Mechanical Power

A Biomarker for the Lung?

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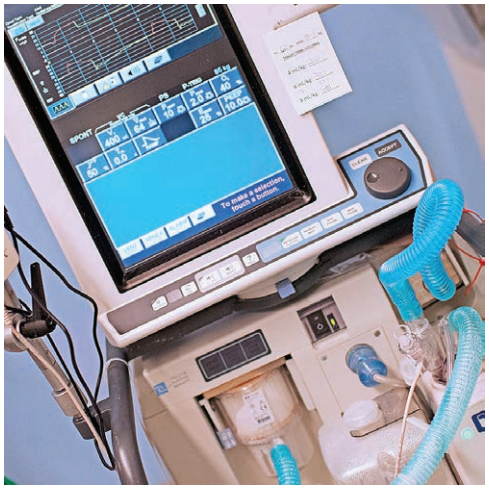
Ventilator-induced lung injury is a multifaceted problem that has progressively become a preoccupation for intensivists and anesthesiologists. It has taken many years to realize that mechanical ventilation, a life-saving technique, could also induce harm. The first randomized controlled trial in critical care compared extracorporeal membrane oxygenation to mechanical ventilation in patients with severe acute respiratory distress syndrome, with the premise that this technique could improve gas exchange and save lives.[1] Because, at the end of the 1970s, the mechanical insult to the lungs caused by mechanical ventilation was not considered as a relevant or important problem (oxygen toxicity was much more of a concern), the two arms in the trials received the same "injurious" mechanical ventilation and had the same dismal outcome. Pioneer experimental work from Webb and Tierney[2] and later from Dreyfuss and Saumon[3] progressively demonstrated the potential of large volumes and pressures to cause injury either in previously healthy or already injured lungs. The concepts of atelectrauma and biotrauma were later proposed by Tremblay *et al.*[4] in Slutsky's group to explain the observed protective effects of positive end-expiratory pressure (PEEP) and to show the link between local mechanically induced inflammatory effects with both the systemic multiorgan failure observed in these patients and their high mortality. Pressure limitation in the alveoli, assessed by the plateau pressure, was introduced in clinical practice by recommendations in the early 1990s[5] and was based on the baby lung concept[6] and an early clinical report by Hickling *et al.*[7] suggesting, in 1990, a marked improvement in survival resulting from deliberately limiting pressures and volumes. The proof of concept was brought by the 12 *versus* 6 ml/kg positive pressure ventilation trial in 2000,[8] which showed that 25% of the actual mortality observed using 12 ml/kg of predicted body weight could be avoided by limiting tidal volume to around 6 ml/kg and plateau pressure to 30 cm H_2O. Numerous studies then discussed how far tidal volume should be reduced to remain protective in acute respiratory distress syndrome, whereas other studies have shown that lung protection needed to be extended beyond the field of acute respiratory distress syndrome, including data suggesting that this concept of lung protection could also apply to the field of intraoperative ventilation.[9]



"How can we determine when mechanical ventilation is harming the lung…?"

From there, clinicians still face a number of important questions, among which two concern everyday practice: Which PEEP level is optimal for protecting the lung of mechanically ventilated patients? How can we determine when mechanical ventilation is harming the lung and/or is inducing systemic inflammation deleterious for other organs (before it is too late)? An impressive animal study by Collino *et al.*[10] from the group of Michael Quintel and Luciano Gattinoni (Department of Anesthesiology, Emergency and Intensive Care Medicine, University of Göttingen, Göttingen, Germany), published in this issue, tried to address these two questions at the same time using an animal model. They applied the concept of mechanical power as a unifying determinant of injury that describes the energy transfer to the lung to predict the potential harm generated by mechanical insufflations at increasing pressures. The mechanical power takes into account the energy delivered to the lung, popularized

