Author’s response to reviews

Title: Application of intraoperative lung-protective ventilation varies in accordance with the knowledge of anaesthesiologists: A single-centre questionnaire study and a retrospective observational study

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Prof. Guangde Tu
Editor in chief
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Dear Prof. Guangde Tu:

Thank you for inviting us to revise our manuscript titled ‘Application of intraoperative lung protective ventilation varied in accordance with the knowledge of anesthesiologists: a single-center questionnaire study and retrospective observational study’ (BANE-D-17-00336).

We greatly appreciate your review of our work and the constructive comments suggested by the reviewers. Our point-by-point responses to the comments raised by the reviewers are listed below. We also revised the manuscript and highlighted the revisions in red.

We hope that our manuscript has been improved through this revision and is now suitable to be considered for publication in BMC Anesthesiology. We look forward to hearing from you.

Sincerely,

Jeongmin Kim
Reviewer reports

Stefan Schumann (Reviewer 1): In their manuscript, Seung et al. describe the combination of a questionnaire and a retrospective study. Although this is unusual, it appears interesting in the given context.

However, I have several comments and suggestions for the manuscript.

Answer: We greatly appreciate your review of our work and the constructive comments. Our responses to your comments are listed below. The manuscript was revised according to your suggestions and the changed parts are highlighted in red. Thank you.

It appears unclear which part of the results are related to the questionnaire and which to the retrospective study. I was not aware that the questionnaire included questions on how the participants would set ventilation in specific conditions as it became obvious when the discussion referred to an 'obesity patient in our questionnaire' and a 'patient in non-laparoscopic surgery in our questionnaire'. This must be clarified in the Methods section and clearly separated in the description of the results.

In this context, please show the questionnaire. It would be relevant for the reader to see the questions and the respective options.

Answer: We apologize for the ambiguous description of the results. The results are divided into two sections: a questionnaire survey and a retrospective study. We also apologize for not commenting on the questionnaire in the manuscript. We have now added the questionnaire as an appendix. The manuscript was revised according to your suggestions and the changed parts are highlighted in red.

The questionnaire consisted of 6 questions (Appendix). The first 3 questions were about the ventilator settings (tidal volume and PEEP) that should be used in certain situations. Question 1, 2, and 3 asked about ventilator settings in laparoscopic surgery, in non-laparoscopic surgery, and in obese patients, respectively.

Abstract
Line 45: It might be helpful for the reader if the correct choice (body height) would be stated within the abstract.

Answer: The manuscript was revised according to your suggestions and the changed parts are highlighted in red.

Anesthesiologists who were able to answer a question related to LPV correctly (respondents who chose 'height' to a multiple choice question asking what variables should be considered most important in the initial setting of tidal volume) applied a lower tidal volume in cases of laparoscopic surgery and obese patients.

Background

Line 17: I would like to suggest to state that however, so far there is no generally accepted strategy for setting appropriate PEEP.

Answer: The manuscript has been revised and references have been included, according to your suggestions, and the changed parts are highlighted in red.

Although the level of PEEP that balances alveolar recruitment against over-distension should be selected and titrated for individual patients [4-7], currently, LPV with low VT (6 mL/kg of ideal body weight [IBW]), limited plateau pressure (< 28–30 cm H2O), and appropriate PEEP is generally accepted for ventilation in patients with ARDS.

Methods

Page 4, Line 33: 'Also, respondents…' Please clarify that respondents who chose the wrong answer but replied "Yes" were considered as having knowledge on LPV. Furthermore, please state, how respondents were classified if they answered correctly 'height' to the first(?) question but declared not to know about the concept of LPV.

Answer: According to your suggestions, we have clearly stated that the respondents’ classification according to the answer to the 2 questions is distinct. We also attached a reference to why ‘height’ is the correct answer, and added an explanation thereof in the Discussion.

