Reviewer’s report

Title: The increase of vasomotor tone avoids the ability of the dynamic preload indicators to estimate fluid responsiveness.

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Reviewer: Jochen Renner

Reviewer’s report:

Comments to the Author

Dynamic variables of fluid responsiveness have been extensively investigated in the past years, and indications and limitations are definitely better known today. One main issue is of course the question whether vasoactive agents affect the ability of these variables to accurately discriminate between responder and non-responder due to volume load. In this regard the study from Bouchacourt et al. is of some interest. Especially, since the available literature is not consistent. However, there are a few aspects that need to be addressed and need to be clarified by the authors.

First of all, in general, the manuscript is well written. However, the main problem with this manuscript is the divergence of the hypothesis (estimation of fluid responsiveness) and the setting of the study protocol (Baseline – Baseline + PHE - Hemorrhage – Hemorrhage + PHE), which is not designed to estimate fluid responsiveness, but to assess the influence of different loading conditions plus/minus PHE on dynamic variables. Whether these variables were able to accurately predict fluid responsiveness under these conditions, i.e. discriminate with acceptable sensitivity and specificity between responder and non-responder has not been shown in this manuscript. Nevertheless, this study is of some interest, especially since the influence of PHE on vasomotor tone and consequently on pulse pressure has been well shown. Consequently, the focus of this manuscript must be the influence of hemorrhage and PHE on the different variables assessed and the potential consequences of their ability to estimate fluid responsiveness have to be discussed (but are not justified by the presented data). The authors interpret the influence of PHE on dynamic variables as a pseudo normalisation, however, the very important point is whether they still have predictive power our not, since in daily clinical routine continuous administration of norepinephrine intraoperatively during major surgery is a common thing.

Another point regarding the decision to perform Bland Altman Analysis: Comparing stroke volume variation, pulse pressure variation and systolic pressure variation are in general variables yielding the same information, but in part with totally different threshold values. I have never heard of any Bland Altman plots comparing CVP and PAOP to prove interchangeability.

So what to?
Please focus more on the assumed effect of PHE on dynamic variables; more pronounced during haemorrhage compared to euvolaemia? Potential effects on the accuracy to predict FR.

Any influence for our daily clinical routine? Another confounder/limitation?

To me it makes no sense to compare SVV / PPV / SPV using Bland Altman.

Please discuss the findings of Monnet et al. Br J Anaesth. 2013 Feb;110(2):207-13. SVV, PPV and PVI under NE, influence of the Perfusion index!

Does the manuscript contain relevant news? Not really, which is basically often an answer to reject a manuscript. However, to me it seems important to dignify work like this helping to more clearly define indications and limitations of any clinically used variable.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'