

Protective Ventilation during Anesthesia: Too Soon for Final Recommendations

To the Editor:

We read with interest the review by Güldner *et al.*¹ on intraoperative protective ventilation. The authors provide an excellent and thorough summary of the mechanisms of ventilation-induced lung injury and the role of lung-protective ventilation. They further review several interventions such as low tidal volumes, positive end-expiratory pressure (PEEP), and lung recruitment maneuvers (RM) and analyze their respective contribution to reducing stress and inflammation of lung tissue. For this purpose, they provide up-to-date information on the clinical trials aimed at optimizing intraoperative mechanical ventilation since the year 2000. In general, and despite unavoidable limitations of such trials, most of these studies support active lung protection during general anesthesia.

However, we are critical of the authors' recommendations as to how to implement such intraoperative lung-protective ventilation strategies. We believe that the recommendations by the team of these well-published authors are too strongly skewed toward the results of the recently published PROVHILO study,² which many of the current contributors coauthored. It appears that ample clinical and experimental results in conflict with their own findings are either neglected or unduly overridden. While addressing a highly relevant hypothesis, this study comparing a high with a low PEEP strategy for intraoperative mechanical ventilation suffers from several drawbacks related to the protocol design and therefore fails to provide an appropriate answer to the primary study questions. First, the RM applying 30 to 35 cm H₂O of inspiratory pressure for three consecutive breaths only must be considered ineffective as it remains below both the known effective recruitment pressures and the minimal duration required for these inspiratory pressures to recruit the collapsed lungs of most patients under general anesthesia.^{3,4} This implies that many lungs never reached the desired recruited state, which in this study was unfortunately not confirmed by appropriate diagnostic means such as oxygenation or lung ultrasound.^{4,5} Indeed, the modest increase in compliance by 9 to 11 ml/cm H₂O observed in the high PEEP group can easily be explained by a redistribution of ventilation toward hypoventilated areas and not by an effective recruitment of anesthesia-induced atelectasis. The comparable incidence of postoperative atelectasis in the high and the low PEEP groups (12%) further supports the suspicion of a lack of lung recruitment in the PEEP group. Second, the level of PEEP after the RM was not individualized. The rationale of choosing one single arbitrary level of 12 cm H₂O

clearly contradicts the authors' explicit opinion stating that "certainly the level of PEEP should be chosen according to the patient's particular characteristics." In this context, it is remarkable that up to this day no study has evaluated the effects of such an individualized PEEP. We believe that this is essential since an unnecessarily high level of PEEP—such as 12 cm H₂O in healthy lungs—could certainly foster many of its known side effects such as hypotension or the need for vasoactive support (as also reported by the PROVHILO investigators) rather than its equally known beneficial effects. Another important confounder of this study is the liberal use of fluids in amounts remarkably larger than current standards recommend.⁶ This fluid overload may account for the overall high incidence of postoperative pulmonary and nonpulmonary complications (40 and 50%, respectively), which are remarkably higher than could be expected for patients of the respective risk category.⁷

We believe that the above bias asks for caution when recommending a ventilation strategy based on low tidal volumes and low or next to no PEEP while discouraging the use of lung recruitment before sufficient evidence warrants such recommendations. The therapeutic advice given by Güldner *et al.* would in fact result in a higher mortality—a harder endpoint than merely the postoperative complications—if the recent evidence from a large series of almost 30,000 patients were taken into account.⁸ Finally, the authors also recommend that future studies should test single interventions in order to be able to extract relevant information for clinical practice more easily. If such single intervention were PEEP, we believe it is time to abandon the useless high *versus* low PEEP debate as there is now enough evidence demonstrating the shortcomings of such a sterile design. It is about time to evaluate the effects of an individualized level of PEEP adjusted to pathophysiologically meaningful endpoints either in conjunction with or without lung RMs under low tidal volume ventilation.

Competing Interests

The authors declare no competing interests.

