Lung Protection: The Cost in Some Is Increased Work of Breathing. Is It Too High?

The need for lung-protective ventilation for patients in acute respiratory distress syndrome (ARDS) has been clearly demonstrated by a number of groups, both in animal studies[1] and, most importantly, in patient randomized controlled trials.[2–4] Lung-protective ventilation has focused on 2 very specific aspects of ventilation: (1) reduction of end-inspiratory overdistention by limiting end-inspiratory plateau pressure and tidal volume (V_T) and (2) elimination of repetitive opening and closing of unstable lung units by the use of appropriately adjusted positive end-expiratory pressure (PEEP).[1] Although controversy does exist over what is the appropriate level of PEEP to avoid injury,[2,4,5] most would support the need to avoid end-inspiratory overdistention by reducing end-inspiratory plateau pressure and V_T.[1–5] Even in patients initially ventilated without lung injury there seems to be a relationship between V_T and development of acute lung injury (ALI) during ventilatory support.[6,7] Gajic et al,[6,7] in 2 retrospective analyses, demonstrated the relationship between delivered V_T and development of ALI[8] (ratio of arterial partial pressure of oxygen to fraction of inspired oxygen [P_{aO_2}/F_{IO_2}] $<$ 300 mm Hg). Their data would imply that ventilating patients who do not have lung injury with $V_T > 9$ mL/kg increases the risk of developing lung injury during mechanical ventilation. However, those data are retrospective, and actual end-inspiratory plateau pressures were not provided.

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As very nicely demonstrated by Kallet and colleagues in this issue of the Journal, the primary cost of maintaining a small V_T (6 mL/kg of predicted body weight [PBW]) in some patients is an increase in the work of breathing (WOB).[9] They demonstrated in 14 patients with ALI or ARDS, and who were spontaneously triggering the ventilator, that regardless of which ventilation mode was used (volume-assist/control, pressure-assist/control, or pressure-regulated volume control), when V_T is maintained at about 6.4 mL/kg PBW, patient WOB exceeds 1.0 J/L. In addition, there was a nonsignificant trend of greater WOB with pressure-assist/control (1.27 $\pm$ 0.58 J/L) and pressure-regulated volume control (1.35 $\pm$ 0.6 J/L) than with volume-assist/control (1.09 $\pm$ 0.59 J/L). To put this into perspective, the normal inspiratory WOB in a healthy adult breathing through the nose is about 0.4 J/L.[10] Many have considered inspiratory WOB $>$ 1.0 J/L during spontaneous breathing unsustainable and an indication for ventilatory support.[11–13] In other words, the WOB performed by these 14 ALI/ARDS patients during assisted ventilation was equivalent to that considered in spontaneously breathing patients as an indication for ventilatory support.[11–13] Is the cost of the small, lung-protective V_T in these patients too high? This is not an easy question to answer! One problem in answering this question is the lack of airway pressure data. No indication of the end-inspiratory plateau pressure is provided. As discussed by Dreyfuss and Saumon,[1] it is local overdistention that causes lung injury, defined by transpulmonary pressure. Without knowing the end-inspiratory plateau pressure it is impossible to even estimate transpulmonary pressure.

The most important question is: Is it beneficial for patients to continue to breathe with this high inspiratory work? Again, a difficult question to answer. The original ARDS Network data would indicate the answer is yes, but a recent editorial by Deans et al[14] would question that answer. Deans et al determined the mortality of 2,587 patients who meet the original ARDS Network enrollment criteria[4] but were not randomized for various technical reasons. The mortality of these patients was 31.7%, as compared to the 31% mortality of the patients in the 6-mL/kg PBW group. Guess what the V_T was in these patients? 10 mL/kg!

Before completing the above discussion, let us consider Petrucci and Iacovelli's meta-analysis[15] of the 5 published randomized controlled trials that have evaluated lung-protective ventilation,[2,4,16–18] which found that V_T did impact mortality among the 1,202 patients in those 5 studies. However, when patients whose plateau pressure was $<$ 31 cm H_2O were evaluated, V_T had no significant effect on mortality. A recent analysis of the actual patient data from those 5 trials,[2,4,16–18] plus the high/low PEEP ARDS Network trial,[5] has been performed by Amato (Marcelo Amato, Pulmonary Division, Hospital das Clínicas, University of São Paulo, Brazil, personal communication, 2005). When Amato assessed the actual data from almost 1,800 patients, V_T did not have an association with mortality. Mortality was primarily related to plateau pressure! The higher the plateau pressure, the higher the mortality.

