

# Prone Position and COVID-19: Mechanisms and Effects\*

**KEY WORDS:** coronavirus disease 2019; mechanical ventilation; lung recruitment; prone position

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Prone positioning was first applied in critically ill patients by Piehl and Brown (1) in 1976 who reported a marked oxygenation improvement in five patients with acute respiratory failure. This observation remained essentially a curiosity until the first CT scan of acute respiratory distress syndrome (ARDS) patients showed that parenchymal densities were disproportionately distributed in the dorsal lung regions. This finding provided the anatomical hypothesis for the improvement in gas exchange and led to an increase in the clinical use of prone position (2). The assumption was that the normally ventilated lung located in the “ventral” regions (i.e., the anatomical concept of “baby lung”) would be better perfused if placed in a gravitationally dependent position, improving the overall ventilation/perfusion (V/Q) ratio, and hence gas exchange. However, further studies of CT scans taken with patients in the prone position disproved the mechanistic hypothesis that change in perfusion determined its effects on oxygenation (3). On the contrary, it became apparent that the main effect following prone position was the redistribution of lung densities from the dorsal to the ventral lung regions. This discovery led to the formulation of the “sponge” model of the lung in which the rapid resolution and formation of atelectasis in different regions of the heavily edematous ARDS lung are primarily due to changes of superimposed hydrostatic pressure which follow the change in gravitational axis (4). The improvement of oxygenation, consistently found both clinically and experimentally, prompted the parallel implementation of clinical trials. Over the ensuing years, diverse studies of prone positioning led on one hand to better understanding of the mechanisms that improve oxygenation; on the other hand, observational and clinical trials that progressively refined the indications for its use in ARDS. Significant survival benefits were demonstrated when prone position was applied for 12–16 consecutive hours in the more severe forms of respiratory failure ( $\text{PaO}_2/\text{FiO}_2 < 150$  mm Hg) (5), whereas its application does not provide convincing survival advantage in patients with milder disease (6). Therefore, what we understood regarding “typical” ARDS might be summarized as follows: prone positioning in ARDS, a condition characterized by extensive inflammatory edema, leads to decreased frontal chest wall compliance, to partial clearing of dorsal atelectasis, and to the development of new ventral atelectasis. In most patients, the balance favors clearing of dorsal atelectasis, thus increasing the net amount of well-aerated tissue. Regarding perfusion, evidence from both experimental models and clinical studies indicated little change with the shift from supine to prone position (7, 8).

As we learned in other landmark trials, however, better oxygen exchange does not satisfactorily explain the survival advantage attributable to prone

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positioning. The improved survival is more likely to result from the greater homogeneity in alveolar dimensions, the reduction in the maximal tissue stretch, and a more uniform distribution of stress and strain throughout the lung parenchyma associated with prone position (9). This possibility is supported by data from human and experimental animals, which show less variation in the size of the individual pulmonary units along the vertical axis in the prone as opposed to in supine position, due to a better anatomical matching of lung and chest wall shapes and compliances (9).

During the COVID-19 pandemic, the use of prone position increased exponentially to reverse hypoxemia not only in patients receiving mechanical ventilation but also in awake patients who breathe spontaneously or receiving noninvasive ventilation (10). A series of epidemiological studies has confirmed that oxygenation improves with prone positioning in 60–80% of COVID-19 patients (11), but little physiologic data are available to understand the relationship between improvement in gas exchange and patient outcome. Indeed, we should understand why some patients do not respond to prone positioning and determine whether this technique is just a gas exchange cosmetic or, conversely, a driver of improved clinical outcomes. Several mechanisms may account for improved oxygenation: 1) global alveolar recruitment, 2) increase of the nondependent lung mass in prone position (60% vs 40% of the supine position), and 3) decrease of the total chest wall compliance due to the functional stiffening of the ventral chest wall. These mechanisms may be discussed in the light of the new information provided by Fossali et al (12), published in this issue of *Critical Care Medicine*.

