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Barotrauma is volutrauma, but which volume is the one responsible?

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The deleterious effects of mechanical ventilation on lungs are usually referred to as barotrauma. For many years, clinicians have defined barotrauma as the occurrence of air leaks resulting in the accumulation of extraalveolar air which can manifest in numerous ways, the most threatening one being tension pneumothorax. Besides these "macroscopic" events whose adverse consequences are usually immediately obvious, more subtle physiological and morphological alterations may result from mechanical ventilation, especially when high airway pressure and high lung volumes are reached. Our knowledge of such manifestations stems mainly from experimental studies and has considerably expanded in recent years. Indeed, alterations of lung fluid balance, increases in endothelial and epithelial permeability, and severe ultrastructural damage have been described as the consequence of lung overinflation. One of the pioneer works was performed by Webb and Tierney [1] who have shown that rats mechanically ventilated with IPPV with a peak airway pressure of 45 cmH_2O developed rapidly a very severe pulmonary edema, responsible for massive tracheal flooding, severe hypoxemia and death of most animals. Closely related observations have been made by Kolobow et al. in sheep after longer periods of mechanical ventilation [2]. The edema resulting from high peak pressure mechanical ventilation is of the permeability type and is associated with a diffuse alveolar damage on electron microscopy examination [3]. It is worth noting that these anatomic alterations are quite similar to those observed during toxic permeability edema as well as during the adult respiratory distress syndrome. An hydrostatic component is also present [4] and may explain the fulminating course of this edema, which may be produced by very short periods of overinflation in small animals [5].

Is it barotrauma? In fact, it has been shown that an increase in airway pressure without concomitant increase in lung volume (binding of thorax and abdomen) has no effect on lung fluid balance [6–8] nor ultrastructure [6], whereas important increases in tidal volume (i.e. of the same magnitude as during high peak pressure ventilation without volume limitation) obtained by negative pressure ventilation resulted in similar lung damage as previously described [6]. Thus, the word "volutrauma" would be more appropriate [5, 9].

We are now left with a much more difficult problem: which lung volume should be considered as potential culprit? Is it tidal volume, especially from a low functional residual capacity? Is it the absolute level of lung distension (the end-inspiratory volume)? Does an increase in FRC (with PEEP, for example) affect the manifestations of volutrauma? These questions are not pure intellectual speculation and may be of clinical relevance. In the preceding issue of *Intensive Care Medicine*, a paper by Sohma et al. [10] addressed the question whether, for a same mean airway pressure, ventilation during 5 h of acutely HCl-injured rabbit lungs with low (3 cmH_2O) PEEP is more deleterious than with higher (10 cmH_2O) PEEP. Despite better lung mechanics and gas exchange in the higher PEEP group, microscopic examination did not disclose any difference in the histological alterations (oedema, haemorrhages, neutrophil infiltration and hyaline membrane formation). Maybe longer periods of ventilation combined with morphometric analyses would be necessary in order to rule out any difference between the two treatments. A recent study by Corbridge et al. [11] reported apparently different findings. The authors studied dogs with acutely injured lungs (intra-tracheal HCl instillation) and showed that the amount of pulmonary edema (post-mortem measurement of wet lung weight) was larger in those animals ventilated with large tidal volume (30 ml/kg BW) and low PEEP (3 cmH_2O) than in those ventilated with smaller (15 ml/kg BW) tidal volume and higher PEEP (12 cmH_2O). In fact 15 ml/kg cannot be considered a "small" tidal volume, and tidal volumes of 30 ml/kg BW have been shown to produce per se pulmonary edema both in rats [1] and sheep [12]. Therefore, the difference in the amount of edema could result from the compounding effects of chemical and mechanical injury. Indeed, when applied on acutely injured lungs, mechanical ventilation with overinflation produces more severe permeability alterations [13, 14] and edema [13–15] than either alone. Thus, previous lung alterations could favor

