Peer Review File

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Reviewer A

1. I congratulate the authors to their systematic review and meta-analysis dealing with an important topic in surgery for acute type A aortic dissection. The choice of the preferred cerebral perfusion technique can be challenging, and today we know that many different and individual factors may influence outcomes. The authors conclude that ACP and RCP are both safe and acceptable techniques to use in emergent settings. However, the RCP technique may be preferred over ACP in terms of PND, and uACP may be preferred over bACP in terms of TND. These are really interesting findings and partially supplement the existing data, however I would like to make some comments for potential improval of the manuscript:

   Reply 1: Thank you for your comment. After reviewing your valuable comments, we encountered some problems in the meta-analysis. Therefore, we asked another professional statistician to perform the meta-analysis. The results of the analysis showed no significant difference between the two main cerebral perfusion methods in terms of mortality and PND; while TND risk in the bACP group was higher than the uACP group, ICU-stay time was longer in the uACP group compared to bACP, CA time during ACP was longer than during RCP, and core temperature was higher in ACP. There were no significant differences in CPB, and operative mortality endpoints, whereas TND in uACP was higher compared to bACP. In meta-regression analysis an increase in age is associated with longer ICU stay time and higher CCT in uACP compared to bACP.

   We sincerely apologize for this incident. However, we wanted to make sure that the most accurate results are submitted for your kind approval.

   Changes in the text: We have changed the results section accordingly.

2. Line 81-82: More in general, main risk factors for mortality in acute type A aortic dissection are advanced age and preoperative malperfusion. I suggest reading and including: https://doi.org/10.1093/ejcts/ezad288

   Reply 2: Thank you for your comment. We added the missing information to the sentence using the mentioned study.

   Changes in the text: Page 3, Line 79:"Besides, postoperative brain malperfusion or advanced age are the leading causes of mortality and morbidity in ATAAD…"

3. Line 135-138: the authors describe the definition of permanent neurologic dysfunction (PND) and transient neurologic dysfunction (TND), which are in common with the current literature and apply to the literature. However, when describing the findings of TND in line 230-231 the authors suddenly talk about the chance of PND (Postoperative Neurologic Dysfunction) occurring in uACP. For me, this is not clear and does not apply to the methods described before. I strongly recommend to revise this paragraph.

   Reply 3: Thank you for your comment. We revised the text accordingly.

   Changes in the text: Page 10, Line 242: " Risk of TND occurring in bACP is higher than in uACP."

4. Line 239: I recommend to use the same terms and abbreviations for cerebral perfusion techniques (e.g. uacp, bacp vs. uACP, bACP).

   Reply 4: Thank you for your comment. We revised the text accordingly.

   Changes in the text: We have changed uacp and bacp to uACP and bACP.

5. Line 263-265: The authors conclude that this meta-analysis showed no significant difference between the two main cerebral perfusion methods regarding PND. There were no significant differences in CPB, CA time, and operative mortality endpoints, whereas PND in ACP was higher compared to RCP. Also, the authors showed that the pooled RR (95% CI) for PND between ACP and RCP was 1.4958 RR, 95%CI, 236 [1.0271; 2.1783] (P value=0.0358) and therefore might be 50% higher than RCP. According to that, the conclusions are contradictory for the reader. I strongly recommend to revise this paragraph.

   Reply 5: Thank you for your comment. We revised the text accordingly.

   Changes in the text: Page 16, Line 398:We have changed the conclusion section: " In conclusion, this meta-analysis demonstrated that the ACP and RCP are both safe and preferable techniques to use in emergent settings. There was no significant difference between the two methods in terms of operative mortality. ACP and RCP both were safe for PND and TND, also uACP and bACP are equivalent in terms of PND. However, the uACP technique is preferred due to the lower risk of TND compared to the bACP. "

6. Line 275-277: The authors conclude that a general agreement on which technique, ACP or RCP, provides superior clinical cerebral protection efficiency is needed. Considering ACP has no advantage over RCP, further research on this topic is essential, particularly in institutions using advancing minimally invasive procedures. Why do the authors refer to minimally invasive procedures? Furthermore, ACP has several advantages over RCP (e.g. core temperature, antegrade body perfusion via innominate artery, ...). I recommend to read and include the following article: 10.3390/jcm12062271

Reply 6: Thank you for your comment. We have added the two sentences based on the mentioned article to the study.

Changes in the text: Page 15, Line 377**:** "These results are in line with the narrative review of 24 original articles published by Pitts *et al.*, in which the authors conclude that use of ACP is favored for surgeries under moderate hypothermia compared to RCP and deep hypothermia. While bACP is suggested for longer circulatory arrest durations, uACP is safe for shorter durations. There's no definitive time threshold established, but 30-50 minutes has been proposed (33). "

7. Line 344-350: The authors discuss their main limitations. However, the associated level of hypothermia in terms of the core temperature is a relevant and really important missing factor, which is not considered in the current meta analysis. The degree of hypothermia has been shown to be a relevant influencing factor in the past, especially in terms of permanent neurologic dysfunction (Czerny et al.). Therefore, I invite the authors to perform a further analysis regarding the degree of hypothermia in case of RCP vs. ACP and uACP vs. bACP and discuss the results.

