Author’s response to reviews

Title: Differential Lung Ventilation for Increased Oxygenation during One Lung Ventilation for Video Assisted Lung Surgery

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Differential Lung Ventilation for Improved Oxygenation during One Lung Ventilation for Video Assisted Lung Surgery

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Reviewer reports:

Reviewer #1: This is a well designed and well written study.

The study findings regarding the utility of low-volume ventilation of the non-dependent lung during on-lung ventilation are clinically relevant.

My only comment is that the axes of the figures need to be labelled appropriately (i.e. "mmHg" etc)

• MB: Changed as suggested (Fig. 1-4)

Reviewer #2: This paper reports a study that compares two methods of preventing hypoxia during lung isolation for VATS surgery and one-lung ventilation that is applying to continuous
positive airway pressure (CPAP) or mechanical ventilation to the surgical lung. The paper has a number of important limitations.

1. The use of improved in the title of ‘improves' is pejorative and insufficiently scientifically objective. Something like ‘increases' would be more appropriate.

- MB: The title is changed

2. An estimate of the study population sample size should have been provided. It is inadequate to justify the population sample size used in the present study simply by reporting a previous study in the area. This is particularly important for the reader to be able to interpret non-significant results such as the surgical exposure when p = 0.073. This marginally non-significant result may caused by Type II error if too few patients were included in the study.

- MB: Sample size calculation is added (page 7 lines 8-10). The main end point was the patient’s oxygenation, and for this goal the group sizing was suitable. The issue of type II error regarding the surgical exposure is added to the Discussion (page 9 lines 13-17).

3. A cross-over study design was used and should have been explicitly stated in the methods section. A cross has strengths and weaknesses. An important weakness is carry-over effects and its influence on interpretation of the findings should have been addressed in the discussion section.

- MB: This issue is added to the Methods (page 5 line 2) and Discussion (page 9 lines 8-13)

4. Multiple statistical tests have been applied to the data greatly inflating the risk of Type I error. A primary outcome was declared in the methods section but the risks of multiple testing in the primary and secondary outcomes should have been controlled using something like Bonferroni's correction.

5. Non-parametric statistics tests were applied without justification. If the distribution was examined then how it was done should have been described. If the data was truly abnormally distributed then the use of non-parametric statistics is justified but their use leads to loss of information. It would have been far better to arithmetically transform the data to near-normal using something like the natural logarithm.

6. Importantly, a more powerful and valid way to have analyse data from a cross-over design would have been to use analysis of variance (ANOVA) and this would have limited the risk of Type I error.

- MB: (answering reviewer’s comments 4-6) This study was designed for 2 groups of patients and 4 modes of ventilation, thus we did not choose ANOVA analysis. Indeed, for some variables, as in any study, large group of subjects may result in more robust results. However, regarding the surgical exposure, in no one of the patients and modes there was grade 3 interference, and lower grades of interference was recorded in 8 patients.
7. Page 5, sentence beginning line 9: one-lung ventilation is not a primary goal in itself but is a consequence of using lung isolation to facilitate surgical access.

- MB: Changed

8. An explanation why the study appears to have been registered after it was undertaken should have provided.

- MB: Added (page 2 line 24)

9. The computerised system used for randomisation should have been described and when and who undertook the randomisation should have been reported.

- MB: Added (page 6 line 11)

10. It is stated that the surgeon was blinded but not how this was undertaken. The way the use of a second ventilator was disguised should have been described. Also, the anaesthetist was not blinded and this limitation should have been discussed in the discussion section.

- MB: The surgeons cannot see the anesthesia machine or the ventilator, since the patient’s sterile covers block their view (page 7 lines 4-5). The issue of the anesthesiologist is added to the Discussion (page 9 lines 16-17)

11. It should have been reported whether positive end expiratory pressure was used on the ventilated lung.

- MB: This is reported (page 6 lines 4-5).

12. This reviewer finds the multiple different terminologies used to described lung isolation in the literature confusing and it is particularly so in the paper. Patients who have lung isolation are not always placed in the lateral decubitus position so dependant and non-dependant are not always accurate descriptions. Something like 'surgical or non-ventilated' and 'ventilated' lung seems a better description and less confusing and should have been used consistently throughout the paper.

- MB: Indeed, sometimes the patient is not in the lateral decubitus position, however, in this study all the patients were place that way (page 6 line 6). We did not choose the “ventilated” and “non-ventilated” since in this study the surgical lung is ventilated occasionally, and that may have been confusing as well.

13. PaO2 has been used as surrogate measure of outcome. Why this was used instead of pulse oximetry should have been explained and if it was measured it would have been useful to report the findings.

- MB: We find the PaO2 to be more accurate than pulse oximetry. Sometimes when the patient is cold the pulse oximetry fail to measure.
14. The figures are poor with no legends to explain the symbols make them extremely difficult to interpret. The PaO2 data should have been described so see the effect of changing technique in both order not just as one overall group to see if there is any carry-over effect.

• MB: The figures are changed as suggested (Fig. 1-4).

15. Differences in PaO2 should have been reported as mean differences and 95% confidence intervals if the data was normally distributed or medians with interquartile ranges to facilitate interpretation of the clinical importance of the findings.

• MB: The differences are in Fig. 1.

16. Just because there are significant difference in PaO2 does not make them clinically important. Reporting the incidences of hypoxia e.g. SpO2 < 85% would have been valuable interpreting the importance of the findings.

• MB: Gladly, we had no event of patient’s hypoxemia. Hypoxemia was one of the criteria to exclude the patient (page 5 lines 9-10) since we rather not put a patient in risk for the completion of this study. Regarding oxygen blood level: we believe that one may deduce the beneficial effect of different ventilation modes without having hypoxemic patient.

17. It is unclear why spirometric findings were collected and there is not explanation provided why they might be affected in the ventilated by the use of CPAP or DLV in the non-ventilated lung. If they add no value to the primary goal of the study then there is not point in reporting them. Similarly, was not explained what the value of reporting pH and bicarbonate was to aim of the study.

• MB: Since the chest is a “closed box”, applying different ventilation mode in one hemithorax may influence on the other (ventilated) hemithorax. This was the reason for spirometry parameters of the ventilated lung (added, page 9 lines 5-7). Regarding the pH and bicarbonate: apart from respiratory acidosis, there may be a metabolic acidosis when one lung is not ventilated. Thus, we believe some of the readers are interested to see whether there are acid base changes during the different stages of ventilation.

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Thank You,

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