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Intraoperative Protective Mechanical Ventilation: Fact or Fiction?

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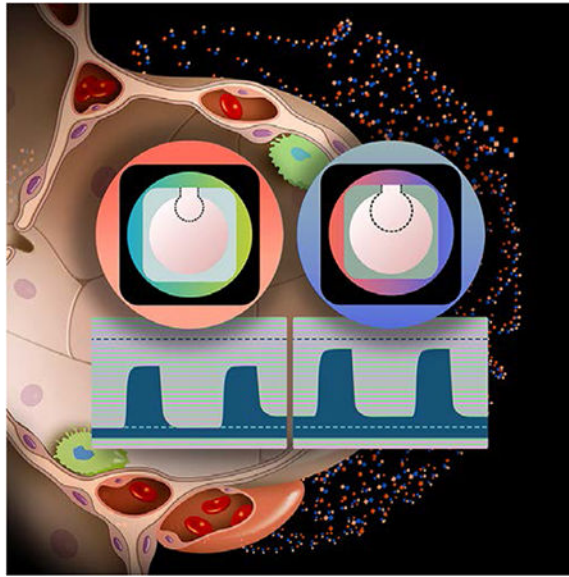
Positive pressure ventilation gained widespread clinical acceptance during the Danish polio epidemic of 1952,¹ when it dramatically reduced the mortality of respiratory failure, and it has saved countless lives in ensuing years by enabling modern critical care and the safe practice of surgery under general anesthesia. Nonetheless, evidence emerged in the 1970s that positive pressure ventilation can itself cause lung injury.² Since then, two fundamental facts have been established. First, large tidal lung excursions are detrimental if they lead to end-inspiratory overdistension and/or cyclical alveolar or bronchiolar derecruitment–recruitment between breaths. Second, the lungs of patients during general anesthesia or with acute respiratory distress syndrome are functionally smaller: functional residual capacity is reduced because some of the airspaces become atelectatic, consolidated, or flooded with edema. A corollary of these facts has been the quest to restore the relationship between tidal volume and functional residual capacity either by decreasing the former or increasing the latter. This concept represents the physiologic underpinning of all “protective” ventilation strategies.

Such framework is helpful to analyze the study by Turan and colleagues³ in this issue of *ANESTHESIOLOGY*. In this large factorial crossover cluster trial, adults undergoing orthopedic surgery during general anesthesia (approximately 50% also with regional block and slightly more than 50% undergoing arthroplasty) were allocated to two levels of tidal volume (6 and 10 ml/kg of predicted body weight) and of positive end-expiratory pressure (PEEP, 5 and 8 cm H₂O). Presumably, ventilation with lower tidal volume and higher PEEP could lead to better postoperative oxygenation and lower incidence of respiratory complications, because such a strategy would limit both end-inspiratory overdistension and end-expiratory derecruitment, the two biophysical triggers of ventilator-induced lung injury. The results instead show no meaningful clinical or statistical difference among the four studied groups in oxygenation within the first postoperative hour, oxygenation later on the ward, frequency of postoperative pulmonary complications, or duration of hospitalization.

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Competing Interests

The authors declare no competing interests.



“When is protective intraoperative ventilation most beneficial?”

It is important to note that the authors did not use excessively high or low tidal volumes^{4,5} and PEEP, but instead values considered acceptable in current clinical practice.⁴⁻⁶ Accordingly, two main inferences can be drawn. First, in a cohort of patients with a low prevalence of lung disease and borderline obesity undergoing nonabdominal surgery of moderate duration (about 3.5 h) and without major physiologic impact (*e.g.*, blood loss), low tidal volumes as well as higher acceptable tidal volumes (10 ml/kg)^{4,5} with higher PEEP were well tolerated. It is interesting that a tidal volume of 6 ml/kg did not result in lower oxygenation even at the lower PEEP, given that atelectasis is usually considered the main downside of low tidal volume. These results suggest that relatively healthy lungs in the studied conditions can withstand a few hours of low tidal volume ventilation during nonabdominal surgery without developing significant atelectasis even at low PEEP. Higher PEEP and tidal volume did not seem to compromise postoperative lung function either. Second, these results release the cognitive anchor to a single optimal PEEP or tidal volume, at least in this patient population, and instead portray a range of equally acceptable values, consistent with a range—not merely a point—of maximal compliance in the pressure–volume curve of a healthy lung. This message is important because it argues against the transposition without qualification of inferences and values derived from critical care studies to the operating room.

