Author’s response to reviews

Title: Neurally Adjusted Ventilatory Assist (NAVA) or Pressure Support Ventilation (PSV) during spontaneous breathing trials in critically ill patients: a crossover trial

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Version: 1 Date: 21 Jun 2017

Author’s response to reviews:

We appreciate the reviewers taking the time to review our manuscript. Your comments have helped us come up with an improved revised version of the report, which we hope will be considered suitable for publication. We address each of the 2 reviewers’ comments one by one.

Reviewer 1

Thank you for your detailed review of our manuscript. We reply point by point:

1) Patients underwent to the SBTs of the study as first weaning attempt or, before the study, have received other (failed) weaning trials? If possible it would be useful to include this information in Table 1

We only included patients in their first SBT attempt, as patients who already have failed one SBT are a special subgroup, classified as difficult weaning or prolonged weaning. We wanted to compare the two types of SBT on a more general population of patients under MV. We added a comment about it in the Methods section.

2) patient n° 4 failed SBT trial according to criteria adopted in the study (RR 39/min)

The reviewer is correct to notice that patient #4 had a high respiratory rate during the SBT, as shown in Table 2S. However, the decision to interrupt the SBT and the final assessment of pass
vs. fail was made entirely by the clinicians, not the investigators. To prevent bias, investigators were not allowed to prompt clinicians to interrupt the SBTs, even if they noticed objective criteria for interruption. The trade-off for avoiding bias was that we had to accept the clinicians’ decision even if they did not completely adhere to the guidelines for interruption.

This patient already had a high baseline respiratory rate (Table 1S), and we can speculate that given this high baseline respiratory rate, clinicians were less strict with the respiratory rate criteria. Moreover, the respiratory rate of 39 is an average for that patient, calculated offline from the ventilator recordings, and it is possible that the clinicians assessing the SBT looked at the ventilator screen when the respiratory rate was a little lower.

To make this point clearer to the readers, we added a comment in the text that the decision to interrupt the SBT or decide between pass or fail was entirely in the clinician’s hand. We also added a comment to tables 1S and 2S that the values for VT, RR and EAdi are average values obtained from ventilator waveform recordings.

3) the subgroup of reintubated patients have a higher duration of MV (8.0±2.7 vs. 5.6±2.7 days. Is this difference clinically or statistically relevant? Please discuss.

The difference may look clinically important but it was not statistically significant, p value = 0.1138, therefore we didn’t add these values (which I assume the reviewer calculated from our tables) to the text. Importantly, these values are for the duration of mechanical ventilation prior to the SBTs, not total duration of mechanical ventilation adding the extra time in MV after reintubation. To make this distinction more clear, we modified the text on the manuscript and on Table 1 footnote. We hope that this clarification makes the values more meaningful.

4) Please discuss better the high reintubation rate and review reintubation rate in other studies with similar patient characteristics.

We agree that the extubation failure was high in our patients, 25% (95%CI 9–49%), but given the reduced number of participants, the confidence interval is relatively wide, which prevented us from making strong arguments around that figure. In larger studies, extubation rates are on average 13% (Boles ERJ 2007), but in a large observational trial conducted in many countries (Frutos-Vivar 2011), the extubation failure rate was 29%.

The reviewer makes a good point that we didn’t discuss this point, so we added this topic to the discussion section.

Reviewer 2:

Thank you for reviewing our paper> below we answer your questions and hope that this clarifications make things clearer.
I have two questions:

1) Why do you have double triggering in NAVA?

This phenomenon has been observed in other studies, and it is related to the fact that, in NAVA, cycling off occurs when EAdi reaches 70% of its peak, to avoid delayed cycling. The cycle off cut off in PSV in our study was adjusted by the ICU clinicians, during pressure support ventilation, and was not changed during the study. It ranged from 20% of peak flow to 60% of the peak flow, with a median value of 30% (Table 1S). In the discussion section, we discuss this phenomenon and reference other studies that also showed an increase rate of double-triggering in NAVA compared to PSV. It is a price to avoid delayed cycling, and since the volume delivered in the second cycle is zero or very low, the clinical consequences are less deleterious than when double triggering occurs in volume-controlled ventilation. It is nonetheless an asynchrony that should be monitored.

2) Why do you set the NAVA in relation of the pressure in PS and no in relation of VT???

That is a very good question. Most studies published in NAVA do that, and this is one of the reasons we also used this strategy. We referenced the papers that use But the rationale is that when the clinician is titrating NAVA, there is no pressure or tidal volume setting, the only parameter to be set is the NAVA level, which is a factor gain that will multiply EAdi to generate airway pressure (not volume). In NAVA, tidal volume is never set; it is a consequence of patient effort, respiratory system compliance and airway pressure. And airway pressure is determined by Paw = NAVA level *EAdi. Now, assuming that patient effort will remain relatively constant if the level of support from the ventilator also remains constant, titrating NAVA to deliver approximately the same pressure than PSV should also result in approximately the same tidal volume, but matching the airway pressure is more straightforward.