

ARDS with COVID-19. An intermediate  $V_T$  (7–8 ml/kg PBW) ventilation strategy was applied to the first four patients to increase pulmonary efficiency to eliminate  $\text{CO}_2$ , and this was used in the next four patients.

Gas exchange consists of oxygenation and ventilation. Oxygenation is quantified by the  $\text{PaO}_2/\text{FiO}_2$  ratio, and this method has gained wide acceptance, particularly since publication of the Berlin definition of ARDS (7). However, the Berlin definition does not include additional pathophysiological information about ARDS, such as alveolar ventilation, as measured by pulmonary dead space, which is an important predictor of outcome (8). Increased pulmonary dead space reflects the inefficiency of the lungs to eliminate  $\text{CO}_2$ , which may lead to hypercapnia.

In our patients with ARDS with COVID-19, hypercapnia was common at ICU admission with low  $V_T$  ventilation. Assuming the anatomic portion of dead space is constant, increasing  $V_T$  with constant respiratory rate would effectively increase alveolar ventilation. Any such increase in  $V_T$  would decrease  $\text{PaCO}_2$ , which would be captured by VR (6). VR, a novel method to monitor ventilatory adequacy at the bedside (4–6), was very high in our patients, reflecting increased pulmonary dead space and inadequacy of ventilation.

With an acceptable plateau pressure and driving pressure, titration of  $V_T$  was performed.  $\text{PaCO}_2$  and VR were significantly decreased when an intermediate  $V_T$  (7–8 ml/kg PBW) was applied. We suggest that intermediate  $V_T$  (7–8 ml/kg PBW) is recommended for such patients. Therefore, low  $V_T$  may not be the best approach for all patients with ARDS, particularly those with a less severe decrease in respiratory system compliance and inadequacy of ventilation.

In summary, we found that hypercapnia was common in patients with COVID-19–associated ARDS while using low  $V_T$  ventilation. VR was increased in these patients, which reflected increased pulmonary dead space and inadequacy of ventilation. An intermediate  $V_T$  was used to correct hypercapnia efficiently, while not excessively increasing driving pressure. Clinicians must have a high index of suspicion for increased pulmonary dead space when patients with COVID-19–related ARDS present with hypercapnia. ■

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## COVID-19 Does Not Lead to a “Typical” Acute Respiratory Distress Syndrome

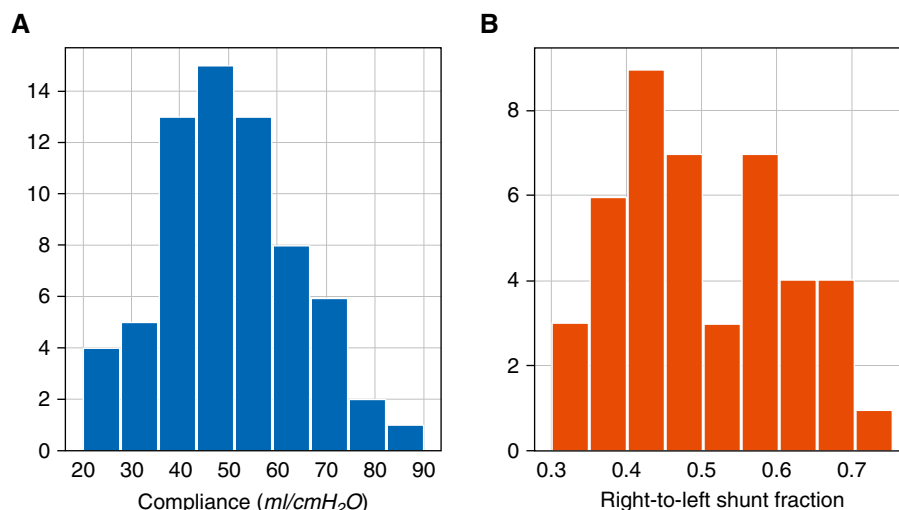


To the Editor:

In northern Italy, an overwhelming number of patients with coronavirus disease (COVID-19) pneumonia and acute respiratory failure have been admitted to our ICUs. Attention is primarily focused on increasing the number of beds, ventilators, and intensivists brought to bear on the problem, while the clinical approach to these patients is the one typically applied to severe acute respiratory distress syndrome (ARDS), namely, high positive end-expiratory pressure (PEEP) and prone positioning. However, the patients with COVID-19 pneumonia, despite meeting the Berlin definition of ARDS, present an atypical form of the syndrome. Indeed, the primary characteristic we are observing (and has been confirmed by colleagues in other hospitals) is a dissociation between their relatively well-preserved lung mechanics and the severity of hypoxemia. As shown in our first 16 patients (Figure 1), a respiratory system compliance of  $50.2 \pm 14.3$  ml/cm  $\text{H}_2\text{O}$  is associated with a shunt fraction of  $0.50 \pm 0.11$ . Such a wide discrepancy is virtually never seen in most forms of ARDS. Relatively high compliance indicates a

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**Figure 1.** (A) Distributions of the observations of the compliance values observed in our cohort of patients. (B) Distributions of the observations of the right-to-left shunt values observed in our cohort of patients.

well-preserved lung gas volume in this patient cohort, in sharp contrast to expectations for severe ARDS.

A possible explanation for such severe hypoxemia occurring in compliant lungs is a loss of lung perfusion regulation and hypoxic vasoconstriction. Actually, in ARDS, the ratio of the shunt fraction to the fraction of gasless tissue is highly variable, with a mean of  $1.25 \pm 0.80$  (1). In eight of our patients with a computed tomography scan, however, we measured a ratio of  $3.0 \pm 2.1$ , suggesting a remarkable *hyperperfusion* of gasless tissue. If this is the case, the increases in oxygenation with high PEEP and/or prone positioning are not primarily due to recruitment, the usual mechanism in ARDS (2), but instead, in these patients with poorly recruitable lungs (3), result from the redistribution of perfusion in response to pressure and/or gravitational forces. We should consider that 1) in patients who are treated with continuous positive airway pressure or noninvasive ventilation and who present with clinical signs of excessive inspiratory efforts, intubation should be prioritized to avoid excessive intrathoracic negative pressures and self-inflicted lung injury (4); 2) high PEEP in a poorly recruitable lung tends to result in severe hemodynamic impairment and fluid retention; and 3) prone positioning of patients with relatively high compliance provides a modest benefit at the cost of a high demand for stressed human resources.

Given the above considerations, the best we can do while ventilating these patients is to “buy time” while causing minimal additional damage, by maintaining the lowest possible PEEP and gentle ventilation. We need to be patient. ■

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