volutrauma. The issue on the effects of PEEP during acute lung injury is further confused by the finding that during mechanical ventilation-induced pulmonary edema, for a same end-inspiratory pressure, less edema was present in animals ventilated with PEEP that in those ventilated with ZEEP [1, 6]. Does it mean that PEEP would have some "protective" effect against volutrauma (in contrast with the absence of reduction or even the increase in edema observed with PEEP during most types of experimental edema), or is it simply the result of hemodynamic alterations due to the higher mean intrathoracic pressure during ventilation with PEEP? This question pertains to the problem of the respective responsibility of large pressure-volume excursions and of the absolute level of lung distension in the genesis of ventilator-induced lung injury. Further studies will be required to provide an answer. Meanwhile, it may be worth noting that microvascular injury occurs in rats submitted to very large tidal volume ventilation as well as in those who received normal tidal volume superimposed to a markedly increased FRC during continuous negative pressure ventilation [16]. In summary, from the present experimental data, one can only conclude that any form of lung overinflation is noxious.

Avoidance of large phasic pressure-volume excursions is the common rationale for the use of nonconventional modes of mechanical ventilation, both during infant and adult respiratory distress syndrome. The strategies proposed have the objective to avoid barotrauma and "put lung to rest". Apneic oxygenation with extracorporeal CO_2 removal (ECCOR) [17–20] and high frequency oscillatory ventilation (HFO) [21, 22] are the subject of considerable work, both experimental and clinical. Has the promise been fulfilled? Not completely, at present. Indeed, impressive survival rates have been reported after ECCOR in adults, but these were compared with historical series [17]. To avoid this potential bias, a randomized study of ECCOR versus conventional mechanical ventilation is under way in the USA. Preliminary results [23] do not seem to favor one strategy over the other. It is worth noting that the authors of this trial have noted that ARDS patients meeting criteria for ECMO study entry had a better prognosis during conventional treatment than historical controls [24]. This emphasizes the need for randomized studies. Similarly, in neonates, a trial comparing HFO and CMV failed to show any reduction of mortality with the former technique [22]. Interestingly enough, the incidence of pneumoperitoneum (a manifestation of "classical barotrauma") was higher in neonates treated with HFO. This study has been questioned because the authors did not "condition" the lungs with maximal recruitment before starting HFO, so that the volume swings were possibly not avoided [25]. A simpler way of avoiding large volume excursions has recently been published in this *Journal* [26] by Hickling et al. who reported that limiting peak pressure (and allowing some degree of hypercapnia, even severe) allowed a striking reduction in mortality when compared with prediction from Apache II score. Here again, no true controls were available.

At this point, we must turn again on the concept of volutrauma. Apart from the semantic aspect, thinking in terms of volume instead of pressure bears practical disadvantages but possibly important theoretical advantages. Indeed, monitoring airway pressure during mechanical ventilation is easy, but we cannot rely on this sole parameter to assess the risk of ventilator-induced lung injury. For instance, application of a continuous distending pressure during HFO or ECCOR may favor a gradual increase in lung volume. If this volume increase corresponds to recruitment of previously closed lung units, it is likely to be beneficial at least in terms of gas exchange, and probably should not cause additional lung damage. Unfortunately, things may not be so straightforward. Indeed, we know that during ARDS, normal zones may coexist with edematous ones [27] resulting in a heterogeneous distribution of ventilation. In keeping with this, Gattinoni et al. [28] proposed that during ARDS, lungs should be divided into 3 zones: a healthy one, a recruitable one and a diseased one unresponsive to pressure changes. They coined the term of "baby lung" in ARDS patients, renewing the concept of "shrunken lung" by Gibson and Pride during lung fibrosis [29], to figure the possibility that the bulk of ventilation during conventional treatment could mainly reach healthy units, with resulting overdistension.

In conclusion, although most information is derived from experimental studies, it seems possible that lung overinflation during treatment of patients with ARDS may actually worsen injury. What we need would be to find a simple way to monitor not airway pressure but lung volume [30], and particularly *regional* volumes. Meanwhile, we must realize that we treat lungs "hidden in a box" and that every effort should strive at not further increasing damage.

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