

## Prone the Lung and Keep It Prone!



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Prone positioning (PP) has been used for a long time as a rescue therapy for severe hypoxemia in patients with ARDS because of its effectiveness in improving oxygenation and in reducing mortality in those with a more compromised Pao<sub>2</sub> to Fio<sub>2</sub> ratio (ie, < 150 mm Hg).<sup>1</sup> Nevertheless, despite that the clinical indication for PP is to improve gas exchange, its benefits on mortality may be related to its veiled effects on stress and strain distribution, lung concentration of proinflammatory cytokines,<sup>2,3</sup> and aeration and ventilation distribution throughout the lung.<sup>4,5</sup> To sum up, its potential effects reduce the risk of ventilator-induced lung injury.

Recently, SARS-CoV-2 infection has put a great burden on the health system all over the world, and physicians have had to struggle with an apparently new form of ARDS associated with great mortality, varying between 43% and 60%.<sup>6,7</sup> One of the most-used strategies for obtaining better gas exchange is PP, which rapidly became a standard of care for most intensivists also for its effect on mortality.<sup>8</sup> However, although substantial agreement exists regarding the need to place these patients in PP, little is known regarding how long they should be kept in this position.

One may think that prolonged PP could be associated with a better outcome, but at the same time, the potential benefits of prolonged PP could expose the

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patients to other risks, such as the need for a higher level of sedation or muscle relaxant infusion and increased risks of pressure wounds, device displacement, accidental extubation, or facial edema. To date, the net balance between potential risks and benefits of prolonged PP have not been determined, and a good clinical compromise has been to apply the Prone Positioning in Severe Acute Respiratory Distress Syndrome (PROSEVA) trial protocol,<sup>1</sup> that is, to keep patients in PP for at least 16 h/d.

In this issue of *CHEST*, the concept of prolonged PP in COVID-19 ARDS was tested in the study by Okin et al.<sup>9</sup> The authors evaluated retrospectively whether prolongation of PP beyond the conventional 16 h may be associated with improved mortality. Interestingly, the authors found that intubated patients undergoing prolonged PP (with a median duration of the first session of 40 h) showed a lower mortality risk at 30 and 90 days as compared with patients undergoing an intermittent pronation strategy. This result was even more evident when patients were sicker, with an initial Pao<sub>2</sub> to Fio<sub>2</sub> ratio of < 150 mm Hg. The prolonged PP group showed, as the only side effect, a higher incidence of facial edema.

This elegant article provides a signal regarding the possible advantages of prolonged PP in invasively ventilated patients with COVID-19 ARDS and integrates the value of time in mechanical ventilation during PP. Moreover, the findings by Okin et al<sup>9</sup> are perfectly aligned with data on spontaneously breathing patients with COVID-19, in which the cumulative time spent in awake PP has been shown to be associated directly to a survival benefit.<sup>10</sup>

Of note, time is a partially neglected element of the delicate relationship between lung injury and lung protection. The results of the study by Okin et al<sup>9</sup> seem to suggest that every time we interrupt PP, we are increasing the risk of ventilator-induced lung injury, and it is tempting to think that in those patients in whom we can reduce ventilator-induced lung injury by using PP, we are obtaining benefits. This is somehow expected when we decide to place patients in PP; what is new is that prolonged PP adds further benefits that we should take into account in our clinical practice. Moreover, because ventilation

and pressure redistribution may require some time after PP, an interruption of PP may determine a reset of the process that therefore must start over at each position change.

However, although the findings by Okin et al<sup>9</sup> increase the knowledge in the field, they also leave some space for many additional questions. First, the precise mechanism associated with the time dependency of PP effect on mortality has not been explored and could be important for further understanding and advancement of the current state of art in lung protective ventilation. Whether the improvement is related to a time-dependent phenomenon or simply to a cumulative reduction of risk must be explored by physiologically targeted trials. In this context, advanced respiratory imaging (ie, CT scan or electrical impedance tomography) can help to evaluate these effects and to identify the appropriate positive end-expiratory pressure to apply in combination with PP strategy. Second, targets for lung protective mechanical ventilation in PP have been translated simply from the supine position. Whether patients undergoing prolonged PP may benefit further from specific ventilatory settings and whether alternative targets of protective mechanical ventilation may exist has to be explored urgently. Third, this article regards patients with COVID-19. We know that COVID-19 ARDS has peculiar characteristics, such as the diffuse involvement of endothelium, the heterogeneous response to positive end-expiratory pressure, and a significant  $\dot{V}/\dot{Q}$  mismatch.<sup>11</sup> The identification of COVID-19 phenotypes<sup>12</sup> underlines that the benefits of treatments could be determined by the presence of different pathophysiologic entities. The authors, unfortunately, did not provide evidence about the phenotypes of COVID-19 ARDS, so that we do not know whether the reduction in mortality is peculiar to a specific group of patients. A one-size-fits-all approach may not always be the correct answer, and seeking a personalized strategy based on the specific patient's phenotype should be encouraged.

As a final comment, we believe that the clinical benefit coming from this study is that we should place these

patients in PP and keep them in PP for a long time. According to our experience, many clinicians realized that prolonged PP was a good strategy in patients with COVID-19 ARDS, but it is extremely encouraging now to know that we were right!

## Financial/Nonfinancial Disclosures

None declared.

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