One more brick in the wall of protective ventilation in surgical patients

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Abstract: On June 14, 2015, Ladha and colleagues published an article in the *BMJ* entitled "Intraoperative protective mechanical ventilation and risk of postoperative respiratory complications: hospital based registry study", which investigated the effects of intraoperative protective ventilation on major postoperative respiratory complications. This study used data of over 69,265 patients in order to investigate patients over the age of 18 who underwent a non-cardiac surgical procedure between January 2007 and August 2014 and required general anesthesia with endotracheal intubation. The investigators found that intraoperative protective ventilation was associated with a decreased risk of postoperative respiratory complications. This study raises important questions about the ventilatory management of surgical patients.

Keywords: Mechanical ventilation; tidal volume; positive end expiratory pressure (PEEP); surgery; postoperative pulmonary complications (PPC)

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Driven by clinical and experimental studies, strategies of protective ventilation combining low tidal volume, low plateau pressure, and application of positive end expiratory pressure (PEEP) have gained widespread acceptance in intensive care units, especially for patients suffering from the acute respiratory distress syndrome (ARDS) (1). However, recent meta-analyses suggest that lower tidal volumes are protective not only during long-term ventilation in critically ill patients with ARDS (2), but also in short-term ventilation during general anesthesia for surgery (3). Indeed, the use of protective ventilation in surgical patients could reduce the incidence of postoperative pulmonary complications (PPC), a condition associated with increased length of stay and mortality in this group of patients (4,5).

In order to limit the risk of ventilator-induced lung injury (VILI), a number of reviews suggested that intraoperative mechanical ventilation should consist of low tidal volume to avoid volutrauma, moderate level of PEEP and periodic lung recruitment maneuvers to avoid atelectrauma and low plateau pressure to prevent barotrauma (6-8). At the cellular level, physical stimuli from mechanical ventilation are transformed into chemical signals, resulting in release of pro-inflammatory and anti-inflammatory mediators by means of direct cell injury or indirect activation of cellular signaling pathways (9). Some mediators may promote local effects such as pro-apoptotic or pro-fibrotic actions, whereas others act as homing molecules recruiting local and remote immune cell populations (10). These local effects as well as their immunological consequences are summarized by the term "biotrauma" (11).

From a physical perspective, the VILI process must be related also to the energy transfer from the ventilator to the lung. Due to the phenomenon of hysteresis the lung conserve energy during one respiratory cycle, resulting in heat and lung tissue damage along each breath. In physical terms, the hysteresis area represents precisely this energy dissipated across the parenchyma and should bear some good correlation with VILI (12,13). For a single patient in which the respiratory system compliance (C_{RS}) is known, the total energy transfer is proportional to (driving pressure)^2 × C_{RS}. Therefore the total energy transferred is strongly determined by the driving pressure (defined as plateau pressure minus PEEP) delivered by the ventilator (12).

In the present study, Ladha *et al*. (14) analyzed the relationship between protective ventilation [defined as a PEEP ≥5 cmH_2O, tidal volume <10 mL/kg predicted body weight (PBW), and plateau pressure <30 cmH_2O] and major respiratory complications in a cohort of 69,265 patients who underwent non-cardiac surgical procedures. The authors found that protective ventilation was associated with decreased risk of complications [adjusted odds ratio (OR) =0.90; 95% confidence interval (CI), 0.82–0.98; P=0.013]. Also, a PEEP of 5 cmH_2O and median plateau pressures of 16 cmH_2O or less were associated with the lowest risk of postoperative respiratory complications. Finally, these results were similar in the propensity score matched cohort.

