Reviewer's report

Title: Exhaled Breath Profiling For Diagnosing Acute Respiratory Distress Syndrome

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Reviewer: Konstantinos Kostikas

Reviewer's report:

The study by Bos and co-workers has evaluated exhaled breath profiling by electronic nose (e-Nose) technology in the identification of ARDS and differential diagnosis from intubated patients with similar conditions (such as cardiogenic pulmonary edema or pneumonia). The study is novel and interesting and tackles a major problem in ICU providing a promising option for the future. My specific comments are the following:

Major Compulsory Revisions

1. The fact that two ARDS definitions were used (references 31 and 1, respectively) should be discussed as a possible limitation of the study.

2. Were bilateral pneumonia and CPE the only alternative diagnoses in the population studied? Were all patients with other causes of bilateral infiltrates (e.g. alveolar hemorrhage or interstitial lung disease) excluded from the analysis?

3. Did the control group consist of intubated patients with normal chest X-rays or was a CT scan used for the exclusion of lung infiltrates?

4. Did the authors take into account in the analysis the differences in minute ventilation (and perhaps not volume as it is expressed in l/min) in their exhaled air analysis?

5. Some of the pneumonia patients present a PaO2/FiO2 ratio <300 (as revealed by the corresponding IQR 241-447). How was ARDS excluded in those patients?

6. The authors need to admit that the discrimination between ARDS and the two competing diagnoses (CPE and pneumonia) presented marginal or no statistical significance, with the exception of moderate/severe ARDS. Even in that case the AUCs of 0.76 represent a moderate diagnostic performance. This needs to be discussed extensively, since this represents the actual challenge in clinical practice. Interestingly, those cases were characterized by a high specificity in contrast to the ARDS vs. control comparisons that were characterized by a high sensitivity with low specificity. The authors also need to comment on this.

Minor Essential Revisions

1. Please define CPE in the Abstract

2. The Ethics Committee approval should follow the design of the study

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests