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Ventilation of the Acute Respiratory Distress Syndrome

Looking for Mr. Goodmode

Recent interest in techniques for ventilating the lungs of patients with acute lung injury has been driven by an evolving knowledge of respiratory mechanics and the potential for iatrogenic lung damage. The protracted need for mechanical ventilation is associated with infection, multisystem organ damage, and increased mortality. Moreover, high stretching forces applied repeatedly to normal lungs may increase permeability and initiate hemorrhage or inflammation without alveolar rupture.[1,2] In view of this, investigators and clinicians have begun to reconsider the fundamental objectives of mechanical ventilation and to design modes to accomplish these revised goals more effectively.

In claiming an advantage, a new technique should either reduce the hazards resulting from ventilation or improve the efficiency of pulmonary gas exchange. Although most innovations have a distinct physiologic rationale, little data address their relative worth. In the current issue of ANESTHESIOLOGY, Lessard *et al.*[3] report a careful comparison of pressure-controlled ventilation (PCV) and volume-controlled ventilation in patients with acute lung injury and find little advantage for pressure control and inverse ratio strategies.

To appreciate the value and limits of the data, it is important to identify those characteristics of the ventilatory pattern likely to influence outcome from acute respiratory distress syndrome (ARDS), as well as understand the basis of concern regarding unregulated airway pressure. Judging from available evidence, all regions of the lung initially sustain injury in ARDS, and inflammation proceeds more or less uniformly. However, although injury may be diffuse, abnormalities of lung mechanics are heterogeneously distributed and change over time. Shortly after disease onset, respiratory compliance decreases—more as a consequence of a reduced number of functioning lung units than of increased elastance. (In severe cases, no more than one third of alveolar units are patent.) *Aerated* regions initially may remain mechanically normal and, therefore, over-distend in response to high transalveolar pressure. Edema and atelectasis concentrate in dependent areas, where the weight of the overlying lung and tendency for airway collapse are greatest. Partly for this reason, prone positioning may dramatically alter the distribution of radiographic infiltrates[4] and oxygen exchange.[5]

In this first stage, the strong collagen framework of the lung, still intact, prevents alveolar rupture. But as inflammation proceeds into the proliferative stage, edema recedes and collagen support weakens nonuniformly. Organizing infiltrates and fibrotic remodeling reverse the tendency for compressive atelectasis and increase lung stiffness. Radiographically evident barotrauma (*e.g.*, pneumothorax and gas cysts) are most likely to occur in these later phases, when the tensile strength of connective tissue is degraded unevenly and inflation pressures are high. This pathologic sequence helps to explain why computed tomography initially demonstrates a predominance of infiltrates in dependent regions,[4,6] whereas fibrosis and cystic changes distribute more evenly later.[7] The evolution from atelectasis to cellular proliferation and fibrosis also seems consistent with the tendency for positive end-expiratory pressure (PEEP) to gradually lose its effectiveness in improving oxygen exchange after the first few days.

In all forms of controlled ventilation, the peak, end-expiratory, and mean transalveolar pressures are the three features of the ventilatory waveform most relevant to gas exchange and healing. Compelling experimental evidence demonstrates that alveolar overstretching disrupts the integrity of the normal alveolar membrane, accentuating edema formation—even when overt rupture does not occur.[1,2,8] Although the safe upper limit for end-inspiratory (plateau) pressure in ARDS is not known, it is unlikely to exceed that corresponding to total lung capacity during health—a *transalveolar* pressure of approximately 30 cmH_2O.[9] In fact, there may be no distinct threshold for enhanced edema formation in tissue already injured and simultaneously exposed to other noxious stimuli, such as hyperoxia.[10,11]

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PEEP is not routinely helpful when ventilating normal lungs at modest pressures.[12] However, when the lung is already injured or exposed to high inflation pressures, providing enough end-expiratory alveolar pressure during the early period may minimize iatrogenic damage and expedite healing. In the first stage of lung injury, maintaining a moderately high end-expiratory lung volume counterbalances the forces favoring atelectasis, prevents tissue collapse and re-recruitment with each tidal cycle, and obliterates the lower inflection point (P_{flex}) of the static pressure-lung volume relationship.[13] More than 15 yr ago, Suter *et al.* noted that "optimum" compliance in ARDS (the quotient of tidal volume and inspiratory alveolar pressure excursion) is jointly determined by PEEP and tidal volume.[14] When little PEEP was applied, larger tidal volumes improved compliance, implicating tidal re-expansion of collapsed tissue. Recently, Pelosi *et al.* extended that observation with elegant computed tomography/densitometric studies demonstrating differences of gas/tissue ratios at the extremes of the standard tidal cycle that are eliminated by 10–15 cmH_2O PEEP.[15]

Preventing tidal recruitment may be instrumental in avoiding further damage. Interdependence amplifies the stresses at the junctions of collapsed and expanding tissue. Even at moderately high lung volumes, junctional tensions may be several-fold greater than those applied to the free walls of patent alveoli.[16] Although decelerating flow or an extended inspiratory time fraction can use this "force lever" of interdependence to advantage in alveolar tissue recruitment, high airway pressure may produce enormous tensions at the interface between aerated and airless units.

