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Ventilatory Management of Severe Acute Respiratory Failure for Y2K

FOR more than 30 years, mechanical ventilation has been a cornerstone of the treatment of patients with acute respiratory distress syndrome (ARDS). Experience has led to value its obvious benefit of supporting gas exchange, but many clinicians have accepted its harmful side effects on the lung as inevitable. Recently, however, mechanical ventilation has undergone an important re-evaluation as an intervention that can support, damage, or even protect the acutely injured lung. Our simplistic practices have been called into question. It is no longer sufficient to merely set a tidal volume (V_T) of 10–15 ml/kg, add a bit of positive end-expiratory pressure (PEEP), and control the respiratory rate to achieve a Pa_{CO_2} of 40 mmHg. The article by Ullrich *et al.*[1] in this issue of ANESTHESIOLOGY describes one approach to ARDS that resulted in a high survival rate. Beyond admiring their superb clinical results, we need to answer a fundamental question: What ventilatory strategy, based on sound physiology and clinical data, can we now recommend to treat severe acute respiratory failure?

Mechanical ventilation with large V_T or high pressure can injure the lung.[2] Although a V_T of 12 ml/kg and an associated alveolar pressure of 30 cm H_2O, commonly used during general anesthesia and surgery, are unlikely to damage normal lungs, similar settings may aggravate lung injury during prolonged mechanical ventilation for acute respiratory failure. This concept is not new, and more than 20 years ago led to the idea of "resting the lung" and supporting respiration by extracorporeal membrane oxygenation.[3] Although extracorporeal membrane oxygenation (ECMO) and its subsequent modifications have not reached widespread use, new physiologic

This Editorial View accompanies the following article: Ullrich R, Lorber C, Röder G, Urak G, Faryniak B, Sladen RN, Germann P: Controlled airway pressure therapy, nitric oxide inhalation, prone position, and extracorporeal membrane oxygenation (ECMO) as components of an integrated approach to ARDS. ANESTHESIOLOGY 1999; 91:1577–86.

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evidence emphasizes the need to protect the lung from the trauma of mechanical ventilation. What seemed to be limited to experimental animals receiving disproportionately large V_T became relevant to our patients after Gattinoni *et al.*[4] demonstrated by computed tomography (CT) that the injury of early ARDS was not homogeneous throughout the lung. Rather, areas of alveolar consolidation coexist with ventilated regions, which may be small and exposed to a relatively large distending volume and pressure. Furthermore, the topographic distribution of the lesions is dynamic, and the dependent lung areas collapsed by the weight of edematous tissues can be reexpanded by changes in body position.[5]

A second important realization was that lung injury could occur not only at high volumes, but also if alveoli were allowed to close at end expiration. The forces generated during repetitive opening of collapsed alveoli are substantial and may induce further damage.[6] This also is not a new concept, but has recently been reexamined with a more complete physiologic perspective: recruitment of the ARDS lung can both improve Pa_{O_2} and limit ventilator-induced lung damage. The level of PEEP necessary to recruit collapsed lung is higher than the level at which the same alveoli would recollapse once opened. Maneuvers to open collapsed lung include using prolonged inspiratory times, applying a high level of continuous positive airway pressure for brief periods,[7] and periodically providing "sighs" during low V_T ventilation.[8] Once recruited, the lung can be kept open by setting PEEP at a sufficiently high level.

The harmful effects of large V_T and end-expiratory collapse in patients with ARDS have been demonstrated by histologic[9] and radiographic[10] studies and by quantification of the release of inflammatory mediators.[11] The practical application of this evidence has not been simple, and clinical data, as often happens, are conflicting. Recently, however, several controlled trials have provided important information. Initial multicenter studies from Canada and Europe failed to demonstrate an advantage of limiting alveolar pressure and V_T in patients at risk for[12] or with ARDS.[13] However, differences in airway pressure and V_T between the study groups were minimal, and PEEP was not set to maintain lung recruitment. In another study, a strategy aimed at reducing ventilator-induced lung injury by enhancing recruitment and limiting alveolar overdistention decreased respiratory morbidity and early mortality.[7] Importantly, the level of PEEP was set above the sharp increase ("lower inflection point") of the slope of a volume–pressure curve of the respiratory system (fig. 1) to promote alveolar recruitment. "Opening" the lung with PEEP and recruitment maneuvers was an essential part of this protocol. Although this study was conducted at a single center and was complicated by a high mortality rate in the control group, its physiologic rationale has attracted intense interest among investigators and clinicians. The National Institutes of Health (NIH) recently completed a multicenter randomized study of limited V_T (6 ml/kg) compared with a traditional strategy (12 ml/kg V_T) in patients with ARDS. Preliminary results released *via* the internet indicate that limiting the V_T was associated with a reduction of hospital mortality rate from 40% to 30%.[14]

