



Hypoxemia and prone position in mechanically ventilated COVID-19 patients: a prospective cohort study

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To the Editor,

During the coronavirus disease (COVID-19) outbreak, patients with severe COVID-19 related acute respiratory distress syndrome (ARDS) were admitted to our tertiary hospital intensive care unit (ICU). The benefits of prone position (PP) on survival have been highlighted in previous ARDS studies.¹ The aim of this study was to report the effects of PP in mechanically ventilated patients with COVID-19 related ARDS.

Between 1 March 2020 and 30 April 2020, we prospectively included all patients admitted to our ICU with COVID-19 related acute respiratory failure. COVID-19 was diagnosed by real-time reverse transcription polymerase chain reaction (rRT-PCR) test on a nasopharyngeal swab. During this period, 70 patients with confirmed COVID-19 were admitted; 64 (91%) received invasive mechanical ventilation during the course of the disease. They were ventilated with low

tidal volume ($\leq 6 \text{ mL}\cdot\text{kg}^{-1}$), plateau pressure below $30 \text{ cmH}_2\text{O}$, low driving pressure ($\leq 15 \text{ cmH}_2\text{O}$), and positive end-expiratory pressure according to the strategy proposed by the ARDS Network.² Patients for whom the ratio of arterial oxygen partial pressure to fractional inspired oxygen ($\text{PaO}_2/\text{F}_i\text{O}_2$) ratio remained below 150 for 12 hr despite this protective ventilation received at least one 16-hr PP session (flow chart, eFigure in Electronic Supplementary Material [ESM]). All patients were sedated and paralyzed before PP. Respiratory parameters were recorded before and at the end of the first 16-hr PP session. The compliance of the respiratory system (Cr_s) was calculated as tidal volume/(plateau pressure minus end-expiratory pressure). Ventilator settings were not modified during PP, and F_iO_2 was adjusted for a target peripheral oxygen saturation (SpO_2) of 92%.

Our local institutional review board waived the need for written consent and data collection was approved by the French licensing authority (number: PI2020_843_0026). Oral and written information was provided to the patients and their families. All parameters were compared using a Wilcoxon rank-sum test and $P < 0.05$ was considered as significant.

Twenty-five patients were analyzed. Clinical data appear in the ESM eTable. Prone position procedures significantly increased $\text{PaO}_2/\text{F}_i\text{O}_2$ ratio (95% confidence interval [CI]) from 91 (78 to 137) to 124 (97 to 149) mmHg ($P = 0.008$). Arterial partial pressure of carbon dioxide (PaCO_2) remained unchanged [from 49 (42 to 51) to 49 (44 to 57) mmHg; $P = 0.55$], as did Cr_s [from 32 (21 to 38) to 32 (23 to 40) $\text{mL}\cdot\text{cmH}_2\text{O}^{-1}$; $P = 0.33$ (Figure)], plateau pressure [from 28 (25 to 30) to 25 (24 to 29) cmH_2O ; $P = 0.16$] and ventilatory ratio [from 2.01 (1.47 to 2.51) to 1.98 (1.42 to 2.46); $P = 0.98$].

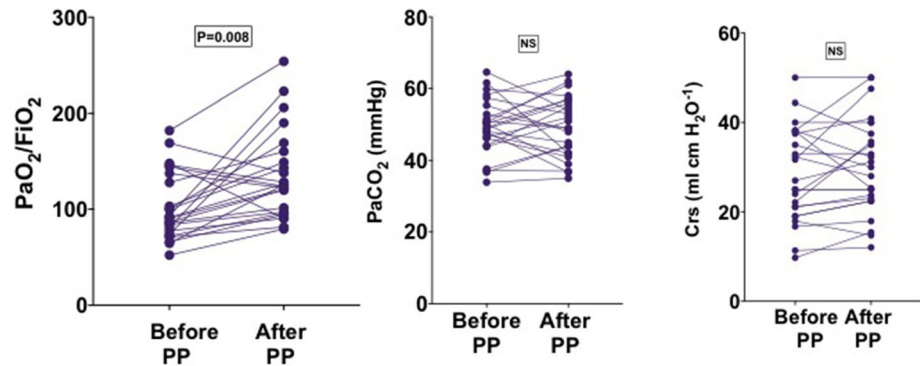
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Figure Effect of prone positioning on respiratory parameters. Changes in the ratio of arterial oxygen partial pressure to fractional inspired oxygen ($\text{PaO}_2/\text{F}_i\text{O}_2$), respiratory system compliance (Crs) and arterial partial pressure of carbon dioxide (PaCO_2) from supine to prone position (PP)



Prone position significantly improved oxygenation without any change in PaCO_2 or Crs in our population of mainly male patients. One of the beneficial effects of PP is the recruitment of non-aerated areas of the lungs. Previous studies have shown that improvement of PaCO_2 with PP suggests lung recruitment.³ We found that PaCO_2 , plateau pressure, Crs, and ventilatory ratio (a surrogate for dead space; see eAppendix, ESM) remained stable suggesting a lack of significant lung recruitment induced by PP. Hence, the increase in $\text{PaO}_2/\text{F}_i\text{O}_2$ ratio may be explained by an improvement in ventilation-to-perfusion ratio (VA/Q). Because ventilation is unchanged, VA/Q increase could only be explained by a decrease in pulmonary capillary flow (Q). If the decrease of Q is sufficient to improve oxygenation, we may suggest that a major mechanism involved in COVID-19 related ARDS is a VA/Q mismatch and probably an intra-pulmonary shunt.⁴ Gattinoni *et al.* have observed an increased shunt fraction in COVID-19 “atypical ARDS” and suggested “hyperperfusion” of gasless tissue.⁵ In this hypothesis, because lung shape is conical, the distribution of the shunt that predominates in the larger (posterior) part may be reduced by PP explaining the significant improvement in $\text{PaO}_2/\text{F}_i\text{O}_2$ ratio.

Despite its limited sample size, this study suggests that PP may improve oxygenation without changing ventilatory parameters, highlighting the possible role of a hidden intra-pulmonary shunt. Further investigations are mandatory before any formal conclusion.

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