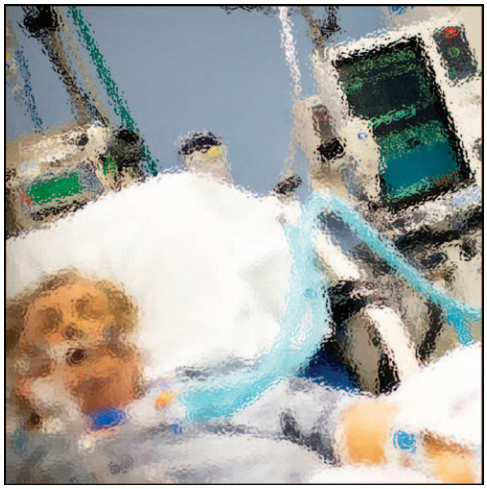
When to Promote Spontaneous Respiratory Activity in Acute Respiratory Distress Patients?

Takeshi Yoshida, M.D., Ph.D., Laurent Papazian, M.D., Ph.D.

IN this issue of Anesthesiology, Dr. Xia *et al.*[1] investigated the potential beneficial effects of a ventilator mode allowing spontaneous ventilation in an animal model. Preventing ventilator-induced lung injuries and achieving adequate gas exchange are the main objectives during the early phase of severe acute respiratory distress syndrome (ARDS). This may be done by maintaining a reduced tidal volume,[2] by using prone ventilation[3] and by eliminating spontaneous inspiratory efforts (during the early phase)[4] in patients with severe ARDS. In contrast, in less severe forms of ARDS, or when the initial phase of severe ARDS associated with severe blood gas exchange impairment has ended, it is generally believed that preserving muscle strength, especially diaphragmatic activity (by allowing spontaneous ventilation), could lead to a better outcome (reduced duration of mechanical ventilation).[5] Various ventilatory modes allowing spontaneous efforts have been proposed such as biphasic positive airway pressure (BIPAP) and airway pressure release ventilation (APRV).



"After this initial period [of severe acute respiratory distress syndrome], it could be of interest to stimulate spontaneous [ventilation] by using ventilatory modes such as [airway pressure release ventilation, biphasic positive airway pressure], or pressure support."

From a physiological point of view, inflation of the lung occurs when the pressure on the lung surface (*i.e.*, pleural pressure) becomes sufficiently negative due to spontaneous breathing effort or when pressure in the airway (from positive-pressure ventilation) becomes sufficiently positive. When spontaneous breathing is preserved during positive-pressure ventilation, negative changes in pleural pressure may be coupled with positive-pressure changes from the ventilator, magnifying transpulmonary pressure = airway pressure – pleural pressure. In normal, homogeneous lungs, development of a more negative pleural pressure due to diaphragmatic contraction is proven to result in a uniform increase in transpulmonary pressure at all points on the lung surface (*i.e.*, the fluid-like behavior of normal lungs).[6]

Thus, spontaneous ventilation is supposed to improve lung ventilation at lower levels of airway pressure and is traditionally encouraged in patients receiving mechanical ventilation. However, expiratory muscle activity triggered by the need for high minute ventilation (agitation, fever, lung disease, and many more) can alter gas exchange by several mechanisms including the cephalad displacement of the diaphragm and reduced end-expiratory lung volume and positive end-expiratory pressure efficiency. Inspiratory respiratory drive can be deleterious by increasing respiratory rate, reducing tidal volume, promoting dynamic hyperinflation, and increasing oxygen consumption.

In this issue of Anesthesiology, Xia *et al.* showed that in a preclinical setting of "*mild to moderate*" ARDS, "*mild*" spontaneous efforts preserved during BIPAP ventilation attenuated histological lung injury, especially in dorsal lung regions. BIPAP also reduced proinflammatory cytokines (interleukin-6 and interleukin-8) at the messenger RNA level. There was an associated improvement in gas exchange and less dead space ventilation.[1] Xia *et al.* offered a plausible explanation for the beneficial effects of spontaneous breathing in mild forms of experimental ARDS: negative pleural pressure generated by diaphragmatic contraction, coupled with positive-pressure changes from the ventilator further help to recruit dorsal collapsed lung, contributing to a better lung aeration and

Image: J. P. Rathmell.

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Accepted for publication March 11, 2014. From the Department of Anesthesiology and Intensive Care Medicine, Osaka University Graduate School of Medicine, Suita, Japan (T.Y.); and Réanimation des Détresses Respiratoires et des Infections Sévères, Assistance Publique-Hôpitaux de Marseille, Hôpital Nord, Marseille, France, and Aix-Marseille Université, Faculté de médecine, URMITE, UMR CNRS 7278, Marseille, France (L.P.).