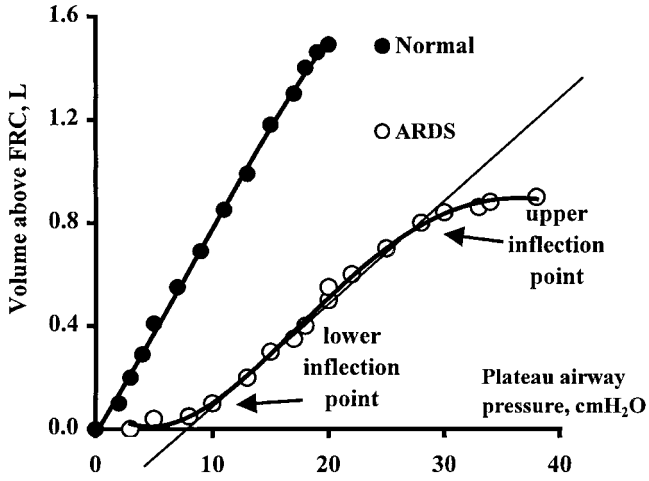

Fig. 1. Idealized volume–pressure curve of the respiratory system of a normal subject (*black circles*) and a patient with acute respiratory distress syndrome (ARDS; *white circles*). The volume–pressure curve of the patient with ARDS has a low compliance, an "upper inflection point" at which overdistention of the lung may occur, and a "lower inflection point" above which optimal recruitment may occur. FRC = functional residual capacity.

A number of ancillary therapies may be used to complement a lung-protective ventilatory strategy. Ventilating patients with ARDS in the prone position often improves their Pa_{O_2}.[15] Although the physiology of this maneuver is not fully understood and its impact on outcome is unproved, its effect on gas exchange is sometimes remarkable. However, keeping a critically ill patient prone for hours requires superior nursing skills and vigilance, and the practice of prone ventilation remains underused.

Inhaled nitric oxide transiently improves Pa_{O_2} and decreases pulmonary pressure in the majority of patients with ARDS.[16] The use of inhaled nitric oxide reduces the need for ECMO in children with acute respiratory failure but has not affected clinical outcome in prospective trials in adults.[17] Inhaled nitric oxide may be of value in

special situations, such as ARDS with severe acute pulmonary hypertension, as a bridge to more complex treatments of severe hypoxemia such as ECMO and lung transplantation and as an antiinflammatory agent.

Carbon dioxide washout techniques include high-frequency ventilation and tracheal gas insufflation.[18] These techniques aim to decrease Pa_{CO_2} while maintaining or improving Pa_{O_2} with less lung trauma than an equivalent level of traditional ventilation. Although their physiologic mechanisms are not completely understood, technical advances have made them more accessible, and clinical trials are ongoing.

Among nonventilatory therapies, the benefit of low-dose, prolonged glucocorticoid therapy for the late phase of ARDS has been suggested by a recent randomized trial.[19]

What, then, can we recommend as a ventilatory strategy for patients with ARDS?

1. Limit V_T size. Multiple randomized studies indicate that a V_T of 12–15 ml/kg should no longer be used to ventilate patients with ARDS. It is reasonable to limit V_T to < 8 ml/kg and end-inspiratory plateau airway pressure to $< 30-40$ cm H_2O. Pleural pressure can be estimated by measuring esophageal pressure if a decreased chest wall compliance is suspected. A moderate compensated respiratory acidemia seems safe in most patients and can generally be offset by a higher respiratory rate.
2. Recruit the lung. Ventilating with low V_T may derecruit the lung. To prevent derecruitment, PEEP can be set above the lower inflection point of a volume–pressure curve (fig. 1), although uncertainties exist about the best way to measure this point. Additional ways to recruit the lung include recruitment maneuvers and repeated sighs. Chest computed tomography can verify the occurrence of recruitment.
3. Limit oxygen toxicity by targeting the Pa_{O_2} to achieve a sufficient oxygen-carrying capacity, *i.e.*, an oxyhemoglobin saturation $> 90\%$. Although the precise role of oxygen toxicity in the evolution of ARDS is unclear, there seems to be no physiologic advantage to increase the Pa_{O_2} above the patient's normal range.
4. Consider the use of a multimodal approach with different options, including early referral to a highly specialized center.[1]

Survival of patients with ARDS may have improved over the past decades.[20] Although the precise causes for improvement are uncertain, better knowledge of the physiology of acute respiratory failure and a general improvement of intensive care medicine may be responsible. To carry these achievements beyond Y2K, clinical investigators must continue to:

1. Test sensible hypotheses based on sound physiologic grounds.
2. Set reasonable outcomes. Single interventions are unlikely to improve the survival of a systemic syndrome like ARDS.
3. Use rigorous, controlled study designs to evaluate new treatments.
4. Consolidate individual resources into networks that can test standardized therapies in prospective, multicenter studies. The success of the NIH *ARDSnet*[14] and similar networks around the world affirm that such studies can be performed in a reasonable time frame. Reports such as those of Ulrich *et al.* form the attractive basis for testable hypotheses but cannot substitute for rigorous clinical trials.

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