Transpulmonary Pressure and Gas Exchange During Decremental PEEP Titration in Pulmonary ARDS Patients

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BACKGROUND*:* Selection of the PEEP associated with the best compliance of the respiratory system during decremental PEEP titration can be used for the treatment of patients suffering from ARDS. We describe changes in transpulmonary pressure (P_{tp}) and gas exchange during a decremental PEEP titration maneuver in subjects with pulmonary ARDS. METHODS: Eleven subjects with early ARDS were included. After a recruitment maneuver they were ventilated in volume-controlled ventilation and PEEP was decreased from 30 to 0 cm H_2O by steps of 3 cm H_2O. Static airway pressure (P_{aw}), esophageal pressure (P_{es}), P_{tp} ($P_{aw} - P_{es}$), the ratio of dead space to tidal volume (V_D/V_T), and P_{aO_2} were recorded at each step. RESULTS: A linear correlation was found between P_{aw} and P_{tp}. Expiratory P_{tp} became negative in all subjects when PEEP decreased below 8.9 ± 5.2 cm H_2O. V_D/V_T was 0.67 ± 0.06 with 30 cm H_2O of PEEP, and decreased 15.4 ± 8.5% during the maneuver, when PEEP and expiratory P_{tp} were 10.6 ± 4.1 cm H_2O and 1.2 ± 2.8 cm H_2O, respectively. V_D/V_T was significantly higher during ventilation at high (> 18 cm H_2O), compared to low, inspiratory P_{tp} values (*P* < .001). P_{aO_2} decreased when expiratory P_{tp} became negative (*P* < .001). CONCLUSIONS: During decremental PEEP titration we sequentially observed high inspiratory P_{tp} that stressed lung tissue and increased V_D/V_T, and negative P_{tp}, indicating high risk of alveolar collapse, explaining worse oxygenation. PEEP selection based on P_{tp} and V_D/V_T in ARDS may help to avoid these situations. *Key words: ARDS; respiratory dead space; mechanical ventilation; ventilator induced lung injury; PEEP; acute lung injury.* [Respir Care 2013;58(5):754–763. © 2013 Daedalus Enterprises]

Introduction

Mechanical ventilation (MV) in ARDS is usually performed with small tidal volume (V_T) and moderate to high levels of PEEP. Several methods to individualize PEEP setting have been proposed to optimize lung mechanics and to improve gas exchange while reducing ventilator-induced lung injury, which has been related to the stress and the strain applied to the lungs during MV.[1-8] Stress depends on the transpulmonary pressure (P_{tp}), which is the difference between alveolar pressure and pleural pressure, while strain refers to the relationship between tidal change and end-expiratory lung volumes.[9] Cyclic opening and closing of alveolar units have also been related to ventilator-

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induced lung injury.[10] PEEP level and resulting expiratory and inspiratory P_{tp} during MV may affect all these mechanisms of injury.

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The PEEP associated with the best compliance of the respiratory system (C_{RS}) can be easily found at the bedside during a decremental PEEP titration maneuver. This procedure has been proposed as a way to individualize PEEP setting.[2] It may be possible to observe a change in P_{tp} and the ratio of dead space (V_D) to V_T when PEEP is progressively decreased from high to low levels. These behaviors have not been well described in clinical settings. The purpose of this study is to describe changes in P_{tp} and V_D/V_T during decremental PEEP titration performed in a group of subjects with ARDS due to severe pneumonia.

QUICK LOOK

Current knowledge

In patients with ARDS, PEEP selection can be based on respiratory mechanics, oxygenation, and/or hemodynamic criteria. The optimum PEEP and best method to set PEEP are controversial. One method includes using the best respiratory system compliance during decremental PEEP titration.

What this paper contributes to our knowledge

The recording of transpulmonary pressure instead of airway pressure and the ratio of dead space to tidal volume during a decremental PEEP trial appears to allow an individualized approach for optimal PEEP setting. Negative transpulmonary pressure was associated with hypoxemia suggesting lung collapse, whereas high transpulmonary pressure increased the ratio of dead space to tidal volume that may be related to alveolar overdistension.

Methods

This study was approved by our internal review board and was conducted in our 19 bed ICU at the Centro de Educación Médica e Investigaciones Clínicas in Buenos Aires, Argentina. Informed consent was obtained from all subjects' next of kin before inclusion.

Subjects and Procedures

Eleven consecutive patients suffering from ARDS, according to the American-European Consensus Conference on ARDS, due to severe pneumonia, were included within 72 hours of admission to the ICU, between May 2009 and May 2010.[11] All subjects' hemodynamic condition was judged stable before procedures. They were ventilated with a Puritan Bennett 840 (Covidien, Mansfield, Massachusetts) or a Servo-i (Maquet, Wayne, New Jersey) ventilator in volume-controlled continuous mandatory ventilation, with a V_T of 6 mL/kg of ideal body weight, F_{IO_2} of 1.0, and breathing frequency between 25 and 30 breaths/min. A humidifier (MR850, Fisher & Paykel Healthcare, Auckland, New Zealand) was used for inspiratory gas conditioning in all cases. The subjects were in semi-recumbent position, with the head of the bed elevated at 30°, and sedated with midazolam and fentanyl. Neuromuscular blockade with atracurium was used as needed. Secretions were suctioned before the start of the study protocol. After a recruitment maneuver using CPAP of 40 cm H_2O for 40 seconds, volume-controlled ventilation was resumed and PEEP was decreased from 30 to 0 cm H_2O by steps of 3 cm H_2O every 3 min (see Fig. 1). An inspiratory plateau airway pressure higher than 60 cm H_2O, a reduction of S_{pO_2} below 85%, a mean arterial pressure lower than 60 mm Hg, or a sudden change in cardiac rhythm were used as criteria for interrupting the decremental PEEP titration maneuver.

