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EDITORIAL

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Tidal volume during acute lung injury: let the patient choose?

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Since the study published by the ARDSNet in 2000 [1], there have been strong debates about the optimal tidal volume to set—and to recommend—for patients under mechanical ventilation for acute lung injury (ALI). This landmark study made very clear that the choice of 12 ml/kg predicted body weight tidal volume was associated with a poor outcome, presumably through the mechanism of ventilator-induced lung injury (VILI), which was already described decades before [2, 3]. The topic is of considerable importance for any clinician, since the mortality difference observed in the 6 ml/kg predicted body weight tidal volume group suggested that 25% of all ARDS deaths in the 12 ml/kg group were caused by this excessive ventilation [1]. For some authors, the choice of 6 ml/kg came to be considered as the new standard. Other authors argued that only two settings had been rigorously tested, that the end-inspiratory level of distension reached, evaluated by plateau pressure as a surrogate, was a key component of the risk of VILI, and that there may also be risks of having an unnecessarily low tidal volume leading to atelectasis, dysynchrony and discomfort [4]. Also, a high tidal volume was proposed as a possible culprit for patients free of ALI on admission but who later develop ALI during the course of mechanical ventilation [5]. Other arguments nourished the debate, such as the distinction between predicted and actual body weight to retrospectively analyze databases, or the lack of relation between tidal volume and mortality observed in some of these studies, as well as the negative results of other randomized controlled trials [6–8]. Taking together the results of clinical trials and of retrospective analysis of some of these data [9], the amplitude of the tidal volume delivered seems to generate a strong signal influencing mortality. The strain forces and shear stress induced by the reopening of repetitively collapsed alveoli or closed terminal airways might play an important role in the poor outcome of patients experiencing VILI. New trials testing different levels of PEEP, supposed to minimize the end-expiratory small airway and alveolar closure through alveolar recruitment, and therefore to limit the strain at end-inspiration induced by tidal volume, did not give a uniform answer to this question. The lack of a clear protective effect of PEEP was possibly explained because the enrolment criteria were unable to distinguish between recruiters and non-recruiters [10, 11]. Since 5–7 ml/kg is considered to constitute a normal physiological range, some authors now consider that 6 ml/kg tidal volume might be recommended for any patient under mechanical ventilation. The clinical picture of a normal breathing pattern is, however, much more complex. In adult awake human subjects at rest, diversity exists in the breathing pattern not only in terms of tidal volume and inspiratory and expiratory duration and derived variables, but also in

the airflow profile [12]. In addition, in every recording of ventilation at rest in steady-state condition breath-to-breath fluctuations are observed in ventilatory variables [13]. Part of this variability is non-random and may be explained either by a central neural mechanism or by instability in the chemical feedback loops. During disease states in general, and ALI in particular, the breathing pattern chosen by the patient may considerably vary from one patient to another, being influenced by the metabolic demand, dead space and the acid–base status on the one hand, but also by respiratory mechanics and respiratory muscle function on the other hand. If one imagines that the latter can be fixed thanks to an appropriate, individualized and optimized ventilatory support, any limitation to respiration due to poor respiratory mechanics or excessive energy expenditure by the respiratory muscles will vanish. The patient's brain will select an "optimal" breathing pattern for the body, including for the lungs, through a myriad of receptors and neuro-chemical signals, enabling a compromise between gas exchange and lung protection. If the increase in ventilation observed in ALI is driven essentially by a respiratory problem, then the tidal volume chosen may be, among other characteristics, one that minimizes or prevents the risk of VILI. This exciting hypothesis constitutes one of the promises of two modes of ventilation now available for patients, proportional assist ventilation (PAV) [14] and neurally adjusted ventilatory assist (NAVA) [15]. The working principle of these modes is to deliver instantaneous pressure to unload the respiratory muscles up to a sufficient level where the patient becomes the entire master of the breathing pattern. PAV is based on the equation of motion of the respiratory system and requires accurate knowledge of patient's respiratory mechanics, whereas NAVA directly records diaphragmatic electrical activity and is therefore able to deliver a pressure directly proportional to the inspiratory neural drive.