### Global Alveolar Recruitment

In “typical” ARDS, a net recruitment, with unmodified perfusion, is the widely accepted mechanism for improved oxygenation (13). However, in this series of COVID-19 patients, studied on the first week after intubation, the recruitment was relatively modest (6% vs a median of 16–20% in “typical” ARDS) and, more relevant, was completely dissociated from the improvement of gas exchange. These data undercut the importance of recruitment in the early stages of the disease, particularly as prone position has been found to improve oxygenation even in early stages of COVID-19 pneumonia, when atelectasis and potential for lung

recruitment are negligible compared with “typical” ARDS with similar Berlin-defined severity. This strongly implies that the mechanisms of hypoxemia and the responses to positive end-expiratory pressure also differ in these COVID-19 patients. Despite the relatively low global recruitment and regardless of the gas exchange, it must be noted that in the study by Fossali et al (12), the dorsal aeration did improve lung homogeneity and may have reduced the stimulus for atelectotrauma—as evidenced by electrical impedance tomography.

### Increase of the Nondependent Lung Mass

In fully supine (0°) position, approximately 60% of the total lung mass is dependent, that is, in the lower 50% of the sternovertebral axis. In COVID-19 pneumonia, the lack of regulatory control of perfusion promotes greater perfusion of these dependent regions, leading to a decrease in the V/Q ratio. As the final arterial  $PO_2$  depends on the weighted mean of the  $PO_2$  of blood flowing from diverse pulmonary units, the greater number of atelectatic units in the dependent lung regions, the more severe will be the hypoxemia. In contrast, in prone position, only 40% of the tissue mass is in the dependent position, that is, fewer pulmonary units will be hyperperfused, resulting in better oxygenation. In summary, the distribution of the lung mass and the regional perfusion may play a significant role in determining oxygenation.

### Decrease of the Total Chest Wall Compliance

The normal mechanical response to prone position is a decrease in the total chest wall compliance due to the functional stiffening of the anterior chest wall. Consequently, regional ventilation becomes less unevenly allocated, resulting in more homogeneous V/Q distribution. Indeed, Fossali et al (12) showed a reduction in dead space in the ventral areas and decrease in shunt in the dorsal areas. The lack of decrease of total respiratory system compliance during prone in position, as observed in the study by Fossali et al (12), suggests that the overall lung compliance improved. It must be noted that the same effect may be achieved by compressing the anterior chest-wall in supine position (i.e., making the anterior chest wall as stiff as the dorsal one), a maneuver which may result in “paradoxical” improvements of gas exchange (13).

In summary, the improvement (or the lack of improvement) in oxygenation in COVID-19 patients depends on the interplay among the mechanisms

described. At this stage of the disease (within 1 wk from intubation), the recruitment is one of the possibilities, but likely, not the most important, as strongly suggested by the lack of correlation between recruitment and oxygenation, a finding similar to what recently found with the CT scan in COVID-19 patients when studied at the same stage of the disease (14, 15).

Although the cure of COVID-19 patients in ICU is often confused with a cure of  $\text{PaO}_2$ , we must remember that increased survival, when related to mechanical ventilation, may not be directly attributable to the  $\text{PaO}_2/\text{FiO}_2$  ratio but instead with a better distribution of alveolar stress and strain. Indeed, the possible decrease of mortality due to a supportive therapy such as prone position is solely due to a decreased harm of mechanical ventilation.

In early stages of COVID-19 disease where the compliance is usually high and the lungs are full of gas, the hypoxemia is dictated by alteration in perfusion. It is difficult to imagine that under such circumstances, mechanical ventilation produces dangerous levels of stress and strain. In this condition, prone positioning is not strictly necessary. However, COVID-19 pneumonia is an evolving disease. As shown in this article by Fossali et al (12) lung weight may increase with passing time causing more atelectasis to develop. At this more advanced stage, prone position may find its place. Finally, in late stages of the disease, the likelihood for oxygenation to improve with prone positioning becomes extremely low. We recently found that this phenomenon may be due to the progression of lung consolidation toward organizing fibrotic pneumonia (14).

We thank Fossali et al (12), who contributed to a better understating of COVID-19 disease by performing an impressive physiologic study under extremely difficult pandemic conditions. When all the data are taken into consideration, we believe that prone position lessens the damage delivered by the mechanical ventilator, regardless of gas exchange. Therefore, given the safety of the procedure and if staffing is available, prone position should be a strong consideration in the care of critically ill ventilated patients.

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