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In Reply:

We thank Dr. Priebe for his interest in our review on intraoperative mechanical ventilation.

Dr. Priebe gives examples of patient's characteristics (obese), types of surgery (peripheral), and positioning for surgery (Trendelenburg) to question our recommendations for intraoperative mechanical ventilation. In fact, our review article clearly states that the recommendations do not apply to those conditions, but rather to nonobese patients with moderate to high risk for postoperative pulmonary complications (PPCs) undergoing open abdominal surgery.[1]

The increase of F_{IO_2} as a first-line measure to treat intraoperative hypoxemia was criticized and the use of lung recruitment suggested instead. Recruitment maneuvers (RMs), when used isolated, are short lasting, and stabilization of the lung volume recruited depends on the use of positive end-expiratory pressure (PEEP).[2] Unfortunately, however, those measures may have relevant side effects. Impairment of hemodynamics is likely the most common one,[3] but RMs have also the potential to injure the lung parenchyma.[4] When classifying the increase of F_{IO_2} as symptomatic treatment and opening of atelectasis as causal therapy, one should ask a simple question: what for? The answer from our systematic review of the literature and meta-analysis is that the "causal therapy" is merely cosmetics in nonobese patients undergoing open abdominal surgery because it does not contribute to the reduction of PPCs. Thus, applying measures that put patients at risk for no benefit in outcome cannot be recommended. The physiologic rationale of lung recruitment and PEEP only deserves the adjective "rational" if accompanied by a clinical benefit or at least no harm.

The fact that our recommendations[1] reflect some of the major findings of the High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO) trial[5] is not due to mutual coauthorship but rather resulted from the systematic review and meta-analysis in our article.[1] Because PROVHILO[5] represented the trial with the largest number of patients, its results much influenced the recommendations. The possible study limitations mentioned by Dr. Priebe, namely protocol deviations, presumed insufficient frequency of RMs, and abrupt withdrawal of high PEEP during emergence from anesthesia, have been already addressed in the replies to the Editorial and correspondence in *The Lancet*.[6] Without exception, they proved to be unfounded. Due to space constraints, we cannot reproduce the replies here but strongly recommend interested colleagues to read them. The claim that the incidence of PPCs was "unusually high" (approximately 40% in both the high and low PEEP groups) in PROVHILO[5] is factually incorrect. PPCs rates corresponded to the incidence as predicted by a risk score.

Dr. Priebe suggests that intraoperative hypotension was as common in the higher as in the lower PEEP group of PROVHILO,[5] which is not accurate. Differences in the frequency of hypotension episodes were clinically and statistically more significant in the high PEEP group of PROVHILO.[5] Also, we do not see the sense of recommending RMs outside of what is common clinical routine for open abdominal surgery, namely combined general and thoracic epidural anesthesia.

A thorough description of maneuvers for rescue due to hypoxemia was beyond the scope of our review article.[1] In the PROVHILO trial,[5] intraoperative hypoxemia occurred in 34 of 449 patients in the low PEEP group and could be reverted by increasing the F_{IO_2} up to 0.6 and PEEP up to 5 cm H_2O in 23 patients. A RM was necessary in only one patient, *i.e.*, ≈ 0.2% of the low PEEP group. These numbers guided the recommended approach for hypoxemia in our review article[1] and reflects the fact that a F_{IO_2} up to 0.8 is not associated with an increase in the amount of postoperative atelectasis or a deterioration of postoperative lung function.[7]

The representation of atelectasis in Figure 3 of our review[1] is of conceptual nature, and its size should not be overemphasized. Amounts of atelectatic and overdistended tissue in that figure are not based on measurements and are intended to illustrate different methods of protective ventilation. We introduced the concept of "permissive intraoperative atelectasis" based on our own meta-analysis from randomized controlled trials, *i.e.*, sound evidence. Accordingly, the fear that other possible complications might outweigh the benefits of low PEEP is unfounded in nonobese patients undergoing open abdominal surgery.

The recent individual patient data meta-analysis mentioned by Dr. Priebe, which has been conducted by our own group, showed that low tidal volumes, but not PEEP, were associated with improved outcome in different types of surgery. In contrast to what the letter claims, moderate to high PEEP (*i.e.*, > 5 cm H_2O) combined with low tidal volume was not associated with decreased incidence of PPCs (adjusted relative risk, 0.93 [95% CI, 0.64 to 1.37], $P = 0.720$).[8] In fact, there was a trend toward higher incidence of PPC in patients ventilated with PEEP between 6 and 8 cm H_2O (adjusted relative risk, 2.08 [95% CI, 0.98 to 4.41], $P = 0.057$).

Comparisons of the PROVHILO[5] and the Intraoperative Protective Ventilation (IMPROVE) trials[9] must be conducted carefully. The IMPROVE trial[9] is unique in that it showed the way we ventilate patients during surgery can have major impact on outcome. In that study, protective and nonprotective ventilation bundles of measures were used. Bundles differed with respect to both tidal volume and PEEP. Although such design revealed a difference between bundles with respect to outcome, it precluded identifying the respective roles of low tidal volume and PEEP with RMs on lung protection. In the PROVHILO trial,[5] the tidal volume was low in both groups, and the effects of PEEP could be addressed. Furthermore, we do not know whether patients in the PROVHILO[5] and IMPROVE[9] trials were comparable in terms of risk of developing PPCs. Also, it must be kept in mind that the average duration of surgery in the IMPROVE[9] and PROVHILO trials[5] differed considerably (≈ 5 and ≈ 3 h, respectively), which makes the comparisons between patient populations difficult. Therefore, data from those trials are not contradictory, but rather complementary. Dr. Priebe states "It is confusing and unsatisfactory for the practitioner to be confronted with recommendations published in the same journal within the same year contradicting each other in central aspects of ventilatory care (*i.e.*, application of PEEP, performance of RMs)." We understand that conflicting opinions may sound frustrating, but they are natural consequences of evolving science, where new information is permanently generated.

Dr. Priebe pleads for a highly individualized setting of PEEP, as well as level of RMs and their frequency, and questions the value of randomized controlled trials in this field. When designing such trials, stratification of patients by their major characteristics, including body mass index and age, risk to develop pulmonary complications, and the type of surgery, represent measures of homogenization of conditions presumed to be responsive to the intervention being investigated. Also, the levels of PEEP and RMs are carefully chosen according to available evidence. Therefore, when a positive effect of a given intervention cannot be demonstrated under the conditions in which it is expected and needed to work, time has come to question whether the physiologic rationale behind the intervention has taken all factors influencing results into account.

The letter title "one size does not fit all" is doubtless attractive, but we are afraid it might also be dangerous. When used uncritically, "one size does not fit all" may result in an extreme behavior that we call "the Cinderella complex." In the fairy tale by the brothers Grimm, the Prince could find Cinderella, because the crystal shoe left behind fitted only her foot. We believe that such a beautiful story should not be transported to our approach to intraoperative PEEP and RMs. Clinical evidence has demonstrated that, in contrast to the Prince, our search for the perfect combination of all factors will not have a happy end.

Competing Interests

The authors declare no competing interests.

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