Low Stretch Ventilation

Good for the Heart?

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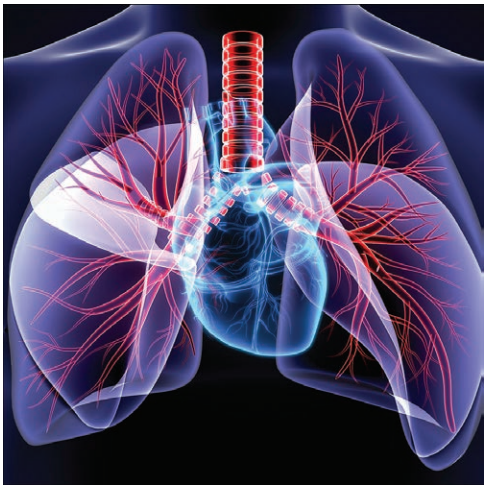
Clinicians have known the circulatory consequences of mechanical ventilation since patients were ventilated. By raising pressure in the chest, positive airway pressure reduces venous return and cardiac preload while it alters the afterload of both ventricles. These responses depend on the interaction of thoracic and pulmonary mechanics, cardiac dysfunction, patient's volume status, and vascular tone. The net result is usually harmful to the patient, but there are exceptions such as left heart failure. Superimposed on the continuous effects of positive end-expiratory pressure, tidal inflation generates swings in biventricular ejection and in pulmonary blood content. If brisk, these oscillations can break the pulmonary capillary barrier and contribute to pulmonary edema when tidal volume is too high.[1] In comparison to its effects on cardiac loading, the interactions of mechanical ventilation and myocardial contractility are underexplored.



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In this issue of Anesthesiology, Cherpanath *et al.*[2] bring novel information to this field. The authors studied 42 patients among those who were recruited in a large multicenter trial (Protective Ventilation in Patients without ARDS trial [PReVENT]) testing the clinical outcomes (ventilator-free days, survival, length of stay, pulmonary complications) of low tidal volume ventilation in patients who did not meet the criteria of acute respiratory distress syndrome (ARDS).[3] Patients were randomized to receive low (6 ml/kg predicted body weight) *versus* moderate (8 to 10 ml/kg) tidal volume within 1 h from initiation of ventilator support. After 24 h with these settings, the subjects studied by Cherpanath *et al.* received a transthoracic echocardiogram. In addition to standard metrics of right and left ventricular function, the authors calculated the myocardial performance index from tissue Doppler measurements of isovolumetric contraction and relaxation of the ventricles. This measurement is considered less dependent on cardiac loading conditions than more familiar echocardiographic variables such as the ejection fraction. The authors found that most indexes of systolic function, including the performance index, were lower in the moderate tidal volume group as compared with low tidal volume ventilation. They hypothesize that these findings may reflect reduced cardiac contractility due to systemic inflammation. Indeed, excessive lung stretch is associated with loss of inflammatory compartmentalization and release of mediators (biotrauma), which may generate nonpulmonary organ damage.[4]

The results of the study by Cherpanath *et al.* are very interesting, but a few considerations need to be addressed by further research, before we opt for lower tidal volume ventilation for the purpose of minimizing impact on cardiac function. First, the mechanistic link among tidal volume, systemic inflammation, and extrapulmonary organ dysfunction is plausible but, as the authors recognize, it is mostly supported by animal studies, where tidal volumes were generally larger than what is typically used in clinical practice. Second, Cherpanath *et al.* recruited a small enough sample size that it is possible that heterogeneity between clinical intervention groups potentially could have influenced study findings. For example, there was a 4-mmHg difference in mean central venous pressures between study groups. While this was not a statistically significant difference, it could represent a clinically significant difference in volume status that potentially could favor the outcome of the low tidal volume study group, since the myocardial performance index is not always preload independent.[5] Third, more vigorous inspiratory effort in the low tidal volume

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group (not measured in the study) could have contributed to the results. When lower tidal volumes are targeted, patient's inspiratory effort increases, whether the chosen modality of ventilation is pressure support (received by most study patients) or volume control. This can have two effects: more negative intrathoracic pressure during inspiration may further increase transmural filling pressures of the heart (compounding the higher central venous pressure in the low tidal volume group); and higher sympathetic activation may increase cardiac contractility. In the second case, the link between cardiac performance and tidal volume may be an adaptive response to the different respiratory muscle workloads.

Irrespective of the limitations of the study, the idea that tidal volume selection might modulate cardiac function is intriguing. Future studies measuring circulating biomarkers will need to convincingly prove that tidal volume size influences cardiac function through release of inflammatory mediators. Furthermore, the work done by Cherpanath *et al.* will hopefully inspire investigations on the effects of tidal volume in heart failure and shock. But overall, there are open questions regarding the role of tidal volume settings in patients who do not have ARDS. In contrast with the stronger evidence supporting low tidal volume ventilation in ARDS,[6] PReVENT—the parent trial of Cherpanath's study and the largest one completed in non-ARDS patients—showed no benefit of this strategy on ventilator-free days (the primary outcome) and on all secondary outcomes.[3] This lack of effect is bothersome to many authors and practitioners, but it is not entirely surprising. Patients who do not have ARDS are less susceptible to stretch-induced lung injury than those with this condition. This may be due to larger capacity of ventilated lung, more stable inflation, or less abundance of stress amplifiers (minute areas of inflation heterogeneity) sparse throughout the lungs.[7] However, critically ill patients display large heterogeneity of biologic, morphologic, and physiologic characteristics affecting treatment responses. The risk factors for stretch-induced lung injury may be present in some patients who do not meet ARDS criteria. Because of this ambiguity, some patients will be harmed if a moderate tidal volume is chosen. Therefore, many experts advocate using low tidal volume ventilation in all patients, assuming lack of harm. But low tidal volume has its own unintended consequences (discomfort, atelectasis, and lung injury generated by diaphragm activity) and its blanket application to a very large population of patients might even do more harm than benefit.[8] Future research will have to respond to these challenges and identify which measurable factors put the patients at higher risk for damage by tidal volume settings.

Do the results of the study by Cherpanathi *et al.* support low tidal volume ventilation as the standard of care in all ventilated patients? Of course not, and a middle ground, slightly more liberal approach to setting the ventilator may be the most sensate option until better evidence is available. More importantly, the results of this study highlight the complexity and distant implications of each decision we make at the bedside, even the simplest ones. Measuring hemodynamic responses to mechanical ventilation, with skilled echocardiographic assessment as championed by the authors, should be incorporated in bedside ventilator management. Supporting this, recently published work suggests that an integrated approach to guide mechanical ventilation with measurements of cardiac and pulmonary physiology may improve the outcome of patients with acute respiratory failure.[9]

Competing Interests

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