Reviewer's report

Title: Influence of tidal volume on pulse pressure variation and stroke volume variation during experimental intra-abdominal hypertension.

Version: 2 Date: 10 April 2015

Reviewer: Simon Vistisen

Reviewer's report:

Major compulsory revisions

Abstract:
Change results and conclusion sections according to the below listed revisions for results and discussion chapters (data does not support that PPV and SVV does not increase following IAH induction when low Vt is applied and fluid responsiveness prediction classification is not really different between the before and after setting of IAH induction).

Introduction:
I miss a clearly stated hypothesis for your study at the end of the introduction

Methods:
Describe if and how respiratory frequency and/or dead space was changed when ventilating the piglets at the three different tidal volumes. Report also for how many minutes the three tidal volumes were applied each. Lastly, state, which tidal volume was used after the randomized 6-12-18 VT protocol. Was it 10 ml/kg which is stated as the initial VT setting?

I miss reasoning for the statistical reporting: If data is not normally distributed, mean (SEM) does not describe the data well and median (inter quartile range, IQR) should be used. Some of the presented data may benefit from log transformation. Please describe, if you tried to log transform with the purpose of applying parametric statistical tests in stead of non-parametric.

Results:
It is unclear which “volemic levels” are compared – there are three levels before IAH induction. Please specify, when you use Baseline, after-FB1 and after-FB2 in the comparisons. Reading the paper, I get the idea that after-FB1 is compared with after IAH induction? Every time a test result is reported, please specify what is tested against each other using Baseline-FB1-FB2-IAH- FB3.

If you use non-parametric testing, report all variables as median (IQR) and not mean (SEM).

All tables and figures must be carefully read through (see comments on minor essential revisions)

As supplemental material, please add scatter plots and ROC curves for all the
AUC analysis reported. The tables are too far away from the raw data to offer interpretation.

At the end of the results section, it is stated that none of the studied variables were good predictors of fluid responsiveness. Looking at the AUCs before IAH and after IAH at VTs of 12 and 18, the average AUC is 0.87 before IAH 0.78 after IAH. I do not think that these data merits the conclusion, that SVV/PPV works under non-IAH conditions and that they don’t work under IAH conditions. Essentially, there is not a big difference here

Discussion

Regarding the main findings (i-ii-iii)

ii. I think, it is nearly as good a prediction as before IAH. At least, be more true to the data and its ‘sparseness’.

iii. Looking at the presented data for SVV (fig 2/3), it is not really true that SVV does not increase with IAH when a low VT is applied. This is clearly a statistical type 2 error and caused by one piglet doubling SVV (7% to 14%) after the FB2, which is difficult to explain.

A lot of the discussion focuses on how SVV and PPV behave at low VT compared to higher VTs. I basically think that a lot of the stated ‘clear-cut’ conclusions in this regard are not merited by the data. For instance, small VTs do produce consistent cyclic swings in PP and SV and SVV and PPV are reduced during low VT by fluid administration. This is erroneously ‘negated’ by the statistical tests because of statistical type 2 errors.

Also, it is stated that ROC analysis showed that PPV and SVV did not predict fluid responsiveness during IAH. I disagree due to the quite small differences in ROC areas before and after IAH.

I would like to see a part of the discussion focusing on the appropriateness of the suggested IAH model. It is stated that this is a new model. The amount of fluids infused in abdomen is around 50% of body weight. What are the thoughts on the model? Can it be ‘recommended’? What are the advantages and/or disadvantages? How does this fit with clinical IAH? In babies, children and adults?

Depending on respiratory frequency/dead space settings, discuss how possible CO2 changes could affect hemodynamics at the different VTs, including PPV and SVV

Minor essential revisions

Introduction:

The use of references appear exaggerated to me. I do not suggest a certain threshold for number of references but think that the reference list should be approximately halved by choosing the 2-3 most relevant references in stead of simultaneously citing 7-13 papers for a single statement at four circumstances in the introduction.
Methods:
State whether the averaging of four consecutive 7.5 second SVV estimates is a PiCCO algorithm or if it was something, you did. Notice, that 7.5 seconds includes >2 respiratory cycles, potentially boosting SVV and PPV if a minimal and maximal value is found for PP and SVV in this interval. If respiratory frequency were reduced at 18 ml/kg and increased at 6 ml/kg, this would be worth a discussion.

Results:
The best cut point changed according to the Vt applied. I have previously suggested tidal volume indexing (Acta Aneasthesiol, 2010, pp. 191-8). How were the cut points if tidal volume indexing was applied?
When reporting the intraperitoneal infusion time, you specify a p-value and state a comparison with baseline (line 11-12 on the last result page). What is tested here?
Report how many piglets responded to the first and the second FB, respectively.
Table 2: HR appears to fall significantly from baseline to AIH, which is not marked in the table. Please add these markings if I am correct. Also check if SBP really changes from IAH to FB3 – I don’t think so. I also believe that CVP is increased at IAH compared to baseline. And finally (but I am not too sure), SVI appears higher at IAH levels compared to baseline.
Table 3: Significant 95% CIs are reported sometimes but such significant CIs are sometimes associated with insignificant p-values. How can that be? – I suppose that you test, whether AUC is significantly different from 0.5?
Specifically Table 3B: The AUC reported for SVV at VT=18 is 0.84 but optimal sensitivity and specificity are 50% and 75%, respectively. I cannot imagine how this can happen? How did you choose an optimal threshold? For instance, if one chose to maximize the sum of sens and spec to find the optimal threshold, these sens/spec values would be associated with an AUC that mathematically cannot exceed 0.72.
Figure 1: Baseline is used as term for the entire period without IAH. Change this such that the term fits with the description in the document (baseline period ends when FB1 begins, right?)
Figure 3: This should have been a figure for PPV but it is for SVV (it’s identical to Figure 2)!

Discussion:
Line 15-18: Erase this sentence or find better explanation and a reference to cite – reference 52 is not existing. There are other references that are not chosen well, e.g. ref. 20 on line 12 on second discussion page, and a few lines above that: ref [9,44,45] where piglets are mentioned in the current paper but all the referenced studies are on humans. Here, it is stated that, in accordance to previous observations, with low VT, one cannot predict fluid responsiveness in piglets. I have published (piglet) data showing that it is possible with low VT in a
study design not very different from this. (Acta Anaesthesiol, 2010, pp. 199-205). At the end of discussion it is stated that by IAH induction, the piglets were euvolemic. At this point, I would refer to the intravascular state as hypervolemic (after FB2).

Author’s contributions:
If TS did not contribute to the manuscript, why is he/she a co-author?

References:
Reduce and choose the most appropriate references at the points mentioned. The fact that non-existing reference [52] is put in the text may indicate other errors in the automatic generation of the reference list and in-text citations. Double check this.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

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