Author’s response to reviews

Title: Relative cerebral hyperperfusion during cardiopulmonary bypass is associated with risk for postoperative delirium: a cross-sectional cohort study

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Author’s response to reviews:

Dear Prof. Biasucci,

dear reviewers,

we again thank you for giving us the opportunity to submit a revised version of our manuscript. We have carefully studied the valuable reviewers’ comments and gratefully acknowledge the helpful suggestions they made to further improve our report. In order to meet their demands, we have made comprehensive modifications within the text, which are further explained in a detailed point-to-point reply.

Rev. #1 Thanks to the authors for their work of implementation of the paper. I think some of my observations are very close to those made by other reviewers. I am satisfied with the integration work done, now the paper is more precise and legible. So no others raccomandations. I only recommend you only if the authors confirm that it is a prospective observational study with a cross-sectional study, it will be precious to use STROBE checklist as platform.

We are glad to have been able to satisfy the reviewer with our revision and appreciate this additional useful comment. We now have added some information to our manuscript to meet the criteria of the STROBE statement, as they can be found at www.strobe-statement.org.
Rev. #3 Misunderstanding is about TCD and hyperperfusion. When hematocrit reduces, cerebral blood flow increases according with Poiseulle’s law to maintain tissue perfusion (Thomas DJ, Lancet 1977). Experimental communication cited by authors in a very particular setting, that is in case of very narrow arteries as in newborn, is not sufficient to question this general physical principle (Paut O). TCD documents this increase, as an increase of cerebral blood flow velocity (Brass LM, Stroke 1988). This is not hyperperfusion, as authors state, but a compensatory mechanism that is of paramount importance to maintain the perfusion. The hypothesis that this is a pathologic hyperperfusion is not proven, and may lead to a dangerous reduction of cerebral blood flow.

We again thank the reviewer for this critical and valuable input. It is absolutely right that decreasing hematocrit might be one underlying cause for increasing CBFV during CPB, as stated by the reviewer and as evidenced by the references he cited. We now included the important reference to Thomas et al. to our manuscript. However, we would like to point out kindly that the results presented by these references are gathered under conditions of pulsatile flow, and non-pulsatile flow may reduce the impact of hemodilution on CBFV (see Thiel et al. [1]). Moreover, compared to hematocrit, the influence of pump flow on CBF is way more pronounced (see Chow et al. [2]). If changing hematocrit questions the validity of TCD to evaluate CBF during CPB is still in doubt (see Gruber et al. [3] vs. Paut et al. [4]).

We think that the relation between hematocrit and CBFV is independent from our finding that relative cerebral hyperperfusion is prominent in patients subsequently developing POD. Yes, we do see hemodilution in our patients, but in all of them and without any association to the development of POD. Pre- as well as postoperative hematocrit values in the POD group absolutely equal those in the no-POD group. And yes, we do see increasing relative cerebral blood flow velocities, but primarily in those patients that develop POD, with a highly significant difference between the two subgroups. And no, neither in the whole cohort nor in any of the subcohorts, relative changes of hematocrit correlated with the relatively changing MCAV. We have added the respective data to our results section. Furthermore, we found an association of subsequent POD not only with increased relative CBFV but also with its duration. Taken together, all this makes a causal relationship between intraoperative hemodilution, increasing CBFV and the development of POD very unlikely in our patients. We have updated our discussion section accordingly.

We hope that these additional clarifications addressed all of your concerns sufficiently and that you agree that the changes improved our manuscript and helped to clarify the report. Please do
not hesitate to contact us if you should have any more questions. We are very looking forward to your decision.

Thank you very much!

Sincerely,

PD Dr. med. Tobias Hilbert, MD, D.E.S.A.

References:


