Editorial

Protective ventilation for lung cancer surgery, the truth likely lies somewhere in the middle

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Comment on: Marret E, Cinotti R, Berard L, *et al.* Protective ventilation during anaesthesia reduces major postoperative complications after lung cancer surgery: A double-blind randomised controlled trial. Eur J Anaesthesiol 2018;35:727-35.

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Pulmonary complications are the most frequently occurring morbidity following pulmonary resection (1). It is no wonder then, that thoracic surgeons have constantly searched for ways to reduce this number. The use of lung protective strategies with low tidal volume ventilation has been shown to reduce mortality in intensive care unit (ICU) patients with acute respiratory distress syndrome (ARDS) (2). Whether or not these strategies also provide benefit for patients undergoing single lung ventilation during lung cancer surgery is the focus of the randomized trial presented by Marret *et al.* (3).

In their article, Marret *et al.* (3) report the results of a double-blind multi-center randomized trial of 346 patients undergoing surgery of lung cancer; randomizing patients to lung protective ventilation (LPV) group (tidal volume of 5 mL/kg and PEEP 5–8 cmH_2O) or control group (tidal volume of 10 mL/kg and no PEEP). The authors found that LPV resulted in significantly lower rates of major complications (13.4% *vs.* 22.2%, P=0.03); with major pulmonary complications reduced by almost half (11.6% *vs.* 21.1%, P=0.02). Length of hospital stay was also less for the LPV group (median 11 *vs.* 12 days P=0.048); however, ICU days and mortality were not different. Randomized trials are the highest level of evidence available to guide clinical practice, much time and effort is needed to implement such important trials and the authors are to be congratulated on the publication of their study. With these results presented by Marret *et al.* (3), it would seem that LPV during lung cancer surgery is clearly the superior strategy; however, prior to accepting this strategy as the "standard of care", one must carefully examine the limitations of this study and also examine the studies reported by others in the literature regarding this topic.

The study by Marret *et al.* (3) has a few methodological problems. First, the trial was designed to enroll 900 patients to achieve appropriate power, but the investigators closed the trial early without an interim analysis, citing that recruitment goals were "unattainable". Second, reported complications were not graded. Since the study's primary outcome was major complications, it becomes important to grade these complications so that "apples can be compared to apples" rather than to "oranges". Grading complications with a validated system, such as the Thoracic Clavien-Dindo classification (4), allows for a more meaningful comparison between the study groups. Third, data regarding important factors that can affect outcomes are not reported. Readers would be interested to know if the two groups were balanced in terms of carbon monoxide diffusing capacity (DLCO), handling of lymph nodes (dissection versus sampling), radiation received, clinical stage, minimally invasive approach, and pain scores; as all of these factors can affect the rates of complications.

When examining the results of this study by Marret *et al.* (3), several peculiar findings are noted, for which explanations are not provided. The pneumonectomy rate was unusually high at 18%, as compared to the 4%

pneumonectomy rate reported from the STS database (1). Despite the requirement for the LPV group to receive positive end-expiratory pressure (PEEP) of 5–8 cmH_2O, the mean PEEP at baseline and during single lung ventilation in this group was under 5 cmH_2O. The median length of hospital stays, although significantly less for the LPV group versus the control group (11 *vs.* 12 days respectively), was unusually long for today's standards. Finally, and most interestingly, the death rate was almost three-fold higher in the LPV group as compared with the control group (3.3% *vs.* 1.2%, P=0.28), although this difference was not significant.

With regards to the published literature, Serpa Neto *et al.* (5) performed a meta-analysis of randomized trials comparing low versus high tidal volume ventilation during surgery, combining general, cardiac, thoracic and spine procedures. Much like the study by Marret *et al.* (3), the authors found that the use low tidal volume resulted in less postoperative pulmonary complications but there was no difference in ICU days, length of hospital stay or mortality (5). When examining randomized trials that specifically focus on single lung ventilation during thoracic surgery, it is interesting to note that all trials found no difference in complications, length of hospital stay, ICU days or mortality when comparing LPV strategy with low tidal volume versus higher tidal volume ventilation (6-10).

At the end of the day, what can we conclude with regards to the optimal ventilation strategy for single lung ventilation? Based on the improved mortality shown by the ARDS Network trial (2), it is easy assume that the benefits of protective lung ventilation seen in ARDS patients should also translate to elective thoracic surgical patients; however, as discussed above, improvement in mortality has yet to be clearly demonstrated in this latter patient population. Unlike patients with ARDS, the lungs of a patient undergoing elective pulmonary resection are more compliant and higher tidal volumes can be delivered with relatively small increases in airway pressures, even during single lung ventilation. The results reported by Marret *et al.* (3) illustrate this point; the recorded peak and plateau pressures at baseline and during single lung ventilation differed by less than 5 cmH_2O between the two study groups. For patients with ARDS, it seems that ventilation with high airway pressure is the major factor associated with adverse outcomes rather than the tidal volume delivered (11,12). In a meta-analysis of randomized ARDS trails, Petrucci and Iacovelli (11) found that the clinical outcome of high tidal volume ventilation was not different than that of low tidal volume ventilation when plateau pressure was maintained at 31 cmH_2O or less. In this study by Marret *et al.* (3), only 13 (7.6%) patients in the control group experienced plateau pressures over 30 cmH_2O, appropriately necessitating a decrease in tidal volume per trial protocol. Finally, it is also important to point out the potential complications of low tidal volume ventilation, such as the adverse effects of hypercarbia (arrhythmia, pulmonary hypertension, intracranial hypertension, and depressed renal blood flow), atelectasis, and higher oxygen requirement (9).

The optimal ventilation strategy during single lung ventilation is currently not known. Intuitively, high tidal volume that results in high airway pressure is undesirable. Conversely, it may be appropriate to avoid low tidal volume ventilation in patients with a history of arrhythmia, pulmonary hypertension, intracranial hypertension, or renal insufficiency as these conditions can be aggravated by hypercarbia. The selection of tidal volume during thoracic surgery should be individualized to achieve desired airway pressure, oxygenation, CO_2 elimination, and surgical conditions. Higher tidal volume can be safely delivered as long as plateau airway pressure is closely monitored and maintained at less than 30 cmH_2O.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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