Tidal Volume in Patients With Normal Lungs during General Anesthesia

Lower the Better?

LUNG protective mechanical ventilation strategies using low tidal volumes ($V_T$) of approximately 6 ml/kg predicted body weight and moderate or high positive end-expiratory pressures (PEEP) have been demonstrated to improve relevant outcome measures in patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS).\(^1\,^2\) Despite the fact that lowering $V_T$ failed to improve outcomes in three other controlled trials investigating $V_T$ in ALI and ARDS patients,\(^3\,^4\,^5\) there is unequivocal evidence that mechanical ventilation in critically ill patients has the potential to aggravate or, under certain circumstances, initiate lung injury.\(^6\,^7\) In addition to mechanical ventilation with lower $V_T$, patients with ALI and ARDS could benefit from strategies that avoid cyclic alveolar collapse and tidal recruitment, including the use of higher levels of PEEP. Meta-analysis suggest this approach can not only waive the need for rescue therapies as a result of life-threatening hypoxemia,\(^7\) it can also reduce mortality in patients with more severe ALI.\(^8\) It is still matter of discussion whether or not lung protective strategies could be beneficial in ventilated patients without ALI or ARDS as well. In this issue of Anesthesiology, Sundar et al.\(^9\) studied the use of low $V_T$ ventilation on duration of postoperative mechanical ventilation among patients with normal lungs who underwent elective cardiac surgery.

Mechanical ventilation is often mandatory for patients who undergo surgery, especially cardiac surgery. Despite its life-saving necessity, mechanical ventilation adds mechanical stress to lung tissues and may cause damage on a cellular level. Potential mechanisms include: (1) stress failure of plasma membrane (necrosis, release of mediators and cytols from damaged cells), (2) stress failure of endothelial and epithelial barriers (loss of compartmentalization, hemorrhage, accumulation of lung leukocytes), (3) damage of the extracellular matrix, (4) overdistension without tissue destruction, (5) effects on the vasculature independent of stretch and rupture (increased intraluminal pressure and shear stress).\(^6\,^11\) In contrast with results from small animal models—in which mechanical stress induced by high $V_T$ and low (or no) PEEP has caused lung injury in normal lungs (and which have been recently seen in larger animals in the context of high $V_T$)\(^12\)—effects of short-term perioperative mechanical ventilation on pulmonary integrity in patients are less well defined.\(^13\) Two retrospective analyses identified high airway pressures and $V_T$ as independent risk factors for ALI and ARDS in critically ill patients who require mechanical ventilation for reasons other than ALI or ARDS.\(^14\,^15\) Studies on mechanical ventilation in perioperative settings often make use of small patient populations and focus at different (and not necessarily clinically relevant) outcomes, such as inflammatory mediators. Such studies have revealed inhomogeneous results.\(^13\) The impression is, however, that major surgery (e.g., cardiac surgery), which per se causes a clinically relevant inflammatory response, makes the lungs more vulnerable to injury caused by mechanical stress.\(^16\,^17\) This effect might be explained by a two- or multiple-hit model. Accordingly, potentially injurious mechanical ventilation as a second hit requires preexisting injury caused by ALI/ARDS. Alternatively, it may also be a marked inflammatory response (e.g., triggered by major surgery) to cause or aggravate lung injury and/or systemic inflammation.\(^16\,^18\)

Different studies on mechanical ventilation strategies during and/or after cardiac surgery are summarized in table 1. The present study by Sundar et al.\(^9\) is the largest one in cardiac surgery patients and it focuses on clinically relevant outcomes. Although the authors failed to show a significant difference in time on mechanical ventilation, the number of patients still on mechanical ventilation at 6 and 8 h after surgery was significantly lower in the protective ventilation group.\(^9\) However, there are several limitations of this study: (1) it is a single-center study, thus its results cannot be generalized to other centers or other groups of patients; (2) obese patients were not included in the study; (3) the level of PEEP was selected according to a specific table and not via individual physiologic parameters like gas-exchange, compliance, or oxygen delivery; and (4) weaning procedures were not specifically standardized.

In this study, PEEP levels in both study groups were approximately 5 cm H$_2$O. Low PEEP levels might increase regional shear stress and lung injury by causing opening and closing of lung units within a ventilatory cycle (atelectrauma), even in absence of high plateau pressures.\(^19\) Tidal recruitment and derecruitment can be minimized by using PEEP levels of 10 cm H$_2$O during anesthesia, at least in healthy nonobese patients.\(^20\) Although it is uncertain whether ventilation strategies that use higher levels of PEEP during the intraoperative period are beneficial to these patients,\(^17\,^21\) higher levels of PEEP could reduce intraoperative atelectasis, decreasing repetitive collapse and reexpansion of dependent lung

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**This Editorial View** accompanies the following article: Sundar S, Novack V, Jervis K, Bender SP, Lerner A, Panzica P, Mahmoody F, Malhotra A, Talmo D: Influence of low tidal volume ventilation on time to extubation in cardiac surgical patients. Anesthesiology 2011; 114:1102–10.
parts, and thereby attenuating pulmonary inflammation and coagulation. Individual factors such as obesity, pneumoperitoneum, preexisting disease, and some surgical interventions may aggravate atelectasis formation.