Because knowing the approximate meaning is different from knowing the exact definition, we assumed that their answers about LPV may differ from their actual knowledge. Therefore, in the subsequent questions, we divided the respondents according to 2 criteria. Question 5 was a multiple-choice question asking what variables respondents consider most important in the initial setting of mechanical ventilation. From the LPV strategy perspective, the correct answer to this question is ‘height’ [22-24]; respondents who answered ‘height’ were classified as the ‘correct answer group’, and those who selected other answers were classified as the ‘incorrect answer group’. This classification was made irrespective of the response to question 6, which directly asked the respondents whether they knew about the LPV strategy. Respondents who replied
‘Yes’ to this question were considered as having knowledge of the concept of LPV, regardless of their answer to question 5, and were classified as the ‘conceptual group’, while respondents who answered ‘no’ were classified as the ‘non-conceptual group’.

Because VT in LPV is based on IBW [22-24], and IBW is determined by sex and height, respondents who chose ‘height’ to question 5 (a multiple-choice question) could be considered to understand the concept of IBW.

Definition of obesity-group is not stated.

Answer: In the questionnaire survey, the obesity group corresponds to question 3, and in the retrospective study, patients with a BMI > 30 kg/m2 were defined as obese patients. A reference is also attached. (Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organization technical report series 1995, 854:1-452)

The questionnaire consisted of 6 questions (Appendix). The first 3 questions were about the ventilator settings (tidal volume and PEEP) that should be used in certain situations. Questions 1, 2, and 3 asked about ventilator settings in laparoscopic surgery, in non-laparoscopic surgery, and in obese patients, respectively.

The ‘obese patient’ in our questionnaire was an extremely obese patient with a BMI of 41.52, and the correct answer group applied a relatively low VT, even in this patient.

Please describe in detail the propensity score matching procedure

Answer: As per your comment, we have added the propensity-score matching in the Methods section.

Ventilator settings, such as VT and PEEP, are determined on the basis of the height, weight, age, and sex of the patient [28]. Since our pre-analysis noted that there were significant differences in the height and sex between the 2004 and 2014 groups, a propensity score (PS)-matching technique was adopted to diminish the compounding effects of height and sex. The calculation of the PS involved the following: (1) using a logit model for matching the variables (height and sex) by considering the 2014 group as the treatment group and (2) predicting probabilities, termed PSs. PS-matching was implemented to pair the 2004 group with the 2014 group within a caliper of 0.01. There were no significant differences in height and sex between the 2004 and 2014 groups after completing PS-matching. In total, 818 matched patients in each group were used in the final analysis (Figure 1).

Please state how ‘Usage of PEEP’ was defined. Was it PEEP >0? Please provide data on the level of PEEP that was set.

Answer: In the questionnaire, respondents were asked to answer ‘yes’ or ‘no’ to whether PEEP was applied, and to define specific PEEP values when answering ‘yes’. Thus, ‘usage of PEEP’ indicates a PEEP > 0; we have added PEEP data with median (interquartile range) in Results and Tables 1 and 2.
In the retrospective study, PEEP ≥ 5 cmH2O was defined as ‘usage of PEEP’. It was described in the Methods and a related reference was included. We also added PEEP data with median (interquartile range) in the Results.

Results

The authors mix labelings for the investigated group. Sometimes they use 'conceptual'- and 'non-conceptual'-, sometimes 'correct answer'- and 'incorrect answer'-group, sometimes 'Anesthesiologists with knowledge' and 'Anesthesiologists without knowledge'. Please standardize.

Answer: We apologize for the confusion with the non-standardized terms. According to your suggestions, the results of questionnaire survey were divided into “Difference between the conceptual group and the non-conceptual group” and “Difference between the correct answer group and the incorrect answer group.” We also added PEEP results that were missing in the “Difference between the correct answer group and the incorrect answer group” section.

Page 7. Line 32 and Line 41: 'The two groups also differed' and 'There was a statistical significant difference…'. It would be helpful for the reader to state which value was larger or smaller for a certain group instead of stating that there was a statistically significant difference.

Answer: The manuscript was revised according to your suggestions and the changed parts are highlighted in red.