Measurements

Flow was measured with a pneumotachograph (TSD137G, ± 3000 mL/s, Biopac Systems, Goleta, California) at the Y-piece. Airway pressure (P_{aw}) at the Y-piece, and esophageal pressure (P_{es}) obtained from a 7 cm long latex balloon inflated with 1 mL of air were recorded using transducers (TSD160D, ± 75 cm H_2O, Biopac Systems, Goleta, California). The esophageal balloon position, between the middle and the distal third of the esophagus to minimize cardiac artifacts, was verified with a chest x-ray before measurements. Data acquisition and analysis were done with an MP100WSW system and AcqKnowledge 3.9.0 (Biopac Systems, Goleta, California), respectively. Inspiratory V_T was integrated from the flow signal. Recordings were performed during the last minute of each step, using an expiratory and an inspiratory pause of 2 seconds, synchronized with the PR interval on electrocardiographic tracing to avoid cardiac artifacts on P_{es} (Fig. 2). P_{tp} was calculated as the difference between P_{aw} and P_{es}. C_{RS}, lung compliance (C_{lung}), and chest wall compliance (C_{CW}) were calculated using standard formulae, and V_D/V_T with the Bohr-Enghoff equation[12]:

$$C_{RS} = V_T/(\text{inspiratory } P_{aw} - \text{expiratory } P_{aw})$$
$$C_{lung} = V_T/(\text{inspiratory } P_{tp} - \text{expiratory } P_{tp})$$
$$C_{CW} = V_T/(\text{inspiratory } P_{es} - \text{expiratory } P_{es})$$
$$V_D/V_T = (P_{aCO_2} - P_{\bar{E}CO_2})/P_{aCO_2}$$

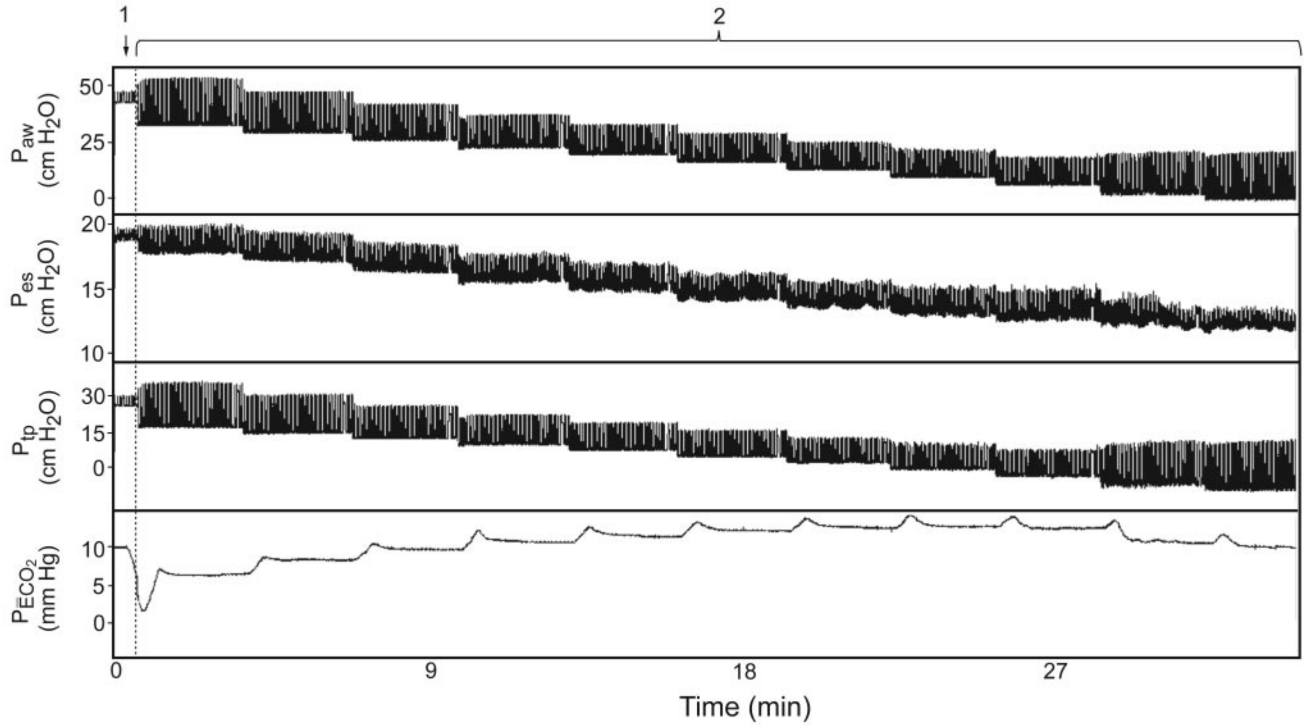

Fig. 1. Study procedures. Tracings from subject 8, showing airway pressure (P_{aw}), esophageal pressure (P_{es}), transpulmonary pressure (P_{tp}), and mixed expiratory P_{CO_2} ($P_{\bar{E}CO_2}$). First a recruitment maneuver was performed, using a CPAP of 40 cm H_2O for 40 seconds. Then volume-controlled ventilation was resumed and PEEP was decreased from 30 to 0 cm H_2O by steps of 3 cm H_2O every 3 min. See how the $P_{\bar{E}CO_2}$ signal stabilizes by the end of each PEEP step.

in which $P_{\bar{E}CO_2}$ is the mixed exhaled pressure of CO_2, measured with a CO2100C module (Biopac Systems, Goleta, California) connected to a 5 L mixing chamber (AFT15A, Biopac Systems, Goleta, California) that collected gas from the expiratory valve. Blood samples for gas analysis were drawn from an arterial line. Values were recorded at the end of each PEEP step, where $P_{\bar{E}CO_2}$ reached a stable value (see Fig. 1). Neither invasive nor noninvasive hemodynamic data were systematically recorded during the titration maneuver.

