



# Effect of prone positioning without mechanical ventilation in COVID-19 patients with acute respiratory failure

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To the Editor:

The efficacy of prone positioning (PP) without mechanical ventilation in coronavirus disease 2019 (COVID-19) patients with acute respiratory failure (ARF) remains uncertain. In a recent trial including 827 non-intubated COVID-19 patients with high baseline peripheral arterial oxygen saturation ( $S_{pO_2}$ )/inspiratory oxygen fraction ( $F_{IO_2}$ ) (around 200), PEREZ-NIETO *et al.* [1] reported that PP use was associated with lower intubation and mortality risk. However, other two large trials [2, 3] have conversely reported that compared with usual care, PP showed no benefit among non-intubated COVID-19 patients with ARF. The reasons for these inconsistent findings remain unknown. We noted that a subgroup analysis of one trial [3] reporting negative outcomes found that PP was associated with decreased intubation rate in the subgroup with  $S_{pO_2}/F_{IO_2} >150$  (HR 0.44, 95% CI 0.23 to 0.87), while this was nonsignificant in the subgroup with  $S_{pO_2}/F_{IO_2} <150$  (p-value for interaction 0.03). In addition, the baseline  $S_{pO_2}/F_{IO_2}$  is also higher in the trial reporting positive outcomes [1] than in the trial with negative findings [3] (baseline  $S_{pO_2}/F_{IO_2}$  200 [1] versus 135 [3]).

In addition, PP-based ventilation has been employed in acute respiratory distress syndrome (ARDS) and ARF for a long period [4]. However, current evidence indicates that PP-based ventilation is only effective in patients with moderate to severe ARDS (arterial oxygen tension ( $P_{aO_2}$ )/ $F_{IO_2} <150$  mmHg) [4] or ARF ( $P_{aO_2}/F_{IO_2} <100$  mmHg) [5]. This conclusion is opposite to the current findings in COVID-19 that PP showed benefit only in patients with mild ARF (high baseline  $S_{pO_2}/F_{IO_2}$  (around 200) [1], or  $S_{pO_2}/F_{IO_2} >150$  [3]). We believe that the mechanism of PP in COVID-19 is quite different from that in ARDS and the severity of ARF plays a key role in these inconsistent findings.

Physiologically, PP (>12 h per day) has been shown to decrease shunt fraction/dead space, and facilitate more homogeneous lung inflation and uniform distribution of mechanical forces [6]. However, all these PP-related physiological changes in the lung were only proven under “keep the lung open” mechanical ventilation strategies (appropriate positive end-expiratory pressure, *etc.*) [7], especially in ARDS (collapsed alveolar). Without “lung open” mechanical ventilation support or adequate duration (>12 h per day), PP alone is not sufficient to maintain lung compliance and regional ventilation of collapsed alveolar. However, most current studies in COVID-19 included non-intubated patients, and only short-period PP (4.2 h per day [2] or 5 h per day [3]) was performed without mechanical ventilation. In addition,  $S_{pO_2}/F_{IO_2}$  of 150 is approximately equal to  $P_{aO_2}/F_{IO_2}$  of 100 [8] (assuming  $F_{IO_2}$  0.6). Therefore, it is understandable that in non-intubated COVID-19 patients with severe hypoxaemia ( $S_{pO_2}/F_{IO_2} \leq 150$ ) [3], short-period PP alone without mechanical ventilation (open lung strategy support) failed to reduce intubation or mortality rate. However, in patients with mild hypoxaemia ( $S_{pO_2}/F_{IO_2} >150$  [3], or high baseline  $S_{pO_2}/F_{IO_2}$  (around 200) [1]), PP, to a certain degree, may exhibit clinical benefits by promoting sputum drainage or improving ventilation/perfusion ratio rather than improving alveolar collapse or lung compliance.



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**The mechanism of prone positioning in COVID-19 is quite different from that in ARDS and the severity of respiratory failure plays a key role in the efficacy of prone positioning in COVID-19**  
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