In a rabbit experiment, Brander, Sinderby and the group of Slutsky [16] tried to determine if NAVA, which delivers pressure in proportion to diaphragm electrical activity, is as protective for lungs with hydrochloric acid-induced ALI and for non-pulmonary organs as volume-controlled ventilation set with a 6 ml/kg tidal volume and compared to 15 ml/kg tidal volume. In their experiment, the animals selected a breathing pattern unique to NAVA: average tidal volume during NAVA was 2.7 ± 0.9 ml/kg during the initial 3 h and increased to 3.4 ± 0.8 ml/kg during the final 2.5 h. Early after ALI induction, the respiratory rate in NAVA was up to three times higher than the ventilatory rate in both controlled ventilation groups, and thereafter decreased towards values in the 6 ml/kg group. In addition, the breathing pattern coefficient of variability varied between 25 and 30% for the NAVA group only, including frequent sighs. With NAVA, lung injury scores, lung wet-to-dry ratio, and lung and systemic biomarkers indicating VILI were similar to 6 ml/kg, whereas other parameters (i.e., PaO_2/FiO_2 ratio, cardiac output, arterial lactate concentration and dynamic compliance) reflecting functional aspects of the cardio-pulmonary system were less affected with NAVA compared to 6 ml/kg. Lung injury scores did not significantly differ from the 6 ml/kg group, but the authors concluded that the use of NAVA, which allowed the injured animals to choose their respiratory pattern, was at least as effective in preventing various manifestations of VILI as conventional, volume-controlled ventilation using a tidal volume of 6 ml/kg in an experimental model of ALI. Both strategies similarly prevented VILI, attenuated excessive systemic as well as extra-pulmonary organ inflammation and injury, and preserved cardiac and kidney function.

The authors thoroughly discuss the numerous limitations of such complex experiments before their results can be translated into clinical practice. As discussed by the authors, we would like to be sure that the animals would adopt the same breathing pattern with a higher NAVA gain. The gain set by the clinician is used to deliver instantaneous pressure in direct proportion to the electrical signal recorded. The way to set this gain remains a matter of research, but experimental and some clinical data suggest that after reaching a certain NAVA level, and presumably only over a certain range, the subject becomes free of choosing his/her desired breathing pattern, the amount of effort becoming the only parameter modified by a further increase in gain [15, 17]. Whether tidal volume would have remained at such low levels with a higher NAVA gain remains speculative, though the authors develop a number of arguments suggesting that the level was adequate. The presence of numerous sighs is also an interesting feature of their breathing pattern. One important concern that remains before using such an approach in a clinical scenario might be the presence of strong extra-respiratory signals driving the patient's respiration, such as acidosis, cardiovascular dysfunction or severe anemia. In an experiment in sheep, Mascheroni et al. [18] showed that direct instillation of sodium salicylate into the cisterna magna, imposing an extremely high level of stimulation on the central chemo-receptors, was able to induce lung injury secondary to hyperventilation. It was concluded from this experiment that sustained prolonged hyperventilation for 24 h while breathing spontaneously can result in severe pulmonary dysfunction, as observed with mechanical hyperventilation. Of note, the rabbits in Brander's study did not have sepsis and/or lactic acidosis, a frequent condition associated with ALI that could induce similar behaviors.

The kind of study by Brander et al. [16] using NAVA opens a new window in our practice of mechanical ventilation and on the degree of freedom that clinicians might give to patients. New ventilatory modes like NAVA offer a fantastic opportunity for exploring this key question, using a now clinically realistic approach.

