Author's response to reviews

Title: Using clinical parameters to guide fluid therapy in high-risk thoracic surgery. A retrospective, observational study

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Author's response to reviews: see over
Dear Professor Koksal,

We hereby submit a revised version of our manuscript “Using clinical parameters to guide fluid therapy in high-risk thoracic surgery. A retrospective, observational study”. In the revised manuscript, changes are highlighted in red.

We wish to thank you for giving us the opportunity to resubmit our manuscript. Also, we would like to thank the expert reviewers for their very useful and constructive comments to our manuscript. When revising the manuscript, we identified a minor error in the results section (line 119); we described a patient who was discharged from the ICU at POD 1, but readmitted within 24 hours. Actually, this patient was discharged at POD 2 and readmitted within 24 hours. We apologise for this mistake, which has been corrected.

Please find below our point-by-point responses to the reviewers comments. We hope that you will find our answers satisfactory and that you will consider our revised manuscript for publication in the BMC anaesthesiology. In case any of our answers are unclear or needs further explanations, please do not hesitate to contact us.

Yours sincerely

Lars Bjerregaard, Hasse Møller-Sørensen, Kristoffer Lindskov Hansen, Jesper Ravn and Jens Christian Nilsson

**Reviewer 1, Sanket Srinivasa:**

*What were the d/c criteria from ICU. Why did patients leave earlier when there were no difference in complications? Were the same objective d/c criteria utilised?*

The same discharge criteria were utilised during the whole study period. These were based on the recommendations from the Danish Society of Anaesthesiology and Intensive Care Medicine for discharge to a ward after surgery. The recommendations are available online (unfortunately only in Danish!) and a reference has been added to the URL (line 61/62).

In response to the question why patients left earlier, we have reviewed the charts from the six patients in the before group who had LOSI > 1 day to determine the main reason for their continued ICU-stay. These are now reported in the results section (line 117-119).

*There is a trend towards earlier operations getting more blood products but having equivalent bleeding- could these results be due to surgical differences rather than changes in fluid management?*

This is of course a potential explanation but for a number of reasons we do not consider it to be likely: Firstly, all operations were performed by the same experienced surgeon using the same...
surgical technique during the entire study period. Secondly, the two groups had equivalent median durations of surgery. What we believe influenced the reduction in the use of blood products, were: 1) That the changed guideline clearly pointed out the use of a restrictive transfusion policy; 2) the “allowance” of higher volumes of colloids and 3) the reduced volumes of intraoperative fluids resulting in less hemodilution. (Please see discussion, line 167-171)

Is multiple regression possible to determine whether fluid management was independently associated with changes in outcomes?

We do agree that multiple regression is worth considering, but we have some concerns about that type of analysis in this study. Our primary concern is that the maximal number of explanatory variables allowed would be no more than three (at best) – depending on the specific type of multiple regression analysis applied. Obviously, this limits the value of the analysis, and even when observing this requirement we believe that the results of such analysis on this small data set would be rather unreliable. For these reasons we have chosen not to go ahead with multiple regressions analysis.

Can you please comment on other methods (e.g. oesophageal doppler) to conduct goal directed therapy and the fact that this strategy is now under scrutiny at least in the context of major abdominal surgery.

In “classic” goal directed therapy fluid boluses are administered as long as this improves the cardiac output (hence moves the patient toward the top of his Starling curve) assessed by different modalities such as oesophageal Doppler or similar devices. Consequently, classic goal directed therapy most often results in increased fluid administration. However, we acknowledge that GDT using haemodynamic monitoring may prove advantageous in pulmonary surgery and a brief discussion of this has been added to the manuscript (line 137-139).

I appreciate that the authors’ acknowledgement that these results are hypothesis generating but it should be noted that the study is likely underpowered to make any assertions regarding risk and benefit.

The small sample size and hereby potential lack of statistically power has been emphasised in the limitations section (line 188-189)

The length of hospital stay is the same- does this mean that patient care was simply handed over to another ward (instead of ICU)?

Yes, the patients were discharged to a thoracic surgical ward, when fulfilling the criteria for discharge from the ICU (please see reference 5 in the revised manuscript). However, although statistically insignificant we also found a reduced median LOS in the after group, indicating that the patients were not discharged earlier from the ICU just to stay longer in the surgical ward.

What do the authors think is the key intervention- permissive oliguria or SCv guided fluids?

In general, we believe that the most important is the balance between two “opposing” measurement to keep the patients dry (permissive oliguria) – but not to dry (ScvO2).

Reviewer 2, Yalim Dikmen:

This manuscript reports the result of implementation of intraoperative hemodynamic goal directed therapy during pneumonectomy operations. This study has several limitations like
the before after design and low subject number, but it shows an indication of better short term outcomes in the goal directed therapy group. However there are some points need to be clarified. On my point of view the most important problem is the lack of information on why the patients in the after group had a significantly lower intensive care length of stay. As the discharge criteria had not been changed during the study period there would be some parameters that would have shown better in the after group for early discharge. I think why this group of patients had a shorter ICU stay can not be seen in the manuscript. Perhaps a comparison of blood gas analysis, respiratory functions, level of consciousness would give better clues for why these patients had been better.

We do agree that the suggested comparisons of blood gas analysis, respiratory function and/or level of consciousness would add valuable information, but unfortunately we have not been able to retrieve sufficient data on these parameters beyond what is already presented in the manuscript. However, in order to describe why patients had significantly shorter ICU stays in the after group, we have reviewed the charts from the six patients in the before group who had LOSI > 1 day to determine the main reason for their continued ICU-stay. These are now reported in the results section (line 117-119).

Another point is the choice of ScVO2 threshold of 60 % for hemodynamic interventions. Although limited, there are perioperative data, which show a ScVO2 value below 70-73% is associated with low tissue perfusion and increased risk of postoperative complications. (Futier E, Robin E, Jabaudon M, Guerin R, Petit A, Bazin JE, Constantin JM, Vallet B. Central venous O# saturation and venous-to-arterial CO# difference as complementary tools for goal-directed therapy during high-risk surgery. Crit Care. 2010;14(5):R193.

and Collaborative Study Group on Perioperative ScvO2 Monitoring. Multicentre study on peri- and postoperative central venous oxygen saturation in high-risk surgical patients. Crit Care. 2006;10(6):R158.) Therefore the argument of preventing hypervolemia by choosing a lower ScVO2 level seems not to be valid, and this issue needs further discussion.

We agree that the referred articles support a correlation between lower perioperative ScvO2 values and an increased risk of postoperative complications in high-risk abdominal surgery. However, these articles primarily report infectious and surgical complications, both of which were rare in our population. In thoracic surgery and pulmonary resection, ALI and ARDS is the main concern and therefore fluid therapy tends to be very restrictive. Also, it should be emphasised that ScvO2 = 60% was an interventional threshold (lowest acceptable limit) and not an intended value. Based on our results (given the limitations of the small sample size) we did not find the used threshold value to increase postoperative complications.

This study can obviously only be hypothesis generating but will hopefully encourage future prospective studies of the optimal way to use ScvO2 for guidance of postoperative fluid therapy, including the optimal interventional thresholds of ScvO2 adapted to specific study populations.
A discussion of the above has been added to the manuscript (line 158-160)