory rate was kept unchanged during the entire protocol. Volume control ventilation was applied during both baseline and PEEP strategies ventilation.

Measurements were obtained before randomization and at the end of each strategy. Sedation with a combination of fentanyl, midazolam, and/or propofol and neuromuscular blockade with atracurium as needed were used to achieve a Richmond Agitation Sedation Scale of to 5 [16].

### 2.4. Statistics analysis

To avoid individual variability, continuous variable comparisons between strategies were done with a general linear model using each patient as a random factor. For proportion comparison, a $\chi^2$ test was used. A $P$ value less than .05 was considered significant. Post hoc analysis was performed with a Bonferroni test. Data were analyzed using SPSS statistical software (SPSS v19 Inc for Windows, Chicago, IL). Continuous data were expressed as median (interquartile range).

## 3. Results

### 3.1. Patients

During a period of 18 months (between April 2009 and September 2011), 25 patients fulfilled the inclusion criteria. Five were excluded