References

1. Network ARDS (2000) Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 342:1301–1308
2. Dreyfuss D, Saumon G (1998) Ventilator-induced lung injury: lessons from experimental studies. Am J Respir Crit Care Med 157:294–323
3. Webb HH, Tierney DF (1974) Experimental pulmonary edema due to intermittent positive pressure ventilation with high inflation pressures. Protection by positive end-expiratory pressure. Am Rev Respir Dis 110:556–565
4. Deans KJ, Minneci PC, Cui X, Banks SM, Natanson C, Eichacker PQ (2005) Mechanical ventilation in ARDS: one size does not fit all. Crit Care Med 33:1141–1143
5. Gajic O, Frutos-Vivar F, Esteban A, Hubmayr RD, Anzueto A (2005) Ventilator settings as a risk factor for acute respiratory distress syndrome in mechanically ventilated patients. Intensive Care Med 31:922–926
6. Brochard L, Roudot-Thoraval F, Roupie E, Delclaux C, Chastre J, Fernandez-Mondéjar E, Clémenti E, Mancebo J, Factor P, Matamis D, Ranieri M, Blanch L, Rodi G, Ferrer M, Dreyfuss D, Mentec H, Brun-Buisson C, Tobin M, Lemaire F, the multicenter trial group on tidal volume reduction in ARDS (1998) Tidal volume reduction for prevention of ventilator-induced lung injury in the acute respiratory distress syndrome. Am J Respir Crit Care Med 158:1831–1838
7. Ferguson ND, Frutos-Vivar F, Esteban A, Anzueto A, Alia I, Brower RG, Stewart TE, Apezteguia C, Gonzalez M, Soto L, Abroug F, Brochard L (2005) Airway pressures, tidal volumes, and mortality in patients with acute respiratory distress syndrome. Crit Care Med 33:21–30
8. Stewart T, Meade M, Cook D, Granton J, Meade M, Hodder R, Lapinsky S, Mazer C, McLean R, Rogovein T, Schouten B, Todd T, Slutsky A, the Pressure-and Volume-Limited Ventilation Strategy Group (1998) Evaluation of a ventilation strategy to prevent barotrauma in patients at high risk for acute respiratory distress syndrome. N Engl J Med 338:355–361
9. Hager DN, Krishnan JA, Hayden DL, Brower RG (2005) Tidal volume reduction in patients with acute lung injury when plateau pressures are not high. Am J Respir Crit Care Med 172:1241–1245
10. Meade MO, Cook DJ, Guyatt GH, Slutsky AS, Arabi YM, Cooper DJ, Davies AR, Hand LE, Zhou Q, Thabane L, Austin P, Lapinsky S, Baxter A, Russell J, Skrobik Y, Ronco JJ, Stewart TE (2008) Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA 299:637–645
11. Mercat A, Richard JC, Vielle B, Jaber S, Osman D, Diehl JL, Lefrant JY, Prat G, Richecoeur J, Nieszkowska A, Gervais C, Baudot J, Bouadma L, Brochard L (2008) Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. Jama 299:646–655
12. Benchetrit G (2000) Breathing pattern in humans: diversity and individuality. Respir Physiol 122:123–129
13. Tobin MJ, Mador MJ, Guenther SM, Lodato RF, Sackner MA (1988) Variability of resting respiratory center drive and timing in healthy subjects. J Appl Physiol 65:309–317
14. Xirouchaki N, Kondili E, Vaporidi K, Xirouchakis G, Klimathianaki M, Gavriilidis G, Alexandopoulou E, Plataki M, Alexopoulou C, Georgopoulos D (2008) Proportional assist ventilation with load-adjustable gain factors in critically ill patients: comparison with pressure support. Intensive Care Med 34:2026–2034
15. Brander L, Leong-Poi H, Beck J, Brunet F, Hutchison SJ, Slutsky AS, Sinderby C (2009) Titration and implementation of neurally adjusted ventilatory assist in critically ill patients. Chest 135:695–703
16. Brander L, Sinderby C, Lecomte F, Leong-Poi H, Bell D, Bell D, Tsoporis JN, Vaschetto R, Schultz MJ, Parker TG, Villar J, Zhang H, Slutsky AS (2009) Neurally adjusted ventilatory assist decreases ventilator induced lung injury and non-pulmonary organ dysfunction in rabbits with acute lung injury. Intensive Care Med. doi:10.1007/s00134-009-1626-x
17. Lecomte F, Brander L, Jalde F, Beck J, Qui H, Elie C, Slutsky AS, Brunet F, Sinderby C (2009) Physiological response to increasing levels of neurally adjusted ventilatory assist (NAVA). Respir Physiol Neurobiol 166:117–124
18. Mascheroni D, Kolobow T, Fumagalli R, Moretti MP, Chen V, Buckhold D (1988) Acute respiratory failure following pharmacologically induced hyperventilation: an experimental animal study. Intensive Care Med 15:8–14