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## EDITORIALS

### Breathing face down

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### Summary

The prone position has been used to improve oxygenation in patients affected by acute respiratory distress syndrome, but its role in patients with COVID-19 is still unclear when these patients are breathing spontaneously. Mechanisms of ventilation and perfusion in the prone position are discussed, with new insights on how these changes relate to patients with COVID-19.

**Keywords:** ARDS; COVID-19; lung injury; noninvasive ventilation; oxygenation; prone positioning

The possible advantages of ventilating anaesthetised and paralysed patients in the prone position were suggested by Bryan<sup>1</sup> in 1974, and markedly improved oxygenation was reported in acute respiratory distress syndrome (ARDS) by Piehl and Brown<sup>2</sup> in 1976. Regardless the improvement in oxygenation, the prone position has been shown to provide survival benefit in patients with ARDS with a  $P_aO_2/FiO_2$  ratio  $<150$  mm Hg.<sup>3</sup> The reason for such survival improvement is likely a decreased risk of ventilator-induced lung injury because of the more homogeneous distribution of stress and strain throughout the lung parenchyma in the prone position. In the prone position, matching between chest wall and lung shape reduces the transpulmonary pressure gradient usually observed in the supine position. Consequently, whilst prone,

the dorsal lung regions (the principal location of atelectasis and consolidation in ARDS) tend to expand, whilst the ventral regions tend to collapse. As pulmonary perfusion in the prone position does not change, the result is an increase in oxygenation, when clearing of dorsal atelectasis prevails quantitatively relative to collapse of ventral lung.<sup>4</sup>

Patients with COVID-19 are characterised, at least in the early stages, by preserved lung parenchyma, near-normal respiratory system mechanics, and little atelectasis and consolidation. Despite the lack of atelectasis, the recruitment of which is the primary mechanism of improving oxygenation in ARDS, oxygenation also usually improves in patients with COVID-19. This suggests a different underlining mechanism. One possible explanation is that in COVID-19, control of perfusion is lost, with hyperperfusion of dorsal regions and a marked decrease in the ventilation/perfusion ratio. This is corrected when the patient is turned prone. Regardless of

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effects on oxygenation, the distribution of parenchymal stress and strain should be more homogeneous in the prone position in patients with COVID-19, as the underlining mechanism (i.e. better matching between lung and chest wall compliance) should be similar in COVID and typical ARDS.

Prone positioning in spontaneously breathing patients started in paediatric patients with respiratory distress to improve oxygenation.<sup>5</sup> The manoeuvre was then used in adults in addition to noninvasive ventilation with similar results.<sup>6</sup> The recent review from Fazzini and colleagues<sup>7</sup> analysed the effect of prone positioning in spontaneously breathing patients affected by severe hypoxaemia. Their analysis was based largely on recent studies conducted in patients with COVID-19. Use of the prone position to improve oxygenation in patients with COVID-19 started in China during the first pandemic wave to overcome the paucity of intensive care beds and to delay the need for mechanical ventilation.

There are some controversial data in this arena that need to be commented on further. Firstly, the prone position has been proved to improve oxygenation in mechanically ventilated patients with ARDS,<sup>8</sup> but it must be applied for prolonged periods of time (at least 16 h) to improve the  $P_aO_2/FiO_2$  ratio in severely hypoxaemic patients.<sup>9</sup> This recent review in the *British Journal of Anaesthesia* shows a significant improvement of the  $P_aO_2/FiO_2$  ratio of  $-3.5$  when patients received awake prone ventilation. A subgroup analysis showed significant improvement when patients maintained the prone position for more than 4 h, although they could not conclude if the duration of pronation was cumulative or consecutive. A recent study in awake patients with COVID-19 revealed substantial efficacy of prone positioning when started early and for at least 10 h daily.<sup>10</sup> This raises a practical concern, as prone positioning has been associated with poor tolerance. This potentially could have been improved by administering sedative drugs, such as dexmedetomidine.<sup>11</sup> Tolerance for the prone position can also be improved when noninvasive ventilation is added.<sup>12</sup>