An interesting finding was an almost dose-response relationship between plateau pressure and major respiratory complications. This indicates that the current thresholds considered protective in critically ill patients with lung injury (<30 cmH_2O) may not be enough for patients with uninjured lungs. There are some concerns over the tidal volume reduction in patients with ARDS whose plateau pressure are already below 30 to 35 cmH_2O. In a study assessing potential reasons why physicians underuse lung-protective ventilation, although not explicitly documented as a reason for not using it, 82% of the patients who never received a protective strategy of ventilation had a plateau pressure ≤30 cmH_2O showing a preference for the plateau pressure as first aim for protective ventilation (15). However, in accordance with the findings from the study by Ladha *et al*. (14), a secondary analysis from the ARMA trial (16) suggests that there was a beneficial effect of tidal volume reduction, regardless of the level of plateau pressure (17). A target plateau pressure selected as low as possible to reduce driving pressure should be applied according to the present findings. In accordance, a recent study showed that decreases in driving pressure owing to changes in ventilator settings were strongly associated with increased survival in patients with ARDS (18).

An important aspect to be considered in studies in this field is the analysis of intervention bundles, in which the effects of single measure in the outcome is prone to criticism. Looking for the individual effects of plateau pressure, tidal volume and PEEP, the study employed separate regression models and found that only plateau pressures and PEEP were associated with the risk of respiratory complications. The rationale for using a bundle of low tidal volume and high level of PEEP with recruitment maneuvers can be that tidal volume reduction would induce atelectasis and higher levels of PEEP with recruitment maneuvers could stabilize the lungs during the respiratory cycle (19).

The use of higher tidal volumes was standard of care in the operating room for several years since use of tidal volumes per se prevents development of atelectasis, and as such improves oxygenation. Furthermore, relatively short use of higher tidal volumes was considered safe (20), despite the fact that animal as well as clinical studies showed that VILI can develop shortly after initiation of ventilation (21). Recently, several studies already strongly showed that tidal volume reduction in surgical patients is associated with decreased incidence of PPC (22-24).

Aiming to determine the impact of PEEP alone in surgical patients, the PROVHILO trial showed that during mechanical ventilation with low tidal volumes in patients undergoing open abdominal surgery, use of a high level of PEEP and recruitment maneuvers alone does not reduce the incidence of PPC (25). Thus, higher levels of PEEP (around 12 cmH_2O) with recruitment maneuvers more frequently results in hemodynamic instability and hypotension compared with low PEEP (around 2 cmH_2O) without recruitment maneuvers. These results were later confirmed in a large individual patient data meta-analysis including several randomized controlled trials in surgical patients, showing that low tidal volumes, but not PEEP, were associated with improved outcome in different types of surgery (26).

An alternative approach during general anesthesia is the so-called “intraoperative permissive atelectasis”, when PEEP is kept relatively low and recruitment maneuvers are waived (19). This concept aims at reducing the static stress in lungs, which is closely related to the mean airway pressure, assuming that collapsed lung tissue is protected against injury from mechanical ventilation (19). Indeed, a recent study showed that a strategy using low tidal volume and minimal PEEP, resulting in a low driving pressure, is capable to protect the lung from VILI in animals model of ARDS, where the amount of atelectatic tissue is in fact much higher than those in uninjured lungs (27).

The influence of outcomes used in the study with other relevant outcomes, including hospital length of stay and mortality still needs further studies. Composite endpoints as used in the present study are useful in that they provide an overall summary of effect, which may be readily appreciated by clinicians. When adequate, they enhance comprehension, study power, and precision, and these should lead to earlier identification of real improvements in care (28). However, composite outcome measures has some major limitations since the component variables can differ importantly in terms of severity and frequency, and differences in the frequency of component variables in a composite outcome may be masked (29).

In conclusion, the findings of the present study are one more brick in the wall showing the potential benefits of intraoperative protective mechanical ventilation. However, the impact of each parameter included in the bundle needs further assessment. According to available evidence and taking into account the present findings, mechanical ventilation of patients undergoing general surgery should include low tidal volume, low plateau pressure, and low driving pressure. However, higher levels of PEEP are still under debate and should be considered in selected cases.

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Footnote

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