

Peer review file

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Reviewer A

Congratulations to the authors for their manuscript which I read with great interest. The study tries to determine the effect of PH on patient's outcome. Despite I agree with the study limitations, my opinion is absolutely positive for the topic of the study and for the results. The manuscript and the tables are clear and immediate, the references updated. Because of the number of patients with PH is low, the conclusions of the study cannot be considered definitive but to be confirmed with a larger cohort of patients. The study, in my opinion, is worthy of publication in its present form.

Reply: Thank you for your comments.

Changes in the text: None.

Reviewer B

Liu et al. are presenting a quantitative retrospective cohort study in patients with acute type A aortic dissection who underwent total arch replacement between 2013 - 2016. The study is centered on a common occurrence of temperature variation and convection body heat loss and its correlation to postoperative outcomes highlighting the risk-exposure relationship. They have modeled this retrospective study with 300 patients from the pool of their experience and expertise. They have illustrated their use of quantitative methods to attain the outcome desired. I congratulate them on this effort, however, have few appraising points that I encourage the authors to consider carefully:

1. Please change the title of your study to indicate that this is an original article, not a review bland article. I suggest the following: Total Arch Replacement Following Type A Aortic Dissection – Multivariate Analysis & Risk Identification for Postoperative hypothermia Occurrence.

Reply1: Agree and thank you.

Changes in the text1: The title was changed into "Total Arch Replacement Following

Type A Aortic Dissection - Multivariate Analysis and Risk Identification for Postoperative hypothermia Occurrence.” Please see page 1, line 4-5;

2. There is certainly a collider bias between temperature recording i.e. from the bladder vs nasopharyngeal. How does the author account for this confounding factor?

Reply2: Although both the bladder and nasopharyngeal temperatures were measured during the operations, only the bladder temperatures were used to represent the core body temperature of the patients. We determined whether or not the patients had developed PH according to the core body temperature. The nasopharyngeal temperatures were used to represent the brain temperature which was an indicator for initiation of the circulatory arrest.

Changes in the text2: None.

3. The DHCA temperature attained presents a further confounding factor, rendering the study unequivocally refutable. How can the author justify that with lag and lack of evidence for robust DHCA temperature the PH could have been better if they needed not to cool down to 22C? Moderate hypothermia would have presented better outcomes and PH recordings?

Reply3: Our study had found that the lowest bladder temperature during DHCA was significantly lower in the patients with PH. So, we may conclude that a moderate hypothermia can have protection effect on the occurrence of PH. However, the impact of the DHCA strategy on the postoperative outcome would be more complicated. We can't conclude the relation between moderate hypothermia and better outcome in this study and we have not done this.

Changes in the text3: None.

4. There is an overly concerning factor and bias in the author's method and outcome reporting. This is related to authors not propagating data analysis in a non-mutually exclusive format. Hence, reporting Type A dissection and arch repair with CABG, MVR, TVR, and other cardiac-related procedures renders the outcome disjoint and the probability of their responses as a single coin toss. Please reshuffle the analysis to

cohort only pertained to have had dissection and aortic arch repair without the need for additional cardiac procedure as this surely would add to PH difference in derivation and reporting.

Reply4:

All the CABGs were performed because of coronary flow compromise due to dissection involvement, which is not uncommon in type A dissection. We think that the CABGs should be considered as part of the “root construction”. We believe it is important to investigate whether or not CABG would influence the occurrence of PH, because you may need to harvest the SVG and result in more heat loss. That’s why we did not exclude patients with CABG. And as you have mentioned, we did find the difference of PH in patients with and without CABG, which suggest a better rewarming strategy may be needed in this group of patients.

We have only a few patients (8) who underwent MVR, TVR and other kind of non-complicated cardiac surgery. All these procedures were performed during the cooling or rewarming period, which did not expand the duration of DHCA, and we assume limited impact on PH by these combined operations. And we did not find any difference in occurrence of PH in patients with and without these procedures.

Changes in the text: None.

5. How scientifically the authors constructed this study on two arms the PH vs non-PH? What methods compelled them to follow?

