VENTILATOR-IDUCED LUNG VORTEX IN PATIENTS WITH SARS-CoV-2

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Materials and method

This study was conducted in the ICU dedicated to COVID-19 patients of an intensive care unit at a university hospital in Argentina. Approval was obtained from local institutional review board (resolution number: 68/2019) and informed consent followed the ethical committee's recommendations.

Inclusion criteria: This single-center prospective observational study evaluated consecutively admitted adult patients who were suffering from ARDS secondary to COVID-19 and needed volume-controlled ventilation (VCV) for at least 7 days. These eligibility criteria were decided in order to allow a minimum monitoring of the mechanical variables. Those who did not meet such requirement were excluded.
ARDS was defined according to the Berlin criteria (19) while the diagnosis of COVID-19 pneumonia was established based on CT images showing such condition and on real-time polymerase chain reaction (RT-PCR) test for coronavirus disease-2019.

Exclusion criteria: Patients with do-not-resuscitate (DNR) orders and pregnant women. Cardiac arrest before ICU admission. Extra corporeal membrane oxygenation (ECMO) requirement within the first 24 h of ICU admission and chronic obstructive pulmonary disease with gold class 3 or 4, or home oxygen therapy (20).

Procedure: Patients were administered sedatives and analgesics (propofol and fentanyl) to obtain a score of -5 on the RASS scale. The protective ventilatory strategy included: low tidal volume ventilation (6 ml/kg/PBW), plateau pressure limitation (PPlat: <30 cmH_2O) and prone positioning for severe hypoxemia (21). FiO_2 and $PaCO_2$ were adjusted to achieve SaO_2 between 92 and 96% and pH >7.20, respectively. PEEP was titrated according to the best compliance of the respiratory system (CRS), without exceeding the PPlat limit set. Neuromuscular blockers were administered to patients suffering from severe ARDS (PaO_2/FiO_2 <100) and to the ones with hypoxemia associated with asynchronies despite the administration of sedoanalgesia, PPlat >32 cmH_2O or that needed prone positioning to improve oxygenation.
Mechanical variables and PaO_2/FiO_2 were registered daily for 14 days or until initiating assisted ventilation. These data were obtained in passive mechanical conditions.
Ventilator-induced lung injury vortex was defined as a progressive increase in driving pressure (ΔP) as Vt remained constant or even decreased.
Refractory hypoxemia was defined as PaO_2/FiO_2 <100 despite the optimization of mechanical ventilation and prone positioning.

Respiratory mechanics: Peak airway pressure, plateau pressure, and total PEEP were measured. The value of driving pressure (ΔP: PPlat - PEEP total), static compliance of the respiratory system (CRS = Vt/ΔP) and specific mechanical power (SMP: mechanical power/CRS) were calculated. Mechanical power was computed as: Peak airway pressure x Vt - (ΔP x Vt/2) x respiratory rate x 0.098 (13).

Complications: The following variables and complications were also observed during the period of analysis: incidence of pneumonia associated with mechanical ventilation (14), need for noradrenaline over 0.1 γ/kg/min for more than 24 h, positive blood cultures, accumulated fluid balance, dialysis treatment, clinical and/or

echocardiographic evidence of heart failure, lactate ≥2 mmol/L in at least two consecutive samples, presence of persistent fever (≥38º at least once a day for three consecutive days), and the highest value of ferritin, D-dimer, C-reactive protein, troponin I and LDH obtained during the first 14 days of invasive mechanical ventilation.

Statistical analysis: Dichotomic data are reported as frequencies and percentages while continuous data are presented as mean (standard deviation) or median (interquartile range) as appropriate, depending on the normality of distribution. Kolmogorov–Smirnov test was used to test normality of distribution for continuous variables. Comparisons between the two groups (VILI vortex vs. No VILI vortex) and intragroup (day: 7 vs. day: 14) were analyzed by either an independent t-test or the Mann–Whitney test. Differences in categorical variables were assessed using the χ^2 or Fisher's exact test.

The mortality predictive model following refractory hypoxemia as well as mortality for any reason was analyzed on day 90 by means of ROC curves. Survival difference between both groups was analyzed through longrank test. Cox's proportional hazards regression test was used to study the relationship between VILI vortex intensity and accumulative risk of death from refractory hypoxia. The difference of driving pressure ($\Delta\Delta P$) between days 7 and 14 was regarded as VILI vortex intensity expression. That was the period in which we more frequently observed VILI vortex development.

Data analysis was conducted with MedCalc 11.4.3.0 statistical software (Mariakerke, Belgium) and a p-value of <0.05 was considered statistically significant.