# Prone Positioning for Patients With COVID-19–Associated Acute Respiratory Distress Syndrome

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**To the Editor:**

We have read with interest the experimental, physiologic study by Fossali et al (1), assessing the physiologic effects of pronation by means of CT scan and electrical impedance tomography. This study raises some interesting issues that might contribute to the study and future investigations.

As shown by the present study, the authors pointed out that prone positioning can improve oxygenation in COVID-19–associated acute respiratory distress syndrome (C-ARDS) by increasing lung recruitment, decreasing atelectrauma, and improving ventilation-perfusion matching. Ventilation-perfusion matching can improve rapidly with the change of body position, which can be explained the dramatically changes of physiologic effects, including oxygenation within a few minutes after prone positioning, as shown by this present study and another study (2), but how long this improvement will be sustained is unknown. Theoretically, with the extension of prone position, pulmonary edema and atelectasis in dependent lung zones will occur in the ventral lung regions and the overall effect will be reversed, just as Fralick et al (3) found that there was no sustained improvement in oxygenation related to prone positioning.

In addition, this article has not yet provided the effects of the prone position on mortality and long-term prognosis. Whether prone positioning is an effective therapy to decrease mortality in patients with C-ARDS remains unclear. A systematic review and meta-analysis showed that patients with mild or moderate ARDS who received prone positioning had improved oxygenation, but the improvement did not correlate with a mortality benefit (4). The physiologic differences between ARDS from COVID-19 and other causes appear small (5). A multicenter pragmatic randomized clinical trial showed that prone positioning of COVID-19 patients with moderate hypoxemia did not improve the risk of the composite of death, mechanical ventilation, or worsening respiratory failure (3).

COVID-19 patients are considered to have heterogeneity in respiratory mechanics and interindividually variable recruitability (5). How longer duration of time spent prone is associated with beneficial clinical outcomes is still uncertain. Previous studies suggested that a mortality benefit was observed only with longer durations (12–16 hr) of prone positioning for mechanically ventilated ARDS patients with or without COVID-19 (4). Considering that many questions about prone positioning remain unknown, such as suitable patient selection, timing of starting, and stopping prone positioning and its cost-effectiveness, rigorous randomized controlled trials that examine clinical outcomes of prone positioning in patients with COVID-19 are needed.

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### The authors reply:

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We thank Wang et al (1) for the interesting comments on our recently published physiologic study (2) in *Critical Care Medicine*, which give us the opportunity to further discuss our results.

The physiology of COVID-19 acute respiratory distress syndrome (C-ARDS) is far from being fully understood. We do not yet know if it can be considered a "separate" syndrome with respect to the so-called "classical" acute respiratory distress syndrome (ARDS). However, we described a different response to prone position in comparison with typical ARDS (2): recruitment was significant but lower (6% vs 16–20%) and dissociated from the improvement of gas exchange; ventilation-perfusion mismatch improved but mostly through decreased dead space (a rather specific hallmark of C-ARDS); and finally, respiratory system compliance was elevated and not affected by prone position, with cyclic alveolar opening and closing (i.e., atelectrauma) playing a major role in determining the impairment of respiratory mechanics.

As underlined by Wang et al (1), C-ARDS has significant inter- and intra-individual heterogeneity. The disease evolves during the clinical course, as does the response to prone position, as shown by Rossi et al (3). These authors observed a larger extent of lung consolidation and poorer response to prone position in patients studied after the third week of mechanical ventilation, becoming more similar to the typical ARDS. Similarly, postmortem pulmonary findings of C-ARDS demonstrated different histopathologic clusters linked to the duration of mechanical ventilation (4), which could represent the anatomical basis for varying response to recruitment, positive end-expiratory pressure, and/or prone position during the clinical course.

Our article (2) did not provide any data on the correlation between prone position and clinical outcomes, and this remains an open issue, as indicated by Wang et al (1). The effects of prone position on long-term outcome and mortality remain unclear. A study by Mathews et al (5) suggested improved survival by

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