Furthermore, although some positive clinical indication on ventilation-free hours or reduced reintubation rate were observed, clinical decisions regarding patient need for reintubation (or any other intervention) were made by these teams based on their clinical assessments. The rate of intubation was determined (or any other intervention) were made by these teams based on their clinical assessments. The rate of intubation was determined mainly by bleeding, arrhythmia, and pancreatitis not specifically related to ventilation management.

Inflammatory responses to cardiac surgery are variable and may depend on individual patient factors, such as co-morbidities, genetic predisposition, previous tissue injury (e.g., cardiac shock), or surgical trauma depending on type of surgery, amount of ischemia-reperfusion injury, and blood loss. Because high-risk patients are usually not included in studies on perioperative ventilation, the issue of protective mechanical ventilation may be even more relevant in daily practice when one treats these patients. Despite an accurately performed sample size calculation in the study by Sundar et al., the number of patients undergoing routine elective cardiac surgery to be studied might be higher to see differences in relevant outcomes depending on mechanical ventilation strategy.

When using lung protective mechanical ventilation more extensively in patients without ALI/ARDS, adverse effects such as hypercapnia, atelectasis formation, and increased requirements for higher fractional inspired oxygen tension and PEEP should be considered. Increased fluid administration or even use of catecholamines might be necessary when treating potential cardiovascular impairment as a result of decreased venous return as associated with higher PEEP. In fact, it is often required when using lower VT. Balancing the risks and benefits of protective mechanical ventilation during anesthesia should include an assessment of preoperative patient status and expected amount and duration of surgical trauma, among other individual factors. There is an increasing body of evidence from relatively small studies directly or indirectly suggesting a potential benefit of protective ventilatory strategies for patients without lung injury. This finding is especially true for patients during cardiac and thoracic surgery (e.g., esophagectomy, which is often associated with a clinically relevant systemic inflammatory response to surgical procedures). Systematic patient scoring methodologies may be useful in assisting clinicians identify patients at risk of postoperative complications. Future studies might consider stratifying patients to include those with more severe illness or injury. This stratification, however, assumes that the more ill a patient is, the more relevant a protective ventilatory strategy may be.

**Table 1. Randomized and Controlled Trials Comparing High versus Low VT Ventilation in Cardiac Surgery Patients**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>N</th>
<th>Setting*</th>
<th>VT, ml/kg</th>
<th>Respiratory Rate, l/min</th>
<th>PEEP, cm H₂O</th>
<th>Outcomes for Intervention (Protective Strategy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chaney MA et al.²⁵</td>
<td>2000</td>
<td>25</td>
<td>OR</td>
<td>6</td>
<td>12</td>
<td>5</td>
<td>Better lung mechanics, less shunt</td>
</tr>
<tr>
<td>Koner O et al.²⁶</td>
<td>2004</td>
<td>44</td>
<td>OR</td>
<td>6</td>
<td>10</td>
<td>5</td>
<td>No difference: plasma IL-6, TNF, ventilation time, hospital length of stay</td>
</tr>
<tr>
<td>Wrigge H et al.¹⁷</td>
<td>2005</td>
<td>44</td>
<td>ICU</td>
<td>6</td>
<td>12</td>
<td>9</td>
<td>No difference: plasma mediators; lower TNF in broncho-alveolar lavage; subgroup showed faster plasma TNF decline</td>
</tr>
<tr>
<td>Zupancich E et al.¹⁶</td>
<td>2005</td>
<td>40</td>
<td>OR</td>
<td>6.8</td>
<td>10.9</td>
<td>9.1</td>
<td>Lower IL-6 and IL-8 in plasma and broncho-alveolar lavage</td>
</tr>
<tr>
<td>Reis Miranda D et al.¹⁸</td>
<td>2005</td>
<td>62</td>
<td>OR/ICU</td>
<td>4–6</td>
<td>6–8</td>
<td>NA</td>
<td>Faster decline in plasma IL-8 (IL-10)</td>
</tr>
<tr>
<td>Sundar S et al.⁹</td>
<td>2011</td>
<td>149</td>
<td>OR</td>
<td>6.2</td>
<td>10.0</td>
<td>5.0</td>
<td>No difference: ventilation time; fewer patients ventilated 6 h after operation; fewer reintubations</td>
</tr>
</tbody>
</table>

* Clinical setting at start of study.

High = high VT group; ICU = intensive care unit; IL = interleukin; low = low VT group; NA = not available (not reported); OR = operating room; PEEP = positive end-expiratory pressure; TNF = tumor necrosis factor-α; VT = tidal volume.

References

2. Parsons PE, Eisner MD, Thompson BT, Matthy MA, Ancuk-
EDITORIAL VIEWS