A second point that has been raised by the review by Fazzini and colleagues is that they were not able to define a threshold  $P_aO_2/FiO_2$  value for initiating prone positioning. Sartini and colleagues<sup>13</sup> performed a 1 day cross-sectional before–after study on pronation, including 15 awake patients with mild-to-moderate ARDS, where the  $P_aO_2/FiO_2$  ratio on medical emergency team arrival was 157 (43). In their cohort, patients receiving noninvasive ventilation plus prone positioning had an improvement in oxygenation and respiratory rate compared with those receiving noninvasive ventilation only.  $P_aO_2/FiO_2$  should not be the only parameter to consider when deciding if a patient might benefit from pronation, as we can potentially create more damage to an already-injured lung because of the excess stress (increased transpulmonary pressure equivalent to airway pressure minus pleural pressure) associated with strain, which is the ratio of volume change to functional residual capacity, or the resting lung volume.<sup>14</sup> We can understand this better from the partitioning of ventilation mechanics,<sup>15</sup> starting from measurement of transpulmonary pressure as changes to oesophageal pressure, as detected by an oesophageal balloon.<sup>16</sup> Other imaging modalities, such as ventilation/perfusion single-photon emission computed tomography (CT) combined with CT (V/Q SPECT/CT)<sup>17</sup> and electrical impedance tomography, allow determination of the most affected lung areas responsible for ventilatory anomalies with relatively preserved perfusion. Point-of-care lung ultrasound has been advocated more recently to evaluate the effect of pronation on non-ventilated areas and

possibly to avoid a longer time in the prone position if no benefit is found in terms of oxygenation or reduction of B-lines.<sup>18</sup>

It is still unclear if awake pronation can reduce the need for intubation,<sup>19,20</sup> and the review by Fazzini and colleagues found similar results with an odds ratio for intubation of 0.73 (0.34–1.56;  $P=0.420$ ;  $I^2=79\%$ ) for patients pronated compared with supine controls. Their subgroup analysis differentiating patients who stayed in this position  $>4$  h favours pronation, but the heterogeneity of the studies was high and leads to uncertainty in interpretation of the results. The mortality of patients who stayed for a prolonged period in the awake prone position was not different to those who remained for a shorter period of time. This is not surprising, as the need for intubation should not be based only on the level of hypoxaemia but also on ventilation mechanics, haemodynamic derangement, and tolerance by the patient of the hypoxaemic state.

Prone positioning could reduce mortality compared with supine positioning, but it is still unclear if the time spent in this position was insufficient to provide benefit or was too long, leading to respiratory fatigue and potentially to patient self-inflicted lung injury.<sup>21</sup> This is one of the worst possible scenarios, as patients could deteriorate quickly once they exhaust the advantage of the recruitment of non-ventilated areas. In this situation, the hypoxic vasoconstriction is already at a stage that is creating a shunt that the patient cannot reduce with the prone position, and the spontaneous ventilation mechanics increase respiratory fatigue and decrease lung function. At this point, the patient could start feeling more discomfort, and many have described a sensation of blowing into a narrow drinking straw.

Intensivists frequently encounter crossroads where they must make critical decisions about intubating patients for mechanical ventilation. In the current pandemic with limited human and logistic resources, awake prone positioning was considered a possible path to improve oxygenation in a patient on the verge of respiratory failure. To answer if this manoeuvre is beneficial to patients, we should first ask the patient if the position itself is tolerable and if there is subjective improvement in the respiratory fatigue caused by hypoxaemia. Second, we should not delay tracheal intubation if the patient is not tolerating the prone position and is not improving, and if we have data showing increased lung stress and strain. In an era of sophisticated respiratory parameters, we should not forget that the first and best monitor is the patient, and we should consider different options (mechanical vs noninvasive ventilation) according to the patient's response and not to single numbers.

## Author contribution statement

The authors contributed equally to this manuscript.

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## Declarations of interest

The authors declare no conflicts of interest.

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## Improving safety and outcomes in perioperative care: does implementation matter?

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