The percentage of respondents who applied PEEP in laparoscopic surgery was also higher in the conceptual group than in the non-conceptual group…

The conceptual group used PEEP more often than the non-conceptual group…

Page 9. Line 23: 'Figure 2 presents …' Please omit describing what a figure/ table shows, rather state the finding and substantiate it with the figure.

Answer: We explained the results in detail according to your suggestions.

In both 2004 and 2014, there was a significant correlation between VT and IBW (p < 0.01), with a stronger correlation in 2014 (R2: 0.49 vs. 0.37; Figure 2).

Page 9 lines 42 to 45: Please specify in the text how Vt was related to the factors

Answer: We apologize for the confusion. The manuscript was revised according to your suggestions and the changed parts are highlighted in red.

Upon regression analysis, in both 2004 and 2014, height, weight, and male sex were the risk factors that increased the VT. The prone position was not associated with VT. In contrast, laparoscopic surgery was the factor associated with a decrease in VT, as compared to non-laparoscopic surgery, in 2004; however, this factor did not affect VT in 2014 (Table 4).
Discussion

Page 11 Line 53: 'Obesity patient…' I could not get this sentence in context to the study. Please clarify what the 'Obesity patient in our questionnaire' is. Page 12 Line 5: Please clarify what the 'patient in non-laparoscopic surgery in our questionnaire' is.

It is not declared in the Methods section nor apparent from the Results section that the questionnaire included questions on how one would set ventilation.

Answer: We apologize for the confusion. The description of the questionnaire, the intent of each question, and the respondents' classification according to the questionnaire answer are explained in the Methods, and the details are given in the Appendix. The Results were written accordingly.

The first 3 questions were about the ventilator settings (tidal volume and PEEP) that should be used in certain situations. Questions 1, 2, and 3 asked about ventilator settings in laparoscopic surgery, in non-laparoscopic surgery, and in obese patients, respectively.

In addition to this, to clarify the meaning, “in cases of laparoscopic surgery” was added to the sentence on page 13, line 5.

Page 13 lines 47ff: Repetition of values already presented in the Results section redundant and therefore not necessary.

Answer: Thank you for comments, we have revised these sentences as follows.

In the present study, the mean VT/kgIBW among obese patients (BMI > 30 kg/m2) had significantly reduced between 2004 and 2014, while the usage of PEEP in this subgroup had significantly increased.

Minor comments

Page 1 line 25: 'ventilaiton' - please correct

Answer: The spelling was corrected according to your suggestion.

Tables: Asterisk markings are not required if p-values are stated within the Tables.

Answer: Asterisk markings have been omitted according to your suggestion.

Table 1 R^2 values >1 are given, please correct (should probably be 0.477 and 0.621)

Answer: We assume that you mean Table 4, not Table 1. We have corrected the values according to your suggestion.
Rujipat Samransamruajkit (Reviewer 2)

Comments

This is a retrospective study to find the application of intra-operative ventilation done by anesthesiologists as a single study. It involved 73 responders. Although, they had more than ten thousand patients involved during the study period, they were mostly excluded due to missing data.

Overall, It is a good study although there are a lot of limitations to discuss.

As the authors have discussed in the discussion part, given that this is a retrospective review.

Answer: Thank you very much for your review and the constructive comments. Considering the characteristics of the retrospective study, there was a limitation in that it was necessary to exclude incomplete anaesthetic recordings. Although this study has inherent limitations as a retrospective study, we believe it provides further evidence of how the concept of LPV affects clinical practice over a period of 10 years. Our responses to your comments are listed below, the manuscript was revised according to your suggestions, and the changed parts are highlighted in red. We will ask for review again. Thank you.

First, the limitation of actual practice from the questionnaire survey, the answers and actual practice may different. The questionnaires were given to predominantly junior anaesthetists such as residents, fellows, of which most would have trained in the era of lung-protective ventilation but the decision on the patient management would depend on staffs.