Statistical Analysis

Linear regression analysis between P_{aw} and P_{tp} or P_{es} was performed. The PEEP value where expiratory P_{tp} became negative was interpolated from each subject's data, assuming that both variables have a linear relationship. To perform this interpolation we calculated for each subject the linear equation linking expiratory P_{tp} as the dependent variable and PEEP as the independent variable, using data points above and below the X axis. Finally, we calculated the PEEP value corresponding to an expiratory P_{tp} of 0. The best C_{RS} PEEP was defined as the highest value of PEEP producing the higher C_{RS} during the decremental titration maneuver.

Receiver operating characteristic curves were built to evaluate the performance of plateau inspiratory P_{aw} for the detection of stressful ventilation (inspiratory P_{tp} higher than 25 cm H_2O). The P_{aw} associated with the greatest sensitivity and specificity was obtained. Additionally, the sensitivity and specificity of a P_{aw} of 30 cm H_2O for predicting a P_{tp} higher than 25 cm H_2O were also calculated with standard formula.

Analysis of variance (ANOVA) for repeated measurements was performed to evaluate the effect of PEEP on compliances, V_D/V_T, and P_{aO_2}. To evaluate the effect of P_{tp} (grouped in intervals of 3 cm H_2O) on these 2 variables, a 2-way ANOVA test was performed using each subject as a block to control interindividual variability, and P_{tp} as a random factor. Post hoc comparisons were made with the Bonferroni test. Continuous variables are expressed as mean ± SD. A *P* value less or equal to .05 was considered statistically significant. Statistics software (PASW 18.0.0, SPSS, Chicago, Illinois) was used.

Results

All subjects had ARDS due to community-acquired pneumonia, 5 secondary to H1N1 2009 influenza virus. Mean age and Acute Physiology and Chronic Health Evalua-

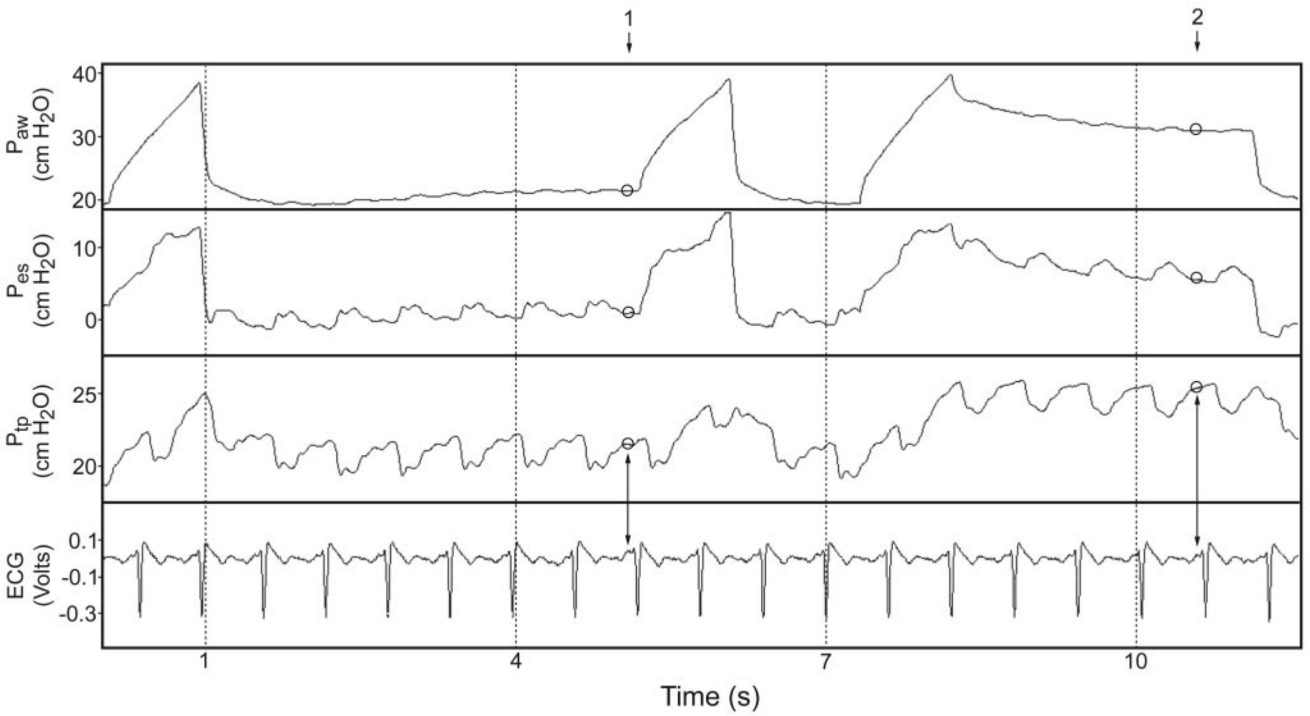

Fig. 2. Influence of cardiac artifact on esophageal pressure recording. Tracings from subject 5, showing airway pressure (P_{aw}), transpulmonary pressure (P_{tp}), esophageal pressure (P_{es}), and electrocardiogram (ECG). Note that the P_{es} signal shows swings of 2–3 cm H_2O, related to cardiac activity. To standardize the measurements, end-expiratory static pressure (arrow 1) and end-inspiratory static pressure (arrow 2) recordings were performed during PR intervals.

Table 1. Baseline Characteristics and Outcomes ($n = 11$)

Mechanical ventilation settings	
Tidal volume, mL/kg	6.35 ± 0.76
Breathing frequency, breaths/min	27 ± 2
PEEP, cm H_2O	18 ± 3
Gas exchange	
pH	7.32 ± 0.06
P_{aCO_2}, mm Hg	45 ± 9
P_{aO_2}/F_{IO_2}, mm Hg	167 ± 128
Outcomes	
Duration of mechanical ventilation, d	27.9 ± 14.7
Hospital stay, d	39.5 ± 24.5
Hospital survival, no. (%)	7 (63)

Data are mean ± SD unless otherwise specified.

tion II were 50 ± 19 years and 20 ± 9, respectively. In all cases chest x-rays showed diffuse pulmonary infiltrates. Baseline MV settings, gas exchange before recruitment maneuver, and outcomes are shown in Table 1. The maneuver could be completed in all cases without signs of major hemodynamic impairment or barotrauma.

Respiratory System Mechanics

During decremental PEEP titration, as PEEP decreased from 30 cm H_2O, mean C_{RS} initially increased until reaching a peak, and then decreased (ANOVA $P < .001$, Fig. 3). The best C_{RS} PEEP was achieved with a mean PEEP of 10.4 ± 3.1 cm H_2O (see Table 1). This behavior was also observed with C_{lung} (see Fig. 3, ANOVA $P < .001$), while C_{CW} was not significantly affected by PEEP (ANOVA $P = .09$).

Figure 4 summarizes the effect on P_{tp} and P_{es} produced by PEEP reduction. A significant correlation was found between both inspiratory and expiratory P_{aw} and P_{tp} ($R^2 = 0.76$, $P < .001$, and $R^2 = 0.73$, $P < .001$, respectively). P_{es} and P_{aw} also showed a linear relationship both during expiration ($R^2 = 0.46$, $P < .001$) and inspiration ($R^2 = 0.56$, $P < .001$). As is shown in Table 2, the PEEP where expiratory P_{tp} equaled 0 could be interpolated in all subjects, with a mean value of 8.9 ± 5.2 cm H_2O (range 0.9–20.1). This value was not significantly different, when compared to the best C_{RS} PEEP (paired *t* test $P = .35$). Maximal individual recorded inspiratory and expiratory P_{tp} were 25.6 ± 5.9 cm H_2O (range 14.4–33.2 cm H_2O) and 13.0 ± 4.8 cm H_2O, respectively. Inspiratory P_{aw} was higher than 30 cm H_2O in 41 out of 121 recordings (33.9%). In 8 (19.5%) of these 41 measurements, inspiratory P_{tp}

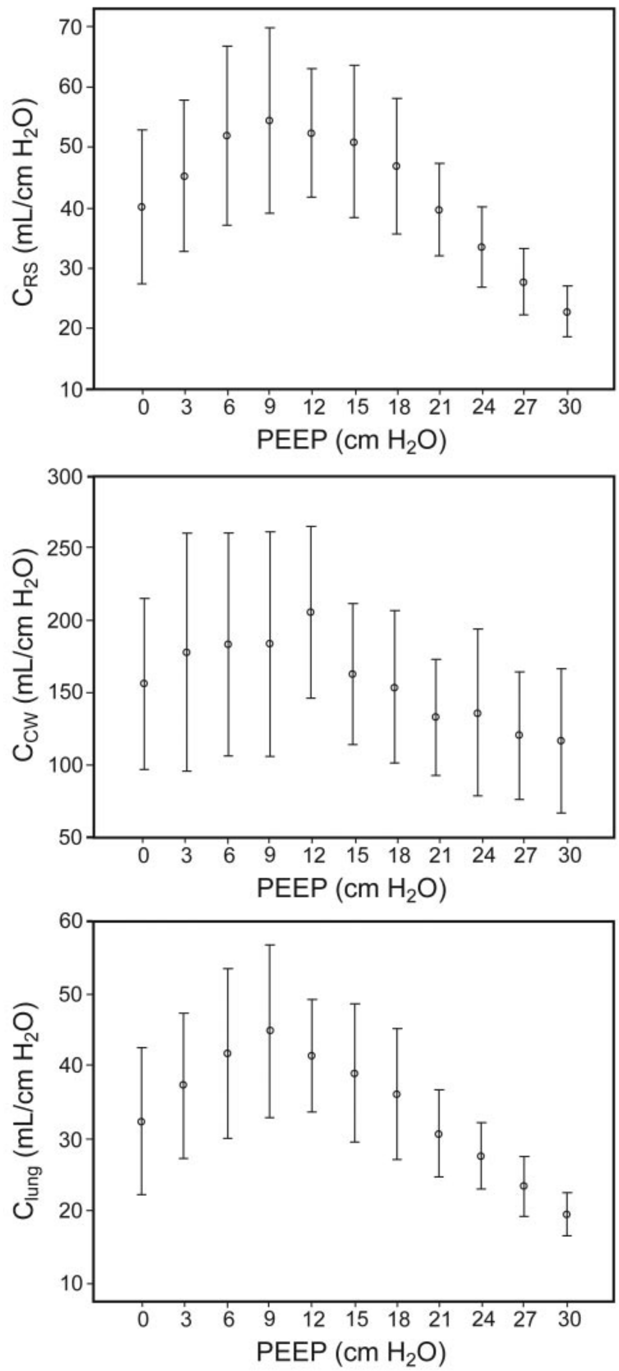

Fig. 3. PEEP versus static compliance of the respiratory system (C_{RS}), chest wall (C_{CW}), and lung (C_{lung}) during a decremental PEEP titration maneuver. C_{RS} and C_{lung} significantly improved as PEEP was decreased ($P < .001$), while C_{CW} was not affected ($P = .09$). The error bars represent ± 1 standard deviation.

was above 25 cm H_2O. On the other hand, inspiratory P_{tp} was below that threshold in all cases when P_{aw} was equal or lower than 30 cm H_2O. Thus, a P_{aw} higher than 30 cm H_2O had a sensitivity of 1.0 and specificity of 0.71 for the detection of an inspiratory P_{tp} higher than 25 cm H_2O. A

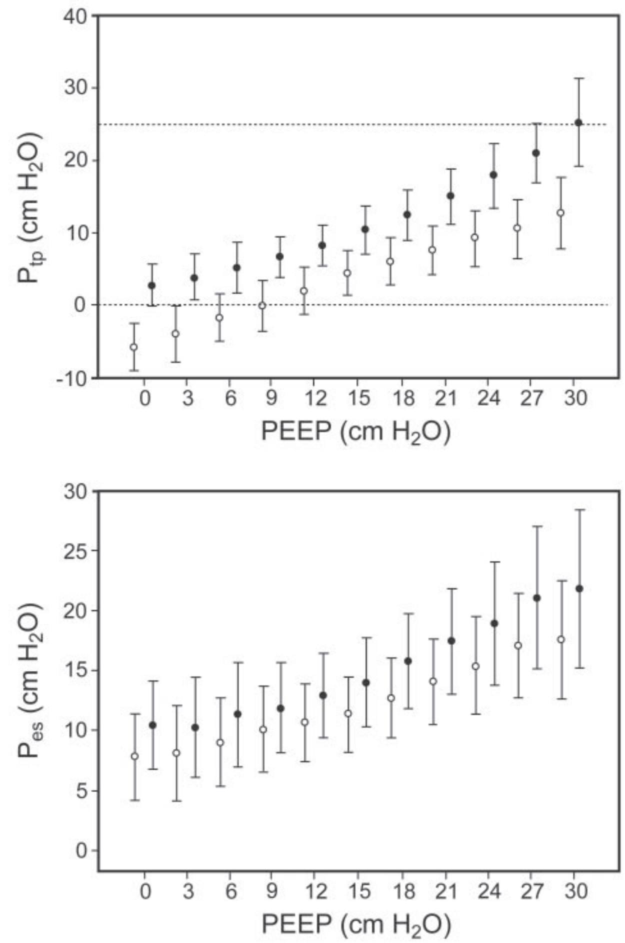

Fig. 4. PEEP versus static transpulmonary pressure (P_{tp}) and esophageal pressure (P_{es}) during a decremental PEEP titration maneuver. Recordings were performed during inspiration (shaded circles) and expiration (white circles). The error bars represent ± 1 standard deviation.

P_{aw} higher than 37.7 cm H_2O showed the greatest combination of sensitivity (1.0) and specificity (0.86) for the detection of an inspiratory P_{tp} higher than 25 cm H_2O (area under the receiver operating characteristic curve 0.93, $P < .001$).

Gas Exchange

During the decremental maneuver, as PEEP was reduced from 30 to 0 cm H_2O, P_{aCO_2} progressively decreased from 57.4 ± 10.6 to 52.9 ± 7.6 mm Hg, respectively (ANOVA $P < .001$). V_D/V_T was 0.67 ± 0.06 during ventilation with 30 cm H_2O of PEEP (see Table 2). From that value, V_D/V_T decreased to 15.4 ± 8.5% during the stepwise reduction of PEEP (ANOVA $P < .001$, Fig. 5A). This peak reduction of V_D/V_T was observed with a PEEP of 10.6 ± 4.1 cm H_2O, which was associated with a P_{tp} of 1.2 ± 2.8 cm H_2O and 7.6 ± 2.8 cm H_2O during expira-

Table 2. PEEP Corresponding to the Best Compliance of the Respiratory System During Decremental PEEP Titration, PEEP Value Interpolated at Expiratory Transpulmonary Pressure Equal to Zero, Ratio of Dead Space to Tidal Volume, and P_{aO_2} With a PEEP of 30 cm H_2O Following Recruitment Maneuver

Subject Number	Best C_{RS} PEEP (cm H_2O)	PEEP Where Expiratory $P_{tp} = 0$ (cm H_2O)	V_D/V_T	P_{aO_2} (mmHg)
1	9	6.6	0.73	204
2	15	20.1	0.56	289
3	9	8.0	0.69	195
4	6	10.3	0.61	108
5	15	7.1	0.69	180
6	12	6.7	0.60	374
7	9	0.9	0.72	427
8	12	13.2	0.71	230
9	12	11.8	0.66	115
10	6	10.1	0.68	85
11	9	3.3	0.73	275
Mean ± SD	10.4 ± 3.1	8.9 ± 5.2	0.67 ± 0.06	225.7 ± 108.8

C_{RS} = static compliance of the respiratory system
P_{tp} = transpulmonary pressure
V_D/V_T = ratio of dead space to tidal volume

tion and inspiration, respectively. V_D/V_T was also affected by expiratory and inspiratory P_{tp} (ANOVA $P < .001$, see Figs. 5B and 5C). Compared to lower inspiratory P_{tp} intervals, when this pressure was higher than 18 cm H_2O, V_D/V_T was significantly increased (Bonferroni test).

P_{aO_2} was 225.7 ± 108.8 mm Hg with a PEEP of 30 cm H_2O, and it changed as PEEP was reduced to 0 cm H_2O (see Table 2 and Fig. 6A, ANOVA $P = .02$). Post hoc comparisons between PEEP levels disclosed no significant differences. Figures 6B and 6C illustrate how expiratory and inspiratory P_{tp} also exerted changes in P_{aO_2} (ANOVA $P < .001$). Post hoc comparison between intervals showed that those including negative expiratory P_{tp} were associated with lower P_{aO_2}.

As shown in Figure 7, V_D/V_T observed during ventilation with the best C_{RS} PEEP showed an excellent correlation with values recorded with the minimal PEEP required to obtain a positive expiratory P_{tp} ($R^2 = 0.96$, $P < .001$). Comparison of P_{aO_2} between these 2 PEEP values showed a good correlation ($R^2 = 0.51$, $P = .14$).

Discussion

This study describes the behavior of P_{tp}, V_D/V_T, and P_{aO_2} during a decremental PEEP titration maneuver performed to detect the PEEP level resulting in the best C_{RS}. Our main findings are:

- All subjects showed negative expiratory P_{tp} at some point of the decremental PEEP titration maneuver.
- An upper inspiratory plateau P_{aw} limit of 30 cm H_2O was not an accurate predictor of potentially injurious high P_{tp} following a recruitment maneuver.

Gas exchange was affected by P_{tp} during decremental PEEP titration. V_D/V_T was mainly increased during ventilation with high inspiratory P_{tp}, whereas P_{aO_2} decreased when expiratory P_{tp} became negative.

Setting PEEP to get the best C_{RS} has been used as a way to optimize cardiopulmonary function since early ARDS studies.[5] We performed a decremental PEEP maneuver using high expiratory and inspiratory P_{aw} in order to enhance the likelihood of lung recruitment, as it has been previously suggested.[13] C_{RS} and C_{lung} were both affected by PEEP in this group of pulmonary ARDS subjects, suggesting that our subjects had recruitable lung units, as has been described in tomographic studies.[14] The greatest improvements were observed with moderate levels of PEEP (mean of 10 cm H_2O) during the maneuver. On the other hand, PEEP did not significantly affect C_{CW}. This has been previously reported in patients with pulmonary and extrapulmonary ARDS.[8]

Effect of Decremental PEEP Titration on Transpulmonary Pressure

During the decremental maneuver all of our subjects exhibited negative P_{tp}, which was calculated as the difference between P_{aw} and P_{es}. Traditionally, P_{es} has been used as a surrogate of pleural pressure in respiratory physiology, although disagreements between both measurements have been recognized.[15] Factors such as lung volume, compression by the mediastinum, and pleural recording site may explain these differences.[15,16] To overcome this problem, authors have suggested performing a correction in P_{tp} calculation, adding an arbitrary value of cm H_2O based on changes observed in P_{es} after body position modification in healthy subjects.[16,17] We did not perform such correction in our calculations because, to our knowledge, there are not enough data about this point in ARDS patients, and we considered that our esophageal recording might estimate pleural pressure between the middle to the more dependent lung regions, as has been suggested in an experimental ARDS model.[18] As expected, during the decremental PEEP titration maneuver, inspiratory and expiratory P_{aw} and P_{tp} showed good correlation. Expiratory P_{tp} became negative when PEEP was decreased below 1 to 20 cm H_2O (average 9 cm H_2O). Negative P_{tp} has been previously described in ARDS patients despite the appli-

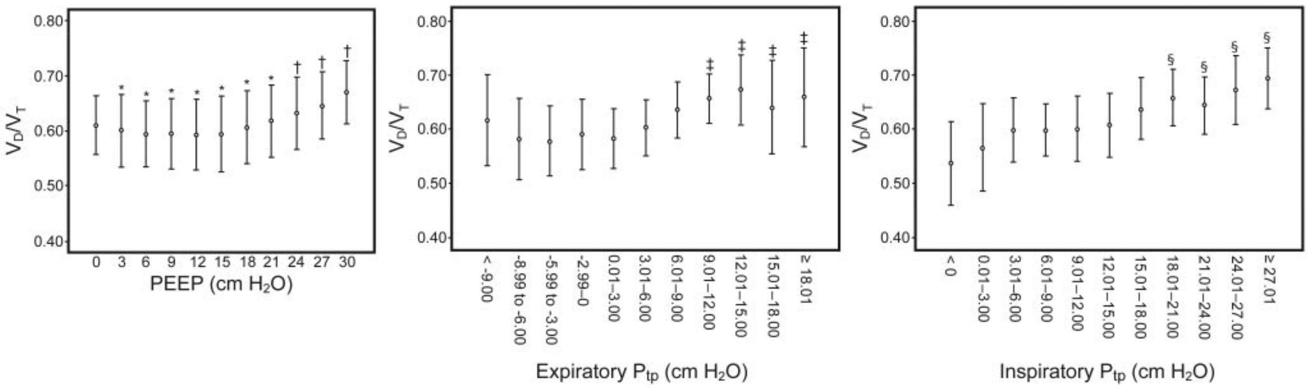

Fig. 5. Mean ratio of dead space (V_D) to tidal volume (V_T) versus PEEP and transpulmonary pressure (P_{tp}) during decremental PEEP titration maneuvers. V_D/V_T significantly changed when PEEP was decreased from 30 cm H_2O ($P < .001$). P_{tp} is grouped in 3 cm H_2O intervals. V_D/V_T was significantly affected by both inspiratory and expiratory P_{tp} (both $P < .001$). The error bars represent ± 1 standard deviation. Post hoc comparison $P < .05$ for multiple comparisons with a PEEP of 30 cm H_2O (*), and for multiple comparisons with a PEEP of 12 cm H_2O (†). Post hoc comparison $P < .05$ for multiple comparisons with the 3.01–6.00 cm H_2O expiratory P_{tp} interval (‡), and for multiple comparisons with the 9.01–12.00 cm H_2O inspiratory P_{tp} interval (§).

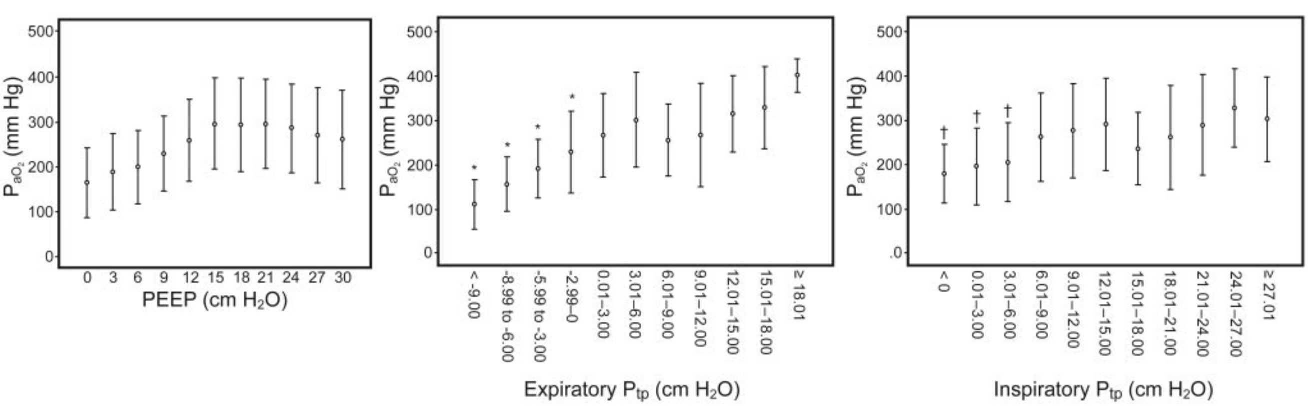

Fig. 6. Mean P_{aO_2} versus PEEP and transpulmonary pressure (P_{tp}) during decremental PEEP titration maneuvers. P_{aO_2} significantly changed during PEEP decrease ($P < .02$). P_{tp} is grouped in 3 cm H_2O intervals. P_{aO_2} was significantly affected by both inspiratory and expiratory P_{tp} (both $P < .001$). The error bars represent ± 1 standard deviation. Post hoc comparison $P < .05$ for multiple comparisons with expiratory P_{tp} intervals higher than 3 cm H_2O (*), and with inspiratory P_{tp} intervals higher than 9 cm H_2O (†).

cation of high PEEP, and this has been associated with low C_{CW}.[17,19] The observation of negative P_{tp} probably represents a miscalculation, because P_{es} might reflect pleural pressure at a given point surrounding dependent lung regions, while P_{aw} only stresses opened alveolar units. The vertical pressure gradient between pleural pressure surrounding these ventilated units and P_{es} seems to be a function of interposed lung weight.[18,20] In other words, when low PEEP is applied, alveoli and small airway may close, at least during exhalation, causing alveolar gas trapping and/or atelectasis. Under these circumstances the static P_{aw} may not reflect the true alveolar pressure. Indeed the high P_{es} could be more representative of the end-expiration alveolar pressure in these poorly ventilated units. These considerations may explain why PEEP interpolated at ex-

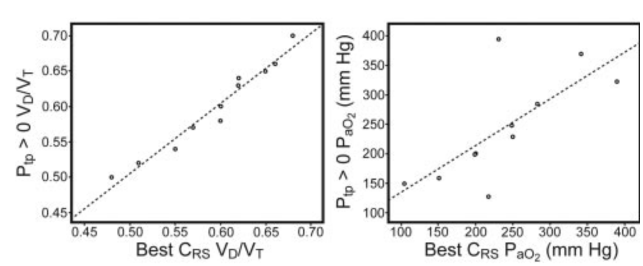

Fig. 7. A: Ratio of dead space (V_D) to tidal volume (V_T) with the PEEP corresponding to the best compliance of the respiratory system (best C_{RS}) versus that with the minimal PEEP required to obtain a positive expiratory transpulmonary pressure (P_{tp}) > 0. B: P_{aO_2} with the PEEP corresponding to the best compliance of the respiratory system (best C_{RS}) versus that with the minimal PEEP required to obtain a positive expiratory P_{tp} > 0..

piratory P_{tp} 0 was highly variable among our subjects and hardly predictable without other tools such as chest computed tomography scans.[18,20] These values were not significantly different from the best C_{RS} PEEP. However, our data suggest that ventilating with the best C_{RS} PEEP based on a decremental PEEP titration maneuver may not always avoid the risk of lung collapse and the tidal cyclic opening and closing of lung units, because some patients will have negative P_{tp}, as was observed in 4 cases of our series (see Table 2).