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by the driving pressure,[11] the dynamic changes in pressure, the energy related to the increase in lung volume induced by PEEP, and the respiratory rate. They had previously shown the influence of respiratory rate on the generation of injury, as predicted by the change in mechanical power.[12] This has important consequences because decreasing tidal volume is often compensated by increasing respiratory rate. Knowing the respective risk (in terms of injury) of respiratory rate *versus* driving pressure will be essential for clinical practice, together with determining safe levels for $Paco_2$. To increase pressures in this series of experiments, they progressively increased PEEP from 0 to 18 cm H_2O in piglets with normal lungs but under general anesthesia, a condition known to generate atelectasis. The study is impressive through the number of experiments performed and their duration but also by the number of ways in which the authors tried to capture ventilator-induced lung injury: lung weight, other organs' weights and wet to dry weights, lung histology, hemodynamics, lung volume, gas exchange including dead space and oxygenation, and multiple measures of mechanics including stress, strain, and mechanical power. The study well illustrates the complexity of the so-called ventilator-induced lung injury, including both atelectrauma (insufficient reopening of the lung at end expiration and/or repeated opening and closing of this atelectatic lung) and volutrauma inducing distension and major hemodynamic effects. As discussed by the authors, such models are complex because you cannot "isolate" the effects of PEEP from the concomitant changes in other pressures or the elastic responses induced by changes in PEEP, and one cannot imagine that a single magic marker will describe every change in every parameter at the same time. Interestingly, they found that PEEP—at "low" values—is an important component of lung protection, a key finding shown for many years, even if its mechanisms are not completely understood. This protection may also be mediated by beneficial hemodynamic effects of PEEP. PEEP can also result in volutrauma when it is too high (in part also because it results in excessively high plateau pressures). Clinical experience and clinical trials have confirmed that excessive PEEP and plateau pressures could be harmful and dangerous.

The experimental model used in the study by Collino *et al.*[10] represents the effects of potentially injurious "standard" ventilation (8 to 10 ml/kg of tidal volume) at different baseline pressures (PEEP) in the presence of general anesthesia with healthy lungs. The chosen model, piglets, makes it difficult to completely infer from these data what would be the equivalent in patients. The authors suggest that the PEEP levels of 4 to 7 cm H_2O, which seem to constitute the transition between lung protection and the start of injury, could represent 8 to 14 cm H_2O in humans, but this has to be taken with great caution. Moreover, the situation of the individual patient must be taken into account, with her/his history and current lung injury. Researchers have looked for inflammatory biomarkers of lung injury, either for prognostication of acute respiratory distress syndrome regarding mortality or for predicting the response to treatment. Because the initial injury results from a direct mechanical insult, it makes sense to propose a mechanical index as a possible biomarker of the risk of ventilator-induced lung injury. The power of breathing is an interesting concept when directly applied to the lung, *i.e.*, using the transpulmonary pressure. Similar to the work of breathing per minute, we are reminded that Otis *et al.*[13] already described in 1950 that the breathing pattern could be optimized to minimize the power of breathing. It is remarkable that across different experiments (assessing respiratory rate or different levels of PEEP in the same animal model), the authors found a similar threshold around 12 to 13 J/min, above which mechanical ventilation may be lethal. As noticed by the authors, this does not indicate a "safe" limit, but being able to use such measurements at the bedside to define dangerous settings of ventilation seems very attractive.

The last paragraphs of the discussion list many unanswered and important questions that merit exploration. We need to see data using a relevant lung injury model where the competing issues of recruitment and overinflation may well influence the data and suggest a different safe power. We also need clinical observational data and ultimately a clinical trial before wholesale adoption of the concept and its potential use. Trying to transpose complex physiologic concepts into useful tools for clinicians at the bedside is very exciting, and the authors need to be commended for their endeavor already showing how promising the mechanical power seems to be.

Competing Interests

The authors are not supported by, nor maintain any financial interest in, any commercial activity that may be associated with the topic of this article.

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