Tidal volume, positive end-expiratory pressure, and mortality in acute respiratory distress syndrome

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In this issue of Critical Care Medicine, Brower and colleagues [1] present the fourth published randomized trial comparing two ventilatory strategies and their impact on mortality in the acute respiratory distress syndrome (ARDS) [2-4]. The rationale behind these studies is that mechanical ventilation can be injurious to the lung and induce an "iatrogenic" death. Many experimental studies have convinced intensivists that the severe pulmonary lesions observed in animal models also could be observed in patients [5]. Unfortunately, no direct transposition of the levels of volume and pressure can be inferred from animal studies to be used as a threshold for the upper limit of ventilation in humans. The specific compliance of the lung, i.e., the extent to which every unit of lung volume can be distended by a given pressure, is similar among all mammalian species. This means that the same distending pressure gives the same degree of lung distension in mice, dogs, humans, horses, and whales. This suggests that the amount of pressure used in the animal studies to generate permeability pulmonary edema could help to indicate the limit of pressure to be used in humans. Other variables that influence this pressure or the number of lesions generated, however, differ markedly between species, such as chest wall compliance or the properties of the vascular bed within the lung, making it difficult to apply any pressure limit to humans. For this reason, a Consensus Conference held a few years ago based its recommendations mainly on normal physiology; its conclusion was that a distending, or transalveolar, pressure of 35 cm H2O should not be exceeded [6]. In the field of ARDS this was sound, if we admit that the specific compliance of the open aerated lung is normal [7]. It thus suggests that submitting the whole ARDS lung to 35 cm H2O exposes the open areas to their maximal regional capacity. Surprisingly, we have very few data on this important aspect of specific compliance in ARDS, with some conflicting studies.

Brower and colleagues [4] mainly compared two settings for tidal volume in 52 patients with ARDS. Positive end-expiratory pressure (PEEP) level, mode of ventilation, respiratory rate, and inspiratory-to-expiratory ratio were kept similar in the two arms. They designed and used an interesting protocol for management of oxygenation in terms of balance between PEEP and FIO2. They also carefully recorded the amount of sedation and neuromuscular blockers, the intake and output fluid balance, and compliance with the protocol. Although the small size of the study is its major limitation, the study offers interesting and important results, especially when combined with the previous recent studies.

It is interesting to see that the standard or control group is referred to as the "traditional" tidal volume group. In fact, this setting of tidal volume (around 10 mL/kg of body weight) had become a standard at the time when all of these recent studies were designed, in part because the animal literature had already
suggested to limit tidal inflation. It is important to remember that much higher levels of volume were used 15 to 20 yrs ago (see Table 1) [8]. Like other recent trials [2,3], this study shows that such a traditional tidal volume setting allows a reasonable level of alveolar ventilation, with a mean plateau pressure of <35 cm H₂ O, and is associated with a very low incidence of barotrauma. No benefit was observed with a further systematic reduction of this volume.

Table 1. Tidal volume range in acute respiratory distress syndrome

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<tr>
<th>Author(s)</th>
<th>Tidal Volume (mL/kg)</th>
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<td>Amato et al.</td>
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Barotrauma and pneumothorax are not only important because their occurrence may influence outcome, but also because they constitute possible markers of ventilator-associated lung injury. There are currently no indicators of ventilator-induced lung injury, because the lesions thought to be generated by the high distending pressures of the ventilator cannot be distinguished from the underlying lung syndrome called ARDS. The study by Amato and colleagues [1] thus offers an interesting comparison. Indeed, in that study, the control group used larger tidal volumes, in the range of 12-13 mL/kg.

These volumes resulted in much higher plateau pressures, reaching rapidly between 35 and 40 cm H₂ O, and were associated with a considerably higher rate of barotrauma (>40%). Finally, the control group in the study by Amato et al. had a mortality rate at 30 days of 70%, which is also higher than in the other studies. Although this value may appear elevated compared with the mortality in the three other studies, it is again worth noting that is it still well below the settings used in this syndrome some 15 yrs ago (see Table 1). Obviously, a comparison between the four recent studies [1-4] is difficult. For instance, the PEEP setting was quite different between the two arms in the study by Amato et al., and the high PEEP level used in combination with the reduced tidal volume may have had a substantial protective effect, in line with experimental studies [9].

Reasonable conclusions must be drawn from all of these studies. First, it seems that the standard or now traditional tidal volume setting of 10 mL/kg is by and large relatively safe and that a systematic and more drastic reduction in tidal volume cannot be recommended. Second, it also seems that an upper limit of plateau pressure and tidal volume above which there is a high risk of ventilator-associated (and presumably ventilator-induced) lung injury does exist, and that, at least as a mean value, the limit of 35 cm H₂ O may be reasonable. Finally, recent important pathophysiologic studies [10,11] have reminded us that the chest wall may play an important role in the pressure read on the ventilator. This pressure, interpreted as a "distending" pressure, would be misinterpreted and could lead to excessive and potentially harmful hypoventilation of patients in case of major impairment of chest wall properties.

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