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In Reply:

We thank Dr. Tusman *et al.* for their interest in our review on intraoperative protective ventilation.¹ They claim that our recommendations neglected experimental and clinical evidence that disagree with the results of the recently published High versus Low Positive End-expiratory Pressure during General Anaesthesia for Open Abdominal Surgery (PROVHILO) study.² Although inappropriate for drawing clinical recommendations, experimental studies provide the physiologic pillars of interventions. Therefore, our review article included a thorough appraisal of the mechanisms of ventilator-induced lung injury and possible strategies to prevent injury. Clinical recommendations must rely on clinical investigations, especially randomized controlled trials. Accordingly, we conducted a literature search and identified a few randomized controlled trials, which were ultimately meta-analyzed. Different from what Dr. Tusman *et al.* assert, selection was objective and unbiased. With 900 patients included in the study, the international, multicenter PROVHILO study² is the largest randomized controlled trial in this field, and the meta-analysis was obviously influenced by this study's results.

When criticizing the recruitment maneuver used in PROVHILO study,² Dr. Tusman *et al.* overlooked some basic mechanisms of recruitment and misunderstood the type of maneuver we applied. In the lungs, reopening of atelectatic tissue mimics avalanches, with different regions opening at distinct pressures and times.³ Furthermore, histologic analysis shows that approximately 5 s is enough to obtain recruitment once a particular opening pressure is exceeded.⁴ In PROVHILO study,² the recruitment maneuver was based on a stepwise increase of tidal volumes at a positive end-expiratory pressure (PEEP) of 12 cm H₂O. The time spent at

different inspiratory pressures, including levels above 30 cm H₂O, was approximately 15 s at each pressure. Thus, comparison with a maneuver based on the sustained inflation with PEEP of 0 cm H₂O⁵ is misleading. In addition, the comparative increase in compliance was 33% on average, which in noninjured lungs ventilated with low tidal volume is more than modest and hardly explained by redistribution of ventilation without opening of atelectatic areas. We decisively disagree that the occurrence of postoperative atelectasis in PROVHILO study² indicates inappropriate intraoperative lung recruitment. Pain, partial immobilization, and limited ability to cough, among many other postoperative factors, likely explain that finding and are obviously not related to intraoperative recruitment maneuvers.

We are aware that intraoperative fluid loading could be harmful in patients undergoing surgery. Accordingly, the PROVHILO protocol recommended “to avoid fluid overload (according to the discretion of the attending anesthesiologist).” When judging this aspect, one must take the whole picture into account and consider that patients in the study underwent major open abdominal surgery, with significant blood loss and intravascular volume shifts.² Therefore, and in contrast to the statement of Dr. Tusman *et al.*, the incidence of postoperative pulmonary complications was as high as predicted in the risk category,⁶ whereas the risk of nonpulmonary complications was not assessed.

Dr. Tusman *et al.* also overlooked the fact that our recommendations targeted nonobese patients undergoing open abdominal surgery only.¹ In the publication that questioned our recommendations, other types of patients and surgical procedures were included.⁷ Furthermore, despite its impressive number of records, that single-center, retrospective study⁷ did not directly evaluate the role of PEEP on mortality.

Future randomized controlled trials will show whether high PEEP level, individually titrated or not, with or without recruitment maneuvers, is superior to low PEEP level in terms of clinical outcome in other types of patients and surgical procedures. The current discussion reminds us of the debate about the studies that failed to demonstrate the usefulness of recruitment maneuvers in patients suffering from acute respiratory distress syndrome. For many years, “inappropriate maneuvers,” “nonindividualized PEEP levels,” “unsuitable therapy windows,” “meaningless endpoints,” and “inappropriate patient selection” were believed to be responsible for the lack of effect of recruitment maneuvers on clinically relevant endpoints. Enchanted by aseptic lung injury models that reproduced some but not all relevant aspects of the complex clinical scenario, passionate researchers have insisted on their own beliefs, denied clinical evidence, and put patients at risk.

For our group, stating that future studies might lead to adjustments in recommendations is not paradoxical but rather reflects our principle of being open to evidence from