Cardiopulmonary Dysfunction During Mechanical Ventilation with Low Level of Lung Overdistention In Severe ARDS

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Background: High levels of Positive End-Expiratory Pressure (PEEP) have been proposed to reduce lung collapse in patients with Acute Respiratory Distress Syndrome (ARDS). However, it may result in lung overdistention, and some researchers have suggested that minimizing overdistention is more important than preventing collapse.

Objectives: To assess the feasibility and safety of setting PEEP at low levels of lung overdistension (0 to 3%), and to compare it with PEEP set at low collapse (0 to 3%) and PEEP set at the crossing point between minimal collapse and distension, on respiratory mechanics and gas exchange over 12 hours of mechanical ventilation in a porcine model of severe ARDS.

Methods: Randomized controlled experimental study in female Yorkshire pigs (30-45 kg). Lung injury was induced by surfactant lavage and high-stretch ventilation. Electrical Impedance Tomography (EIT) was used to estimate lung collapse and lung overdistention during a decremental PEEP titration. The pigs were randomized in one of three intervention groups: low overdistension group, the pig was ventilated with PEEP set at 0-3% of overdistension; the crossing point group, PEEP set at the crossing point of collapse and overdistension; or low collapse group, PEEP set at 0-3% of collapse. We ventilated the pigs for 12 hours on pressure-controlled ventilation with low tidal volume. Respiratory mechanics, hemodynamic variables and blood samples were collected every three hours. At the end of the protocol, we also did biological and histological analysis. For comparisons between groups, we used One-way ANOVA, and for comparisons between group with repeated measures, we used Mixed ANOVA. We used Bonferroni correction for post hoc analysis. In the Low Overdistention group, we also compared pigs that survival the whole experiment (12h) versus pig that died, using t test.

Results: A total of 36 pigs were included, 12 per group. Mean PaO_2/FiO_2 after lung injury was 113 ± 68 and mean recruitment-to-inflation ratio was 1.20 ± 0.36. Median set PEEP was 7(IQR:6-8) cmH_2O for the low overdistension group, 11(10-11) for the crossing point group, and 15(12-16) cmH_2O for the low collapse group, $p<0.001$. In the Low Overdistention group, six (50%) pigs died before 12h of mechanical ventilation. None of the pigs died in the two other groups. In this group at time zero (the beginning of intervention) non-survivors had higher percentage of lung collapse (47% ± 9% vs. 24% ± 9%, $p<0.01$); higher transpulmonary driving pressure (20 ± 4 cmH_2O vs. 15 ± 4 cmH_2O, $p=0.04$); lower respiratory system compliance (9 ± 1 mL/cmH_2O vs. 12 ± 2 mL/cmH_2O, $p=0.01$); lower PaO_2 (47 ± 8 mmHg vs. 81 ± 17 mmHg, $p<0.01$); lower PaO_2/FiO_2 (47 ± 8 vs. 85 ± 27, $p=0.02$); and higher pulmonary shunt (77% ± 20% vs. 42% ± 11%). They also required higher doses of epinephrine (1.14 ± 0.85 mc/kg/min vs. 0.04 ± 0.09mc/kg/min, $p<0.01$) and had a higher wet-to-dry ratio at time of death (9.49 ± 1.01 vs. 7.31 ± 0.75, $p<0.01$). At time zero, transpulmonary gradient pressure and right ventricular transmural pressure were higher in the Low Overdistention group than in the Crossing Point and in the Low Collapse groups, 30 ± 7 vs. 23 ± 6 vs. 22 ± 5 mmHg ($p<0.01$), and 30 ± 7 vs. 22 ± 7 vs. 23 ± 5 mmHg ($p<0.01$), respectively.

Conclusion: Our preliminary results suggest that, in a highly recruitable model of severe ARDS, minimizing lung overdistention as a priority may be dangerous and it is more important to prevent lung collapse. Adjusting PEEP at very low level of overdistention (≤3%) resulted in high mortality from cardiopulmonary dysfunction.