 Anesthesiology 2014; 120:1313-5

a resulting reduced risk of ventilator-induced lung injury.[1] This is in accordance with previous experimental and clinical findings.[5,7] To promote the beneficial effects of spontaneous effort in ARDS, however, it is quite important to stress that Xia *et al.* meticulously avoided strong spontaneous effort in their model and mimic mild to moderate form of ARDS.[1]

Although APRV and BIPAP modes have been used for more than 20 yr, there has been no convincing evidence that they should be used early in the course of ARDS. In an international cohort study, it has been shown that patients who developed respiratory failure after intubation with or without the criteria of moderate or severe ARDS were less likely to be ventilated with APRV/BIPAP.[8] When compared with assist-control ventilation in this nonselected intensive care unit population, there was no improvement in the duration of mechanical ventilation or mortality.[8] However, spontaneous ventilation during mechanical ventilation, such as using APRV or BIPAP, clearly improves gas exchange in selected patients with mild or moderate forms of ARDS.[5]

It is important to note that the review of BIPAP ventilation performed during the past 24 yr demonstrates that plateau pressures applied during BIPAP ventilation were less than 20 cm H_2O in patients with ARDS.[9] In contrast, plateau pressures applied in clinical studies showing beneficial effects of muscle paralysis on severe ARDS were higher (25 to 27.5 cm H_2O) because of the severity of ARDS.[4] The observed higher incidence of barotrauma in the placebo group of the ACURASYS (ARDS et Curarisation Systematique) study at a comparable plateau pressure as the muscle paralysis group suggests that spontaneous efforts may have generated injuriously high transpulmonary pressure, combined with already high plateau pressures.[4] In addition, Richard *et al.*[10] suggested that ventilatory modes with an inspiratory synchronization such as BIPAP can lead to large transpulmonary pressure swings and substantial high tidal volume, both of which are major contributing factors to ventilator-induced lung injuries. Therefore, strong spontaneous efforts must be avoided (*i.e.*, less pleural pressure variations) and relatively low plateau pressure must be maintained (*i.e.*, less airway pressure variations) during both BIPAP and APRV. Xia *et al.* carefully adjusted spontaneous effort activity by titrating sedatives and mechanical breaths.[1] In contrast to the fluid-like behavior observed in normal lungs, pleural pressure variations generated by diaphragmatic contraction in injured lungs are not uniformly transmitted across the lung surface, but rather concentrated in dorsal lung regions. This locally increased pleural pressure variations cause underdiagnosed local overstretch in dorsal lung regions, accompanying alveolar air shift from ventral to dorsal parts of the lung (*i.e.*, pendelluft).[11] This pendelluft effect is enhanced as spontaneous ventilation becomes stronger during mechanical ventilation. Thus, mild spontaneous effort may be beneficial to recruit the collapsed lung, whereas excessive spontaneous efforts may cause local overstretch because of a significant pendelluft effect.[11]

Another issue is the use of BIPAP/APRV allowing spontaneous efforts when prone position is used. In this situation, it is difficult to guarantee the comfort of the patients while maintaining the tidal volume in the range of 5 to 8 ml/kg and while ensuring the efficacy of positive end-expiratory pressure in increasing end-expiratory lung volume.

It may be too simplistic to oppose assist-control ventilation combined with the use of paralytics to APRV/BIPAP which preserve spontaneous respiratory efforts. In the ACURASYS study, the use of pressure support ventilation was mandatory, in a population of patients with severe ARDS, after the initial 48-h period of paralysis, when an F_{IO_2} of 0.6 or less was reached. In an ongoing study (NCT01862016), the use of APRV with a 1-day period of paralysis will be evaluated in patients with moderate to severe ARDS. This could be an important contribution to the management of patients with ARDS.

From our point of view, in severe forms of ARDS, paralytics should be used early in the course of ARDS, combined with prone positioning. After this initial period, it could be of interest to stimulate spontaneous ventilator efforts by using ventilatory modes such as APRV, BIPAP, or pressure support. However further knowledge, skill, and experience are required in the clinical use of BIPAP/APRV to define its role in the management of patients with ARDS.

Competing Interests

The authors are not supported by, nor maintain any financial interest in, any commercial activity that may be associated with the topic of this article.

Correspondence

Address correspondence to Dr. Papazian: laurent.papazian@ap-hm.fr

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