In addition, the recent data from the last adult partial-liquid-ventilation trial must be considered.[19] That was a negative trial, but the mortality of the control group, who received conventional volume-assist/control, was only 15%—the lowest mortality ever published for a group of ARDS patients. On day one of randomization, the V_T of that group was 9 mL/kg PBW, the PEEP was 14 cm H_2O, and the plateau pressure was 28 cm H_2O. That is the same plateau pressure as in the ARDS Network's 6-mL/kg group[4] on day one, in which the mortality was 31%, and even in the ARDS Network high/low PEEP trial[5] the mortality was only 25%. The first question that comes to mind is: Were different patients studied in the partial-liquid-ventilation study than in the ARDS Network studies? They most likely were, and from a pulmonary perspective it would appear that the sicker patients were in the partial-liquid-ventilation study! Enrollment into the ARDS Network trials required that the P_{aO_2}/F_{IO_2} was < 300 mm Hg, regardless of PEEP or F_{IO_2}, whereas in the partial-liquid-ventilation study, first, patients were enrolled only if the P_{aO_2}/F_{IO_2} was < 200 mm Hg, regardless of PEEP or F_{IO_2}. Then patients were placed on a PEEP ≥ 13 cm H_2O and an $F_{IO_2} \geq 0.5$. Only those with a $P_{aO_2} < 300$ mm Hg were then randomized! Why the low mortality in all of these studies, despite the use of different V_T? *The answer is low-end-inspiratory plateau pressure!*

Now let's go back to the Kallet and colleagues[9] data. In my opinion, the cost of using a small (6.4-mL/kg PBW) V_T with these patients, from a WOB perspective, is too high. What are our options when managing patients who clinically clearly have increased WOB, rapid respiratory rate, increased use of accessory muscles of ventilation, retractions, cardiovascular stress, etc? Well, that depends on the end-inspiratory plateau pressure. Plateau pressure is difficult to measure in patients actively participating in ventilatory assistance, but if pressure-assist/control or pressure-regulated volume control is used, plateau pressure can be no higher than the peak airway pressure. It can be argued that high transpulmonary pressure may be developed in actively breathing patients on pressure-assist/control or pressure-regulated volume control, even when the peak pressure is low. But I disagree with that assumption, because with a patient who is actively breathing, the set pressure-assist/control level is never established at the alveolar level unless inspiratory flow is zero before the end of the breath, which is a very unlikely situation in the highly stressed patient.

The options, then, for these patients are: (1) eliminate the increased ventilatory drive by correcting those issues (eg, oxygenation and temperature) that increase ventilatory drive, (2) sedate the patient to markedly depress respiratory drive, (3) accept the high WOB as a necessary cost of lung protection, or (4) allow the V_T to increase. The most ideal option is number 1, but in ARDS/ALI patients it is frequently difficult to eliminate the cause of the increased drive to breath. Sedation does work in many patients; however, frequently sedation to apnea with paralysis is required to eliminate the high ventilatory drive in ARDS/ALI patients—a scenario that itself causes many additional complications, potentially increasing the duration of mechanical ventilation. Accepting the high WOB increases oxygen consumption and cardiovascular work, frequently resulting in cardiovascular instability, but clearly this is an option in many patients. Finally, there is the possibility of letting the V_T increase, provided the plateau pressure remains low; but how low is low? Based on the available data discussed above, it would seem safe to allow V_T up to 9 mL/kg if the plateau pressure is maintained below 25 cm H_2O. The higher the plateau pressure, the greater the need to maintain a low V_T, but in patients with a low plateau pressure, the risks of the alternatives would appear to outweigh the benefits of forcing a V_T of 6.0 mL/kg PBW!

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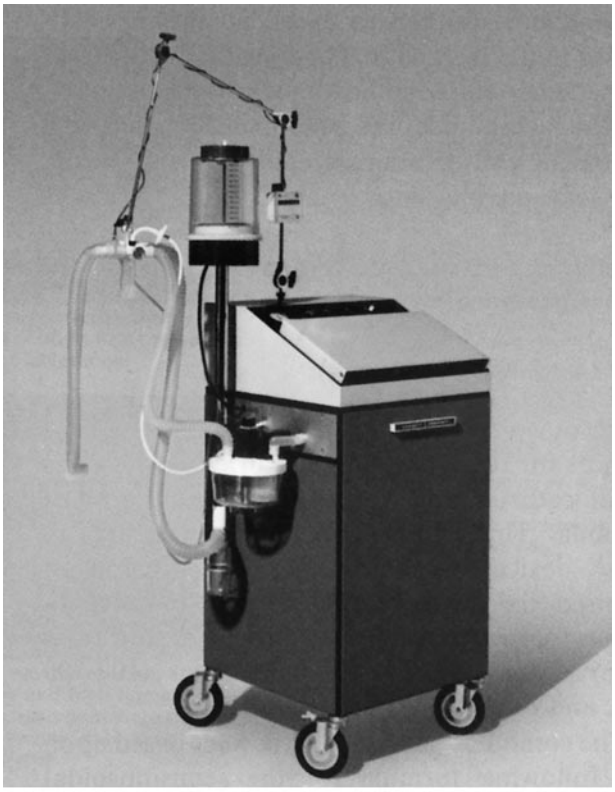

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