Reply5: The study was a case-control study in nature, as the aim was this study was to identify the risk factors for PH.

Changes in the text: None.

6. The authors acclaimed their primary endpoint was PH, defined as the bladder temperature < 36.0°C upon ICU admission after surgery. Why? What scientific justification/s for this? The comparable entity with postoperative tympanic recording would have been wise as used in the preoperative setting? Extrapolate!

Reply6: The postoperative hypothermia was defined as core body temperature less than

36.0°C in most publications and consensus. The bladder temperature is a widely accepted standard to represent the core body temperature. And our ICU nursing team records only the bladder temperature after the surgery with urinary catheter with temp probe already in situ. We do have some patients with preoperative bladder temperature but not all, because some patients were transferred into the OR after a few minutes stay in the ICU and no urinary catheter was inserted in the ICU. As a result, we use preoperative tympanic recording instead. That might be a limitation of our study, however, we believed that the difference between tympanic and bladder temperatures would be limited in the preoperative setting.

Changes in the text⁶: None.

7. What was the authors' overall skin -skin times over their bandwidth of operations performed and how did this correlate to end of the procedure, closure of sternotomy, the occurrence of bleeding per se before primary closure, trainee/fellows involvement (bias of different operators), anesthetic involvement and interventions to prevent convection heat loss, post-operative protocols for maintaining temperature normalcy, infusion of product at what temperature and the bias of contributors? Those are the confounding factors that would render the study unjustifiable and the approach and analysis utterly misleading.

Reply⁷:

We have demonstrated and analyzed the skin-to-skin time in table 2 without a significant difference between the two groups. As the CPB time were comparable between groups, we can assume no difference in time for chest closure between groups. We did not have the data of amount of bleeding per se before primary closure, however, we did have the RBC transfusion units demonstrated in table 2 without significant difference between groups. Most of the RBC units were order during the surgery in our practice, which could represent the comparable bleeding per se before primary closure. All these operations were performed by staffs who were specialized in aortic surgery. Chest closures were performed by staffs or clinical associates with expertise in all cases. The techniques including anesthetic involvement and interventions to prevent convection heat loss and post-operative protocols for maintaining temperature normalcy and rewarming, infusion of product was quite uniform in our protocol. We

have introduced the maintaining and rewarming protocol in detail in the discussion section.

Changes in the text7:

We added “All operations were performed by staff surgeons who were specialized in aortic surgery. Chest closures were performed by staffs or clinical associates with expertise in all cases.” in methods-surgical technique. See page10, line 140-143.

8. The authors yet again created a conflicting bias by stating that “The incidence of PH after total arch replacement in acute type A aortic dissection is relatively low”. I would recommend rewriting the discussion pertaining to your restructuring of the analysis and developing a stringent conclusion that best describe their objectives.

Reply8: Agree.

Changes in the text8: Please see response in reply 4.

Reviewer C

The authors conduct a study to investigate the incidence, risk factors of PH and its impact on early outcomes after arch surgery in acute type A aortic dissection

They conducted a retrospective cohort study in patients with acute type A aortic dissection who underwent total arch replacement from January 2013 to December 2016 at our institution.

300 patients (age 53.8 ± 11.5 years, female 63, 21.0%) were enrolled.

Forty-four patients (14.7%) developed PH. The independent risk factors of PH are age and the intraoperative lowest bladder temperature. There is no significant difference in major postoperative morbidity and mortality between patients with or without PH.

The authors concluded that incidence of PH after total arch replacement in acute type A aortic dissection is relatively low the PH is easy to be corrected, and the adverse effect of transient PH on early outcomes after arch surgery is minimal.

I congratulate the authors; the article is well write. This is a retrospective study conducted with a good methodology. The limitations are described. The authors affirmed that previous studies focused on this topic are limited and for this reason it is necessary to conduct this study to investigate the incidence of PH as well as its impact

on early outcomes after aortic arch surgery with DHCA.

I apologize but I think it is an article that not say anything news and it is not very interesting compared to other information in the literature.

Reply: Thank you.

Changes in the text: None.