**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:** 0  **Date:** 01 Sep 2019

**Reviewer:** Elena Spinelli

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Weber and colleagues performed a randomized controlled trial of PEEP titration using the gliding-SLICE method (based on intratidal compliance profile analysis) during anesthesia. Individualization of ventilation settings is of great interest not only in patients with respiratory failure but also during anesthesia.

My major concerns about this study are related to the patient selection and the interpretation of the results of the trial. Previous studies from the same group (references 15 and 29) provided a preliminary investigation of the gliding-SLICE method to PEEP evaluation during intra-operative ventilation with interesting results. Indeed, they found that both a fixed PEEP of 5 cmH2O and a PEEP selected according to the anesthesiologist clinical judgement result in suboptimal PEEP levels in a significant proportion of patients (up to 92%), as detected by the increasing compliance profile indicating intratidal recruitment/derecruitment. Of note, these two studies included obese patients (20/35 in the first one) and the mean duration of surgery was at least 2 hours (184 minutes and 120 minutes, respectively). In order to explore whether a protocol of PEEP titration based on the gliding-SLICE method allows individualized PEEP titration during anesthesia for otorhinolaryngeal surgery, a randomized controlled trial was performed and reported in the current manuscript. The trial control group always received a PEEP of 5 cmH2O, while PEEP adaptation based on intratidal compliance was performed in the intervention group. Quite disappointingly, despite a slightly higher mean PEEP level in the intervention group compared to controls, there were no differences in the intratidal compliance profiles, in the respiratory mechanics and in the ventilation distribution between the two groups.
Major comments:

The study endpoint is not clearly defined. The authors define "nonlinear intratidal compliance" as the main endpoint of the study in the methods (paragraph "endpoint and data collection"). The hypothesis is that PEEP titration based on the intratidal compliance improves respiratory system mechanics and regional ventilation. According to these premises, the trial results are negative. Data do not support that the intervention improved none of the endpoint variables. Unless I misunderstood the EIT results, it is not correct to say that regional ventilation was improved. The discussion should be more focused on the reasons why the differences between the two groups in terms of PEEP level, compliance profile, respiratory mechanics and regional ventilation are lacking: compared to previous studies, the patient population has a much lower incidence of increasing compliance profile (also in the control group), obesity was an exclusion criteria and anesthesia duration is shorter. The type of surgery could also affect the results.

According to the negative results, the conclusions should be completely rewritten. We might say that individualized PEEP titration might be of limited value in low-risk patients (identified by characteristics such as BMI and type and duration of surgery?)

Other comments:

Background:

"application of adequate PEEP and the performance of recruitment maneuver was shown to improve…": this is not consistently supported by studies (see PROVHILO and PROBESE trials)

Discussion:

"our PEEP titration strategy is based on … data which are available from standard monitoring": I understand that a dedicated monitor is required for the Decision Support System based on the gliding-SLICE.

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

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