Author's response to reviews

Title: Elevated central venous pressure is associated with impairment of microcirculatory blood flow in sepsis: a hypothesis generating post hoc analysis

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Author's response to reviews: see over
To:
T. Rowles, Executive Editor BMC Anesthesiology

Leeuwarden, the Netherlands, June 28th, 2013

Dear Editor, dear reviewers,

Thank you for your valuable remarks and for offering us the opportunity to submit a revised version of our manuscript ‘Elevated central venous pressure is associated with impairment of microcirculatory blood flow in sepsis: a hypothesis generating post hoc analysis’. Please find below our point-by-point response to the comments of the reviewers; the corresponding changes in the manuscript have been made in red.

Sincerely,

Namkje Vellinga

Dr Donadello:

- The formulation of the last sentence of the abstract is not correct, at least for the use of commas; for “finding” I would put an “s” at the end.
  
  We changed the text according to your suggestions (p. 2).

- Introduction: the sentence “attempts to improve” is too heave with the double negative form.
  
  We changed the text to omit the double negative form (p. 4).

- Results: after “statistic measurement” I would put either “:” or “,” or get to the following line; the same for the “dynamic “part
  
  We transferred the results for both subheadings to the following line (p. 7).

- Discussion: I personally would omit the sentence “we, however encourage the reader....”
  
  We deleted this sentence (p. 10).

- Key messages: I think that no guideline suggest to resuscitate to levels of CVP higher than 12, thus I might change the last message.
  
  We changed our message accordingly (p. 12).

Dr Walley

- Major Compulsory Revisions: I think the analysis and manuscript would be greatly improved by using a more robust statistical model, including some measure of severity of illness (and possibly other factors) as covariates in the model. If the CVP-microcirculation association holds up after correction for these covariates then I think they have a valid hypothesis.

  We thank Dr Walley for his suggestions regarding the statistical analysis.

  We applied multivariate analysis in order to detect associations between elevated CVP and a capillary MFI < 2.6. This is the lower bound of the 95% CI for capillary MFI in healthy volunteers. In a recent study, this cut-off value was confirmed for the response of the microcirculation during fluid therapy, underlining the clinical significance of this threshold.

  Tested predictors were perfusion pressure, lactate level, norepinephrine and dopamine dose, PEEP, cardiac index, SvO₂, CVP as a continuous variable, CVP > 12 mmHg and MAP.

  The only remaining significant predictor for an abnormal MFI was a CVP > 12 mmHg (Odds...
ratio 2.5 (95% confidence interval 1.1-5.8), p=0.026). Illness severity scores (APACHE II, SOFA) could not be included for logistic regression for all measurements (i.e. T0 and T30), because these scores were calculated once for the first 24 hours in ICU for these patients, and cannot be calculated for every time point at such a short interval. We changed the text of the abstract, methods, results and discussion in line with the above.

Editorial remarks: we added an acknowledgements section on page 12.