Reviewer’s report

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

Version: 0 Date: 27 Nov 2018

Reviewer: Anselmo Caricato

Reviewer's report:

In this paper the authors tried to investigate if changes in cerebral blood flow, relative to the pre-bypass baseline, are associated with the risk for postoperative delirium.

To this aim, in 47 patients on cardiopulmonary by-pass (CPB) they measured cerebral blood flow velocity on middle cerebral artery by transcranial doppler (CBFV) as surrogate of cerebral blood flow. They found that in patients with delirium an increase of CBFV during CPB was observed if compared with patients without delirium. They suggested a critical role for cerebral hyperperfusion in the pathogenesis of delirium following on-pump open-heart surgery.

The study is interesting, and adds new informations on this topic.

In my opinion there are some problems that should be addressed in this paper.

Several different physiologic mechanism may be involved in cerebral flow velocity regulation during CPB. In fact, temperature may be reduced, hematocrit may change, and systemic flow can be artificially regulated by machine. Each parameter may influence not only cerebral blood flow, but even cerebral flow velocity, changing diameter of cerebral arteries. So, the equivalence between CBFV and CBF is not warranted after starting of CPB. The authors should report this important limitation of the study in the discussion.

The authors studied autoregulation during CPB in these patients, and found that autoregulation was preserved with no differences between patients with or without delirium. If this is true, CBF must be independent from systemic parameters as pressure or flow. This cannot explain results. How can you explain hyperperfusion, when autoregulation is present?

I think that the term hyperperfusion should be changed in increase of CBFV. Can you exclude that these results may be the consequences of increased cerebral metabolism? Have you any data about depth of anesthesia? Did you measure BIS or any other similar index? Did you measure regional oximetry to confirm that the increase of flow is related to hyperperfusion or not the effect of increase of increased metabolism, reduced viscosity or other?

Did you measure hematocrit pre and during CPB? I think that this may be an important bias.

Is there any phase of CPB when CBFV was increased?
Did you measure CBFV after CPB?

Zazulia (ref 6 of the paper) reported an autoregulation index based on cbf measurements. In this case you measured flow velocity through tcd. Method should be standardized according with correct reference.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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