   Reply 7: Thank you for your comment. We analyzed the core temperature and have added the results to the study.

   Changes in the text: Page 11, Line 268: "Core temperature
   The difference in means for the core temperature in the ACP-RCP comparison is demonstrated in Figure 16A. …"

   Page 14, Line 364: " Furthermore, we observed that the core temperature was notably elevated in the ACP group, resulting in reduced durations for cooling and rewarming, as well as the operation and CPB times (32). Nonetheless, we did not identify any significant difference in the CPB durations between the groups. "

8. Line 354-356: The authors conclude that RCP is preferred due to the lower risk of PND compared to ACP. But, both strategies can be used in operations, and the approach depends on the patient's conditions and considering clinical centers or surgeons' experience and preferences. Given an example, in which scenario the authors would decide for RCP vs. ACP?

   Reply 8: Thank you for your comment. We revised the text accordingly.

   Changes in the text: Page 15, Line 385 " However, if a surgeon is faced with a scenario where the risk of TND is a significant concern (such as poor preoperative mental status, diabetes and manifest peripheral arterial disease) and they have the expertise and resources to manage ACP, they might opt for uACP (35)."

Reviewer B

1. Please provide figure legends in the following format:
Figure 2. XXX (a summary legend). A. XXX (separate legend for each subfigure). B. XXX (separate legend for each subfigure).
Below is an example of the presentation of a legend when there are subfigures in one figure.

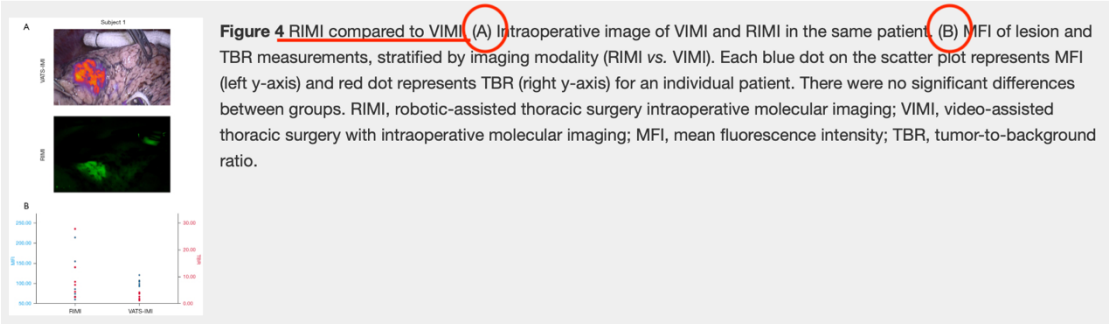

Figure 4 RIMI compared to VIMI. (A) Intraoperative image of VIMI and RIMI in the same patient. (B) MFI of lesion and TBR measurements, stratified by imaging modality (RIMI *vs.* VIMI). Each blue dot on the scatter plot represents MFI (left y-axis) and red dot represents TBR (right y-axis) for an individual patient. There were no significant differences between groups. RIMI, robotic-assisted thoracic surgery intraoperative molecular imaging; VIMI, video-assisted thoracic surgery with intraoperative molecular imaging; MFI, mean fluorescence intensity; TBR, tumor-to-background ratio.

Note that only the final figures should be described in the figure legends. Therefore, revised versions should not appear in the legend.

Reply: We apologize, but we think the current format is exactly the same as the method you have kindly mentioned.

2. Figure 6C: A first and last tick should be added to the y axis.
-20 and 5 are suggested to be added in the y axis.
Reply: We have revised the figure 6c.

3. Table 4: Please add the unit for the below column headers.
Reply: We have added units.

4. Definitions for some of the abbreviations are still not provided in each legend. (e.g. Q and etc.)
Reply: We have added full terms of all abbreviations.

5. Please provide a full citing information or a link of Ref 16.
Reply: We have added the full citing information and the DOI.

6. Line 642: It is a forest plot. Forest plots were named wrongly as funnel plots in the manuscript file. Please check the entire article and revise.
Reply: Edited.

7. Line 307: Please provide the definition on first use.
Reply: Done

8. Line 388/395/402/433/448/472/473/481/494/539/542/586/593/641: Please check the correctness of the number and be consistent with the figure.

Reply: Edited.

9. Line 398: There are nine studies in the figure. Please confirm whether revision is needed.

Reply: Edited.

10. Line 540: Please check the correctness of the numbers as 0.0013 is out of the range in the brackets.

Reply: Edited.

11. Line 685: Should it be ACP instead? If changes are made, please check whether the third line of this paragraph should be simultaneously.

Reply: Edited.