Traditionally, static P_{aw} has been used as a surrogate of stress applied to alveolar units. Excessive stress on lung tissue during MV has been implicated in capillary and alveolar barrier disruption (stress failure) and in enhancing systemic inflammation.[21,22] From a mechanistic point of view, alveolar transmural pressure (static airway minus pleural pressure) is a more accurate stress parameter than airway opening pressure itself. Nevertheless, keeping static plateau inspiratory P_{aw} below 30 cm H_2O during ARDS ventilation has been recommended to avoid ventilator-induced lung injury, and this threshold has been evaluated as an objective for PEEP titration, aiming to increase recruitment.[3,4,23] P_{tp} may be a more accurate predictor of the real alveolar transmural pressure because it is not influenced by chest wall mechanics.[17,24] In fact, although the sensitivity for the detection of an inspiratory P_{tp} higher than 25 cm H_2O (which represents the expected value at total lung capacity in subjects with normal lungs) of an inspiratory P_{aw} greater than 30 cm H_2O was 1.0, its specificity was only 0.71. Moreover, in this series a P_{aw} equal to or higher than 37.7 cm H_2O was identified as the best cutoff value for predicting an inspiratory P_{tp} exceeding 25 cm H_2O. Taken together these results strongly suggest measuring P_{es} and calculating P_{tp} for setting MV in patients at risk of having decreased C_{CW}, including patients with pulmonary ARDS.

Gas Exchange Variations During Decremental PEEP Titration

V_D/V_T is increased in ARDS patients and has prognostic value because it reflects microvascular disruption and ventilation inhomogeneity. It has been suggested that different PEEP levels do not affect V_D/V_T of lung injured subjects.[25] According to our data, after a recruitment maneuver, V_D/V_T decreased during decremental PEEP titration, indicating that very high PEEP levels may overstress alveolar units and jeopardize lung perfusion. Another explanation, suggested by a previous study, is that high inspiratory P_{aw} may only increase airway V_D/V_T partition measured by volumetric capnography.[26] In contrast with our observations, in this study involving acute lung injury patients where PEEP was increased from 0 to 15 cm H_2O, respiratory system mechanics and P_{aO_2} were not improved by PEEP, indicating that there was no lung recruitment. An experimental study using a highly recruitable animal model and volumetric capnography found that alveolar V_D/V_T may be improved by moderate to high levels of PEEP.[27]

However, in our study the highest V_D/V_T values were observed when inspiratory P_{tp} exceeded 18 cm H_2O, suggesting that high P_{tp} may enhance ventilation-perfusion mismatching. P_{aO_2} was also affected by variations of PEEP and expiratory P_{tp} during a decremental titration maneuver. Comparisons between PEEP levels were not significantly different in post hoc analysis. This finding may be explained by the short equilibration time (3 min) between PEEP steps during the maneuver. However, P_{aO_2} significantly decreased when expiratory P_{tp} became negative, probably due to alveolar unit collapse and increased shunt fraction. This observation linking negative expiratory P_{tp} (and not specific PEEP levels) and worse oxygen exchange may be considered when evaluating the potential for recruitment of lung units.[14,20,28] Additionally, our findings also indicate that expiratory P_{tp} may be used for PEEP titration, as has been suggested by Talmor et al.[6] Nevertheless, in this scenario, quantification of V_D/V_T may add to the identification of an excessive pressure setting.

V_D/V_T recorded with the best C_{RS} PEEP was highly correlated with its value during ventilation, with the minimal PEEP producing a positive expiratory P_{tp}. P_{aO_2} also showed a good correlation between these 2 PEEP values. These observations suggest that PEEP titration during a decremental maneuver may provide short-term gas exchange comparable to a strategy aiming to get a positive expiratory P_{tp}. However, as has been stated above, best C_{RS} PEEP produced negative expiratory P_{tp} in some patients. The latter may explain why gas exchange benefits obtained with the best C_{RS} approach are not always sustained in the long term.[29]

This study has some limitations. Our subjects had diffuse ARDS due to severe pneumonia, so these findings should not be generalized to other ARDS etiologies. Second, the occlusion maneuver has been recommended to evaluate the accuracy of P_{es} recordings.[30] We did not perform this validation. This test was originally described to verify the quality of P_{es} measurements in spontaneously breathing subjects.[31] A modified maneuver has been validated in sedated patients with normal lungs, and also in COPD and ARDS patients.[32-34] One potential pitfall of this occlusion test in a heavily sedated ARDS patient would be produced by inadvertent airway position of the esophageal catheter. We had observed (unpublished data) this problem in one case before initiating the present study. Thus, we routinely verified the position of the catheter with a chest-x-ray to avoid that issue. Third, PEEP steps during the maneuver lasted 3 min. This short time might have been insufficient to reach a steady state in gas exchange variables.[35] Fourth, V_D/V_T was calculated using mixed $P_{\bar{E}CO_2}$, measured from a mixing chamber, instead of using volumetric capnography. Both methods provided similar results when comparing physiological V_D/V_T in ARDS patients.[36] However, volumetric capnography also allows partitioning of V_D/V_T into its airway and alveolar components. These parameters may be of interest for the understanding of the relationship between lung mechanics and dead-space ventilation. Finally, measurements were performed during derecruitment, so mechanical behavior was actually influenced by previous recruitment history. Even in the absence of solid evidence, recruitment maneuvers are usually performed to improve gas exchange and to increase C_{lung}.[29] Thus, both expiratory and inspiratory P_{tp} values observed in our study may be lower than those expected during an incremental PEEP titration maneuver.[2]

Conclusions

In this study describing mechanics and gas exchange during decremental PEEP titration in pulmonary ARDS, we observed that P_{aO_2} decreased with negative expiratory P_{tp}, indicating lung collapse. On the other hand, a higher V_D/V_T was observed with high inspiratory P_{tp}, possibly related to alveolar overdistention. Although the best compliance PEEP selection approach may be useful in some cases, accurately predicting these P_{tp} lower and upper limits is difficult when only airway measurements are considered. Keeping MV within these boundaries may be of clinical interest in order to reduce ventilator-induced lung injury in ARDS patients. Further studies focused on clinical outcome are required to demonstrate the impact of a more individualized ventilator setting protocol guided by a multimodal monitoring strategy including esophageal pressure and V_D/V_T measurements.

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