Driving Pressure–guided Ventilation: Comment

To the Editor:

I read with interest Park *et al.*'s article "Driving Pressure during Thoracic Surgery: A Randomized Clinical Trial" which appeared in March's edition of Anesthesiology.[1] In this double-blinded, prospective study, the intraoperative utilization of driving pressure guided ventilation, in which positive end-expiratory pressure (PEEP) was incrementally titrated to achieve the lowest plateau pressure minus PEEP value at 6 ml/kg tidal volume (V_T), reduced the incidence of postoperative pneumonia and acute respiratory distress syndrome following thoracic surgery.[1] Despite the success of this study, a potentially important concept which was not evaluated was the optimization of delivered tidal volume (V_T) during the transition from two-lung to one-lung ventilation. Per the study protocol, subjects from both arms were ventilated with a fixed V_T of 6 ml/kg, throughout all stages of the procedure. As the authors mention, a 6 ml/kg predicted body weight V_T target is central to intensive care unit lung-protective ventilation, but the supporting data and practice itself may not be extrapolatable to one-lung ventilation. It is certainly possible that utilization of 6 ml/kg predicted body weight V_T during one-lung ventilation could lead to more volutrauma and barotrauma than it would during two-lung ventilation.

Currently there is only sparse literature to guide ventilation, and particularly V_T, during one-lung ventilation. Maret *et al.* found that utilization of V_T of 5 ml/kg ideal body weight and 5 to 8 cm H_2O of PEEP during one-lung ventilation compared to 10 ml/kg without PEEP resulted in reductions in major postthoracic surgical complications (pneumonia, acute lung injury, acute respiratory distress syndrome, pulmonary embolism, shock, myocardial infarction, or death) and hospital length of stay.[2] Similarly, a retrospective study of pneumonectomy patients identified an increasing incidence of postoperative respiratory failure with each 1 ml/kg predicted body weight increase in V_T.[3] At this time, it is unclear if the outcome benefits of minimization of driving pressure during thoracic surgery would increase, decrease, or remain the same if smaller V_T targets were incorporated into the ventilation strategy. For example, targeting a V_T of 3 to 4 ml/kg predicted body weight during one-lung ventilation, representing a 50% reduction of V_T goals from two-lung ventilation, would be an intuitive approach to maintaining lung-protective ventilation throughout thoracic procedures, but this range has not been studied and could result in undesirable increases in driving pressure as respiratory rate is increased and inspiratory time is decreased to maintain adequate minute ventilation. Further research is needed to determine the optimal V_T for one-lung ventilation, with a focus on patient-oriented perioperative outcomes.

Nonetheless, the study group should be applauded for contributing to the growing body of evidence-based medicine which supports utilization of intensive care unit–based lung-protective ventilation strategies in the operating room, and their results certainly support the utilization of driving-pressure guided ventilation during thoracic surgery.

Competing Interests

The author declares no competing interests.

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To the Editor:

I read with interest the randomized clinical trial by Park *et al.*[1] on the novel approach of using driving pressure–guided

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ventilation during one-lung ventilation as a method to reduce postoperative pulmonary complications in comparison to conventional protective ventilation. There are several significant limitations to the study that impact interpretation of the results and conclusions. First, the inclusion of lung resection and esophagectomy patients in assessing the effects of driving pressure manipulations on combined pulmonary outcomes is the most important limitation of this study. In comparison to lung resections, esophagectomies are different in that preoperative chemoradiation is standard, the operation typically involves an abdominal and/or neck incision in addition to the thoracic approach, intraoperative ventilation includes a significant period of two-lung ventilation, and there are greater fluid requirements, as well as higher risks of aspiration and greater postoperative morbidity and mortality.[2,3] The Society of Thoracic Surgeons (Chicago, Illinois) maintains two separate databases for these operations. For example, the reported incidence of pneumonia within 30 days of lung resection is 4.8% (1,116 of 27,844)[2] and 12.2% (529 of 4,321)[3] after esophagectomy. Similar to the authors' efforts to focus on the effects of intraoperative ventilatory parameters during one-lung ventilation on the combined incidence of postoperative pneumonia and/or acute respiratory distress syndrome (ARDS), we reported an overall incidence of 4.0% (24 of 608) following anatomic lung resection.[4] It would be more informative if the authors could share their outcome data by the type of surgery and not combined as presented even if the results were negative.

