Reviewer’s report

Title: Effect of individualized PEEP titration guided by intratidal compliance profile analysis on regional ventilation assessed by electrical impedance tomography – a randomized controlled trial

Version: 2 Date: 10 Jan 2020

Reviewer: Elena Spinelli

Reviewer's report:

I truly appreciated the efforts that the authors put into this revision of the manuscript.

Three major issues were raised by the peer-review:

1) Research question not appropriate/not clearly stated:

In the current version of the manuscript, the authors decided to maintain the intratidal linear compliance as the main endpoint. Respiratory mechanics and regional ventilation were defined secondary endpoints. Of note, the intratidal linear compliance is also the target of intervention, so it might be expected to be different in the two groups by study design. Nevertheless, it did not differ between the two groups. I think that both the methodological issue and the unexpected result are disclosed and discussed in the manuscript.

2) EIT analysis underexploited/not clearly described:

The current version of the manuscript has greatly improved in this respect. The methods and the results of EIT analysis are now clear and quite detailed.

3) Interpretation of results and inconsistent conclusions:

This remain the major drawback of the current version. I think that none of the study endpoint was positive: intratidal linear compliance, respiratory mechanics and regional ventilation did not differ between the two groups. I think that global increase in aeration indicated by the calculations of regional gain and loss and change in tidal volume might just indicate the slight increase in aeration cue to the small PEEP increase in the intervention group. The authors seem to suggest this interpretation in the discussion (page 17), while in other parts of the manuscript (mainly in the conclusions) this result is overemphasized and it is used to support the idea that the intervention (PEEP titration according to the intratidal compliance profile) was effective. For example:

- Page 2: "Individualized PEEP titration according to bedside compliance profile analysis improves regional ventilation in terms of global aeration gain without affecting respiratory and hemodynamic variables negatively and might be a promising approach to patient-individual ventilation settings."
- Page 14: "The main findings are that only small PEEP adaptations are required to transfer increasing to horizontal compliance profiles and that the individualized PEEP titration improved regional ventilation without affecting impedance distribution and respiratory or hemodynamic variables negatively"

- Page 19: "Differences in regional ventilation gain and loss might suggest that the individualized PEEP titration could reduce the loss of ventilation in the dependent lung areas."

All these sentences are misleading and they confuse the message of the manuscript. They should be deleted/rewritten in order to be consistent with the study data.

Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English  
Please indicate the quality of language in the manuscript:

Acceptable

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