So, is intraoperative protective ventilation all fiction? Substantive observational evidence has identified tidal volume as a risk factor for postoperative pulmonary complications after general anesthesia.^{7,8} These studies indicated that “protective” ventilation (generally defined as lower tidal volume plus PEEP and/or recruitment maneuvers) may reduce such complications^{4,8} that are associated with increased mortality, intensive care unit admission, and length of stay.⁷ The Intraoperative Protective Ventilation (IMPROVE) trial confirmed a marked beneficial effect of protective ventilation on major abdominal surgery.⁶

Yet, as with Turan's trial, several trials on protective ventilation did not demonstrate a difference between groups.^{5,9,10} What could explain these inconsistencies, and when is protective intraoperative ventilation most beneficial? It has been increasingly recognized that the ratio of tidal volume to end-expiratory lung volume, proportional to the driving pressure and a surrogate for lung strain, is the biophysical mediator of the effects of tidal volume and PEEP on ventilator-induced lung injury.⁴ In fact, the potential of different tidal volumes to reduce postoperative pulmonary complications depends on the patient's respiratory compliance.¹¹ This physiologic individuality may be a reason for discrepancies. Patient population is another factor. The IMPROVE trial targeted a high-risk population for pulmonary complications⁶ (major open abdominal surgery, pre-existent respiratory risk factors), whereas Turan and colleagues studied a population at lower risk³ based on the Assess Respiratory Risk in Surgical Patients in Catalonia risk score.¹² There is evidence that pulmonary outcomes are less likely to depend on PEEP in nonabdominal/noncardiothoracic surgery, *e.g.*, neurologic *versus* abdominal surgery.¹³ This also implies that Turan's results should not be extrapolated to abdominal or cardiothoracic surgery, when additional injury mechanisms are present and, consequently, the effects of different ventilatory settings could be more evident.¹³ Time may also be an important variable. Normal lungs show only limited inflammation after 2 h of ventilation even at high driving pressures.¹⁴ Sixteen to 24 h were necessary for a significant pulmonary inflammatory response and mechanical deterioration to develop in experiments applying clinical tidal volumes (6 to 8 ml/kg) in initially uninjured lungs.¹⁵⁻¹⁷ Finally, the separation between ventilator settings is relevant. The IMPROVE trial acted on multiple variables (tidal volume, PEEP, recruitment maneuvers) setting them apart enough (tidal volumes of 6 to 8 ml/kg with PEEP = 6 to 8 cm H₂O *versus* 10 to 12 ml/kg with PEEP = 0 cm H₂O) that, presumably, the effect could be detected in contrast to current practice used by Turan and colleagues.³

If there is a range of equally acceptable values for ventilatory settings, it may be hard to show an effect, especially when clinical practice has already converged toward such a range. Turan and colleagues studied a large population and observed a smaller SD for the primary outcome than that initially presumed, which ultimately yielded a high power to detect the predefined mean effect. The 97.5% CIs for the effect estimates were a time-weighted average SpO₂/Fio₂ of -0.4 to 7.3% for tidal volume and -4.0 to 3.6% for PEEP, numbers that convincingly demonstrate comparable postoperative oxygenation in the studied groups. These results also imply that, although previous clinical studies documented the presence of an effect, they did not necessarily provide the best or single setting of the variable of interest to achieve that effect.

The hemodynamic impact of mechanical ventilation is frequently a concern. A clinically meaningful finding by Turan and colleagues³ in this regard was the similar intraoperative use of vasopressors and incidence of hypotension in all combinations of PEEP and tidal volume. This finding reinforces the concept that the mild-to-moderate range of ventilatory settings explored does not usually result in major hemodynamic effects.

The study opens several questions. Many patients were excluded by anesthesiologists, or due to comorbidities, instability, or other reasons. Such subset of potentially higher-risk patients could represent those patients who would most benefit from specific ventilatory

interventions. Although the primary outcome of SpO_2/FiO_2 in the first hour is a sensitive marker of oxygenation impairment, it could be affected predominantly by factors other than ventilatory settings. The absence of differences in the ward reinforces that any influence of intraoperative settings on postoperative oxygenation was unlikely. Also, even if there was an intraoperative effect of the interventions, this could be lost at extubation, without subsequent benefit. Finally, the reported rate of pulmonary complications was quite low, implying a low-risk group and the potential risk for false negatives, given that the occurrence of those complications derived from registry and billing data not from prospective collection.

Such limitations will deserve future exploration to advance this relevant area. For now, Turan and colleagues provide evidence that mild-to-moderate differences in key ventilator settings—tidal volume and PEEP—within currently accepted ranges do not result in substantial differential effects on postoperative oxygenation and other pulmonary outcomes during orthopedic surgery. Mechanical ventilation in the operating room requires its own specific set of knowledge, with ranges different from those of patients with acute respiratory distress syndrome in intensive care units. Protective ventilation is not defined by single arbitrary numbers, but by ranges of ventilatory settings that likely differ in distinct conditions and in relation to patient-specific physiopathologic features.

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