Second, in the third paragraph of the results and in figure 2, a chi-square test was incorrectly used for analyzing the incidence of ARDS between the driving pressure group and protective ventilation group (0 of 145 *vs.* 5 of 147; $P = 0.025$) where it would have been more appropriate to use the Fisher exact test of this result which would yield a nonsignificant $P = 0.060$ value. Third, the authors discuss the importance of finding a median difference of 1 cm H_2O lower in the driving pressure group *versus* the protective ventilation group as being associated with a lower incidence of pulmonary complications (fig. 2),[1] however, with the exception of the incidence of ARDS which was not statistically significant (as mentioned previously), pneumonia occurred more frequently in the operated (nonventilated) lung compared to that of the ventilated lung in either group, theoretically protected by a lower driving pressure. Finally, although the two patient groups were well matched with respect to preoperative baseline characteristics, it would be interesting to know, regardless of group assignment, whether major pulmonary complications after lung resection only were associated with proven and independent negative prognostic factors[5,6] such as reduced preoperative diffusion capacity of carbon monoxide, preoperative chemotherapy, and increasing intraoperative fluid administration.

Competing Interests

The author declares no competing interests.

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Driving Pressure–guided Ventilation: Reply

In Reply:

We thank Dr. Fierro for his emphasis on tidal volume reduction in response to our recent article "Driving Pressure during Thoracic Surgery: A Randomized Clinical Trial."[1] The definition of driving pressure is: plateau pressure − positive end expiratory pressure. Another formula of driving pressure is: tidal volume / static lung compliance. Therefore, reduction of tidal volume can also reduce driving pressure. However, the key point is that reduction of tidal volume can

increase driving pressure if it deceases lung compliance (as in atelectasis), or increased tidal volume can decrease driving pressure if it increases lung compliance (as in recruitment). Therefore, reduction of tidal volume would decrease driving pressure until it reaches to the point where lung compliance starts to decrease. No study ever tested tidal volume in terms of driving pressure and it would be another interesting study subject. We think optimal tidal volume would be different in each individual if it is based on the lowest driving pressure.

We thank Dr. Amar for his careful review of our study.[1] As he said, lung resection and esophagectomy are two different surgeries. However, our hospital has many esophageal cancer surgeries (more than 300 cases per year). All included patients underwent the Ivor Lewis operation which usually takes only 4 to 5 h. All patients had no preoperative adjuvant chemoradio therapy. We only studied complications until postoperative day 3, thus a lot of delayed complications (graft failure, aspiration pneumonia, among others) were not included. For this reason, we did not see inclusion of esophageal cancer surgery as a problem. The number of esophageal surgeries was small (control group n = 12 *vs.* driving pressure group n = 16) and the incidence of pulmonary complications diagnosed by Melbourne Group Scale was control group n = 3 and driving pressure group n = 4. Dr. Amar's other concern was the use of statistics. As he said, it is correct to use the Fisher exact test when expected frequencies are less than 5. Our concern was that the Fisher exact test runs an exact procedure especially for small-sized samples and is more conservative than the chi-square test. Our institutional statistician advised that acute respiratory distress syndrome (ARDS) is a small part of our primary outcome (pulmonary complications); therefore, showing the incidence itself is enough (ARDS: control group n = 5, driving pressure group n = 0). $P = 0.05$ cut is a consensus, some argue $P = 0.10$, or $P = 0.001$ is meaningful. Our P value by two different statistics was 0.025 *versus* 0.060, and the difference mostly came from small incidence of ARDS. Dr. Amar questioned why pneumonia occurred more frequently in both operated and nonoperated lungs in the control group. We think direct surgical injury and one-lung ventilation are associated with a profound inflammatory cytokine release because of abundant immune cells on the lung endothelium and alveolus.[2] Excessive neutrophils recruited in response to the proinflammatory cytokines increase pulmonary vascular permeability in both dependent and nondependent lungs.[3] These reactions often precede systemic inflammatory response syndrome, ARDS, and pneumonia.[4–6]

Competing Interests

The authors report no conflicts of interest.

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Extracorporeal Membrane Oxygenation 1-yr Outcome: Comment

To the Editor:

Current trials published in medical literature, and especially the critical care literature, measure similar primary endpoints, namely, mortality. This measure is often an appropriate way of examining the effectiveness of some of our most novel and innovative treatments. Many trials also measure a number of other secondary endpoints, including time free from a ventilator or time spent in the hospital. But often these trials do not describe a patient's neurologic status or functional status after these interventions. Treatments for medical conditions once thought nonsurvivable have advanced rapidly in recent years. Patients can be kept alive in the face of complete failure of multiple organs, often for