

Ventilator-induced lung injury in the excluded lung during one-lung ventilation

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Rationale: Non-ventilated lung regions are usually thought to be spared from ventilator-induced lung injury. Pilot data show activation of inflammation in atelectatic lung areas during mechanical ventilation. We aimed to investigate, in a model of 24-hour one-lung ventilation (OLV), development of injury in the excluded lung and, to identify underlying mechanisms, if it could be prevented by lower tidal volume (V_T).

Methods: Twenty-seven healthy pigs (weight 35 ± 5 Kg) were ventilated for 24 hours after randomization to 3 groups: (1) OLV (left lung excluded) with V_T 15 mL.kg^{-1} , RR 15 min^{-1} and PEEP $1 \text{ cmH}_2\text{O}$ (OLV15 group); (2) OLV with V_T 7.5 mL.kg^{-1} (OLV7.5 group); (3) Two lung ventilation with the same settings of OLV15 (Control group). Respiratory mechanics, hemodynamics and regional lung ventilation and perfusion by Electrical Impedance Tomography (EIT) were obtained at 2 hours after the start of experiment (T2). At 24 hours, bronchoalveolar lavage (BAL) was performed to measure IL-6 and regional tissue samples were obtained to assess lung histological score (HS, range 0-30).

Results: Right ventilated lung HS showed higher values in the OLV15 in comparison to OLV7.5 and Control groups ($p < 0.01$) (Figure 1A). Left lung HS was significantly higher for OLV15 group than Controls ($p < 0.0001$) and OLV7.5 showed intermediate values, higher than Controls ($p < 0.05$) (Figure 1B). BAL IL-6 was higher in OLV15 animals in comparison to the two other groups ($402 \pm 650 \text{ pg/mL}$ in OLV15 vs $51 \pm 90 \text{ pg/mL}$ in OLV7.5 and $27 \pm 15 \text{ pg/mL}$ in Controls, $p = 0.004$).

In terms of underlying mechanisms, driving pressure ($p < 0.01$) and EIT-based % of overdistended pixels ($p < 0.05$) were higher in OLV15 vs. OLV7.5; EIT-based “risk of collapse index” for the non-ventilated left lung was higher in the OLV15 group as compared to the OLV7.5 ($p < 0.05$); % of pulmonary perfusion reaching the left lung was low and similar between the two OLV groups ($16 \pm 6 \%$ in OLV15 and $19 \pm 5 \%$ in OLV7.5, $p = 0.304$).

Conclusions: Left non-ventilated lung develops injury within 24 hours of mechanical ventilation to the contralateral lung. Lowering V_T reduces non-ventilated VILI, but only in part. Of the 4

investigated mechanisms (stress, inflammation, collapse and hypoperfusion) lower VT reduces all, apart from hypoperfusion.

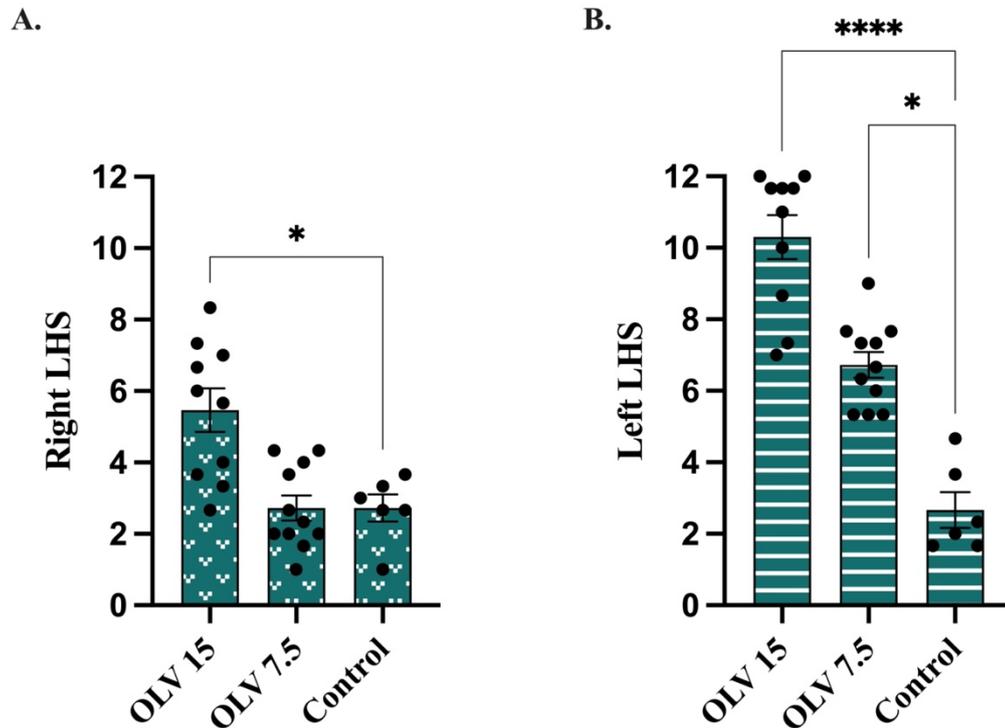


Figure 1. Right and left lung histological scores (LHS). In the OLV15 group the right LHS (A) was significantly higher than in OLV7.5 and Control groups ($p < 0.01$). Left LHS (B) showed higher values in both OLV15 and OLV7.5 groups compared to Control group ($p < 0.0001$); however, OLV7.5 LHS was lower than OLV15 group.

Data are expressed as scatter plot with bars and error bars (mean \pm SEM). Comparisons are obtained with Kruskal-Wallis test for non-normally distributed values followed by Dunn's multiple comparison test.

* $p < 0,05$, ** $p < 0,005$, *** $p < 0,001$ vs Control group.