Reviewer’s report

**Title:** EFFECT OF PEEP AND I:E RATIO ON CEREBRAL OXYGENATION IN ARDS: AN EXPERIMENTAL STUDY IN ANESTHETIZED RABBIT

**Version:** 1 **Date:** 22 Dec 2018

**Reviewer:** Pablo Cruces

**Reviewer's report:**

I read with interest the manuscript entitled "EFFECT OF PEEP AND I: E RATIO ON CEREBRAL OXYGENATION IN ARDS: AN EXPERIMENTAL STUDY IN ANESTHETIZED RABBIT". Although the study has some potential relevance, I have major concerns -see the enclosed comments. Serious confounding methodological issues must be analyzed. Note that substantial revision will be necessary before publication can be reconsidered.

I have several specific comments, which are listed below and you may consider for improving your manuscript.

**INTRODUCTION**

Paragraph 1: It is necessary that the authors base more deeply the need to use (and study) reverse radio ventilation. References mentioned are more than 20 years old. Hemodynamic risk of autoPEEP is not mentioned, which is very relevant in the context of evaluation of oxygenation and cerebral perfusion.

Paragraph 2: The prevalence of cognitive impairment in ARDS has not been studied in patients ventilated with IRV

**MATERIALS AND METHODS**

I'm not clear if the subjects were euvoletic. Was the preload evaluated? The fasting time prior to the experiments is not mentioned.

It would have been relevant to measure cardiac output, to determine if changes in perfusion and cerebral oxygenation are secondary to changes in CO.

There is a lack of information on the manufacture of drugs used.

I do not understand why not use volume control mode, which would have simplified lung mechanics measurements. I'm not sure how they measured intrinsic PEEP without performing an expiratory pause.

The authors used a 3-hit model of ARDS (LPS / surfactant depletion / VILI). Why?

Authors do not explain what is the relevance of measuring "muscle oxygenation indices"
Also you must state whether a sample size calculation was conducted. Despite the reason mentioned by authors, I believe that using information on known changes in tissue perfusion and oxygenation induced by IRV
Please add if a randomization method was used.

Please report temperature

RESULTS

The respiratory rate is not mentioned under different conditions. As I understood the methods, the respiratory rate was adjusted according to ETCO2 target. However, in conclusions it is mentioned that the respiratory rate was constant. Please explain

Is it possible to affirm, using CVP, MAP and CF, that "increasing the I:E ratio decreased venous return"?

Figure 2: Imperfect legend.
FIO2 was 100% in subjects injured. Why PaO2 differs from PaO2/FIO2?

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.

Yes

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 recommend additional statistical review
Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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