Excessive junctional strain may contribute to capillary stress failure and help account for the hemorrhagic edema formed in normal lungs when high pressures are applied without adequate PEEP.[17] If minimizing peak alveolar pressure and avoiding the tidal recruitment cycle limit injury, it may be important to use relatively high levels of PEEP and relatively low tidal volumes in the earliest phase of ARDS. Later, PEEP should be withdrawn as tolerated to reduce peak alveolar pressure—provided there are no serious consequences for oxygen exchange and no inflection point reemerges on the pressure-volume curve.

The wisdom of maintaining Pa_{CO_2} at near-normal levels was challenged recently by the recognition that pressures that are too high or too low may extend tissue injury or retard healing. Placing bounds on the end-inspiratory and end-expiratory alveolar pressures limits the pressure available to drive ventilation and, in severe cases, results predictably in carbon dioxide retention. Reducing the *frequency* of tidal cycles also may help limit damage, but it elevates Pa_{CO_2} as well. Intriguing data from several sources now suggest that pressure-limited ventilation with "permissive hypercapnia" may improve lung mechanics, gas exchange, and survival.[18–20] Confirmation awaits a prospective controlled study.

When evaluating ventilatory options, the importance of mean airway pressure (MAP) in assuring adequate arterial oxygenation and oxygen delivery also should be well understood. Under passive conditions, increasing MAP, a correlate of mean alveolar pressure, recruits collapsed lung units and redistributes lung water but also may impede venous return and reduce oxygen delivery.[21,22] At specified levels of tidal volume and minute ventilation, MAP can be raised by increasing PEEP, extending the inspiratory time fraction, or inducing dynamic hyperinflation (which also causes mean alveolar pressure to exceed MAP).[21,22]

As demonstrated in the data presented by Lessard *et al.*,[3] relatively minor differences in gas exchange efficiency and tissue damage are expected between different patterns of ventilation when peak and mean alveolar pressures are matched at a similar minute ventilation and sufficient end-expiratory alveolar pressure (P_{ALV}) is used. The comparison of volume-cycled ventilation with PCV is of particular interest, however, because virtually all newer modes of ventilation can be considered variants of PCV, a time-cycled mode in which approximately square waves of pressure are applied and released from the airway opening. Controlling pressure, rather than flow, relaxes the guarantee on alveolar ventilation, and the decelerating flow inherent to PCV theoretically generates high shear stresses at inflation onset. In exchange, PCV offers several theoretical advantages. Early alveolar filling sustains more alveolar tractive force than constant-flow ventilation of similar duration, potentially aiding recruitment. In support of this, other recent comparisons of volume-controlled ventilation and PCV found more rapidly improving compliance when PCV was used.[19,23] The decelerating flow profile may also help distribute ventilation and pressure evenly among units with different time constants, an advantage not shared by constant-flow ventilation.[24] Finally, whatever its potential advantages for gas exchange, PCV ensures that alveolar pressures everywhere within the heterogeneous lung never exceed the targeted value. This is an especially important safety feature during inverse ratio ventilation (IRV).

IRV may simply offer an alternative means of increasing mean alveolar pressure while satisfying the pressure constraints of a "lung-protective" approach.[25] Yet, because certain closed airways may require moderately high and *sustained* pressures to open,[26] the increased traction of IRV could conceivably open adherent channels more effectively than transient application of the same peak alveolar pressure. Refractory units of this type may be more prevalent during the edematous and proliferative phases of the disease, when atelectasis is widespread and the surface tension and viscosity of the fluid lining the small airways are high.[26] Almost two decades ago, Lamy *et al.* identified a subpopulation of patients with advanced lung injury who responded very slowly to a PEEP increment.[27] More recently, investigators have reported a tendency for compliance and arterial oxygenation to steadily improve for hours after the ventilatory pattern changes to IRV.[28–30]

In the study by Lessard *et al.*,[3] two of three crucial variables (peak and end-expiratory P_{ALV}) were well matched between comparison groups. However, although carefully collected, these data do not quite settle the issue of IRV utility. This would require an extended study of patients more likely to benefit from IRV and match *mean* P_{ALV} while ensuring an appropriate *minimum* P_{ALV}. In this study, oxygen exchange did not improve in response to increased MAP, the greater MAP of IRV depressed cardiac output, and the high mortality rate suggests an advanced stage of illness. Finally, any *delayed* effect of either method may have been missed by stopping observation too soon (30 minutes) after each change in mode.

Despite these minor shortcomings, the authors should be commended for carefully executing a difficult study of considerable practical interest. In an era of increasing scientific emphasis on molecular biology and outcome-based investigations, applied clinical physiology of this high standard is welcome.

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