Answer: Thank you for your constructive comments. We fully agree with your view that the answers and actual practice may be different, and we have added that view in the limitations section. Additionally, a survey study of various barriers that interfere with LPV application, including knowledge deficit, is attached as a reference. The changed parts are highlighted in red. Nevertheless, we think that it is a meaningful study in that the majority of anesthesiologists who have been in charge of anaesthesia for more than a decade have participated in the survey, and that the responses of anesthesiologists on all levels were used in the analysis. It is also clear that junior anesthesiologists can also set ventilator settings according to their knowledge when performing anaesthesia alone. This questionnaire survey is based on this assumption, and the results of the survey that the cognizance of LPV is related to the adoption of LPV strategy is in line with the result of the retrospective study that adoption of LPV increased significantly over 10 years.

Secondly, the definition of LPV (VT < 10 mL/kgIBW and PEEP ≥ 5 cmH2O) may not apply to other study in LTV - ARDS.

Answer: Thank you for your comments. We fully agree with your view that the definition of LPV (VT < 10 mL/kgIBW and PEEP ≥ 5 cmH2O) may not apply to other studies on LTV–ARDS. However, this definition is based on previous studies in patients without acute lung injury undergoing general anaesthesia. In the meta-analysis (2015) based on randomized
controlled trials, the benefits of low tidal volume ventilation (< 10 mL/kgIBW) in patients without acute lung injury, including a decreased need for postoperative invasive ventilatory support, postoperative pneumonia was reported. (Guay J, Ochroch EA: Intraoperative use of low volume ventilation to decrease postoperative mortality, mechanical ventilation, lengths of stay and lung injury in patients without acute lung injury. The Cochrane Database of Systematic Reviews 2015(12):Cd011151) The manuscript was revised according to your suggestions and the changed parts are highlighted in red.

Secondly, the definition of LPV (VT < 10 mL/kgIBW and PEEP ≥ 5 cmH2O) in our study—although based on previous studies [20, 26, 27] in patients without acute lung injury undergoing general anaesthesia—is arbitrary and differs from the standard ARDS treatment guidelines.

Thirdly, the retrospective study involves many uncontrolled co-factors—including intake fluid, operation time, blood products, and type of surgery and intravenous fluid—which cannot be controlled in this study.

Answer: We agree with your view that this retrospective study involves many co-factors that cannot be controlled. Therefore, we only used the initial ventilator settings for analysis. Your valuable point of view is reflected in the Methods and limitations sections.

Only the initial settings were used for the analysis because there are many uncontrolled factors in such a retrospective study.

Also, the study may benefit to further analyse by category of different level of training and answers that may effect the results.

Answer: Thank you for your constructive comments; we agree with your point of view. However, the sample size is small, and thus it is difficult to perform the analysis according to the training level. We plan to conduct prospective studies based on this study. It would be another meaningful study to observe the change in practice or learning curve before and after the education of first-year residents.

Lastly, the author mentioned that there is no previous study that look at intra-operative mechanical ventilation lung strategy during anesthesia. Actually, there was at least one recent study done by Guldner, A et al that look at intraoperative protective mechanical ventilation for prevention post-operative complications.

Answer: We agree with your point of view that previous studies about intraoperative protective mechanical ventilation already existed and have mentioned this in the Discussion. We still believe that this questionnaire survey is meaningful in that it shows the relationship of cognizance of LPV with adoption of an LPV strategy in general anaesthesia, and we changed the phrase ‘no study’ to ‘few studies’. According to your suggestions, the conclusion was rewritten to emphasize the originality of our study. We appreciate your careful attention and constructive advice.
In summary, in a questionnaire survey, we found that anesthesiologists with cognizance of LPV applied LPV more often during general anaesthesia than those without cognizance of LPV. This finding explains the results of our retrospective study, which demonstrated that adoption of LPV during general anaesthesia increased significantly over a period of 10 years. Further studies assessing the impact of intraoperative LPV on clinical outcome are required, and more research to determine the efficacy of intraoperative LPV education is needed.