Reviewer's report

Title: High-frequency power of heart rate variability can predict the outcome of thoracic surgical patients with acute respiratory distress syndrome on admission to the intensive care unit: a prospective, single-centric, case-controlled study

Version: 0 Date: 05 Sep 2017

Reviewer: Tobias Kammerer

Reviewer's report:

This prospective trial focused on a new non-invasive method to estimate survival in post-thoracic-surgery ARDS patients. Even if the statistical methods seem to be correct, there are still some serious shortcomings, especially regarding the trial design and patient recruitment.

The main critics are, in my opinion, the missing information about the patients included in the trial, insufficient information about patient recruitment and randomization, missing intraoperative data, a lack of description of the trial design, an insufficient description of the ICU data, and a short discussion.

In detail I have the following general questions and comments:

1. P1 title: Please add information about the trial design into the title (e.g. prospective, single-centric, randomized).

2. P3 L20: Insert the number and percentage of patients in both groups.

3. P3 L33: here and everywhere else: please avoid terms like "greater". Instead use phrases like "higher" or "increased".

4. P3 L49 - 59: The Abstract Conclusion is nothing more than a restatement of the results. What is the interpretation and conclusion?

5. P5 L42: Please delete "plays an important role in". Consider "is important for" or a similar phrase.

6. P5 L58: please add a reference regarding the method of HRV measurement.
7. P6 L4: Please add some references here.

8. P6 L26: The last sentence sounds like a part of the discussion. Please delete.

9. P6 L58ff: Important information about the trial design is missing. For example, no information is given about the intraoperative procedure, neither regarding the surgery, nor the anesthesia management. How many patients received one-lung ventilation? How was the airway management (double-lumen tube, airway blocker etc.)? Was volatile or intravenous anesthesia used? What about neuraxial regional anesthesia? How was the respirator setting in the OR? Was a lung protective ventilation setting used there? Please provide more information about the management before transfer to the ICU.

10. P7 L7-11: Was the trial registered in an online trial register? If yes, please add the trial registration number. Furthermore, to the best of my knowledge, a written informed consent from the family members is not the correct procedure for a prospective trial. Even if only data are collected, the consent of the patients should be done in advance. Especially, as it was a matter of elective interventions. This point seems to me particularly critical in view of a possible publication.

11. P7 L23ff: Please give much more data about the included patients (kind of surgery, duration of surgery, duration of ventilation, ASA classification, comorbidities, co-medications, intraoperative PaO2/FiO2, intraoperative fluid balances, transfusion rate etc.). You can include these data into table 1 (demographics).

12. P7 L26: When exactly was the diagnosis of ARDS done after arrival on the ICU? Which monitoring was used for diagnosis (chest x-ray, CT scan)? How many patients had infiltrates and where were they localized? And if the diagnosis "ARDS" was done only after admission to the intensive care unit, how is it possible that the ventilation was already adapted (for example: PEEP=5mbar in the non-ARDS group)?

13. P7 L30: Please add here all exclusion and inclusion criteria.

14. P7 L49: When exactly upon admission were the different scores determined?

15. P7 L52: Why were the patients without ARDS not extubated immediately after surgery? What were the decision criteria for postoperative mandatory ventilation?
16. P8 L26 ff: I’m not sure whether the reader is familiar with the method of HRV analysis. Please provide more details about this procedure (which device was used etc.).

17. P10 L17: Please add additional data about the patients: how many patients were screened during which time period, how many declined consent, how many were randomized for the trial etc.). Please add also the percentage of patients in each group. Furthermore, the proportion of ARDS patients is surprisingly high (>65%). Therefore, more data about the overall population of screened patients would give important information.

18. P10 L20: Here and everywhere else: please change µg/hr to µg^-1 h^-1.

19. P10 L23: the phrase "produce a state of calm" is not precise enough. Please give data like RASS score or similar sedation scores. Additionally, it is uncommon, that no analgesia was given. Which kind of post-surgical pain management was performed and how long was it done. Was spontaneous breathing allowed during mechanical ventilation? What was the ventilator mode (PCV, BiPAP etc.)?

20. P10 L26: it seems unlikely, that vasopressors were used only in the ARDS group. Please give information about vasopressor, catecholamine, co-medication and analgo-sedativa in table 1.

21. P10 L30: what is the definition of "adequate blood pressure"? Did you define hemodynamic target values in dependence of comorbidities?

22. P10 L30: when exactly and how often were ECG recordings taken within 4 hours?

23. P10 L36: here and everywhere else in the results section: please add exact p values to show significances.

24. P10 L46: the phrase "as expected" should only be written in the discussion section, but not in the results section. Please delete.

25. P10 L49-55: This sentence is an interpretation of the results and should therefore be moved to the discussion. Furthermore, isn’t it possible, that other variables could have been predictive too? Have you also done a multivariable analysis for parameters like duration of ventilation, fluid balances, postoperative pulmonary complications, re-intubation etc.?
26. P10 L58 to P11 L7: Please provide a more detailed description of the results. Also, please avoid terms like "greater". Add mean and p values whenever you show your results.

27. P11 L1: Please give the information, that Murray’s ALI score was used and add a reference.


29. P11 L39: Please delete "marginally" and give the exact p value.

30. P12 L1: Please add p values here.

31. P12 L10: The entire discussion is too short and requires a substantial revision. For example, less pathophysiologic description of increased vagal modulation and their possible influence on ARDS is given. This is especially important as most readers will not be familiar with this topic. A limitations section is completely missing.

32. P12 L17: Please avoid words like "we" or "our" and use a different term.

33. P13 L14: please give some possible pathophysiologic declaration to underline your assumption.

34. P13 L17-36: Here, only the results of previous trials are listed. Please add also, as a short resume, the possible explanation and interpretation of the results, given by the different authors in the original publication and compare them with your results.

35. P13 L45-52: This conclusion seems premature. The descriptive character of the study does not allow such a statement. For this purpose, prospective intervention studies are required. Please formulate this sentence more cautiously. Additionally, why should this be interestingly only in cancer surgery? Here again, more data about the diagnoses and surgical procedure of the included patients would be meaningful.

36. P14 L7-20: Again, your conclusion is nothing more than a restatement of the results. What is the interpretation and conclusion?
37. Figure 1: Please avoid interpretative statements in the figure legends. Delete the last sentence here.

38. Table 1 and other tables: give data as no. (%).

39. Table 1: please add additional demographic data (see above). As a minimum the reader should know: underlying disease, comorbidities, ASA classification, co-medication, perioperative antibiotics, preoperative lung function (FEV1, blood gas analyzes etc.), duration of surgery and anesthesia, kind of surgery (open vs. thoracoscopy, wedge resection, pneumonectomy etc.), duration of one-lung ventilation, lung separation technique, intraoperative blood loss, urinary output and fluid balances, neuraxial or other regional anesthesia). Add also statistical analysis to compare these variables.

40. Table 2: Please give more data about the ARDS patients. As a minimum you should provide: length of ventilator support, hospital stay, ventilator free days, fluid balances, vasopressors and catecholamines, re-thoracotomy rate, rate of adverse events (reintubation rate, resuscitation etc.), antibiotics, sedation, co-medication, SAPS and TISS score, RASS score, incidence of postoperative delirium and neurocognitive disorder. Add also statistical analysis to compare these variables.

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

No

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.

Unable to assess

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.

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