

Peer Review File

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Reviewer A

In this submission, the authors aimed at investigating the impact of preemptive intubation under sedation and analgesia on the prognosis of patients with acute Type A dissection at rupture risk. This is a retrospective review covering the period 1/2019 – 1/2020. One hundred and eighteen patients were divided into two groups (25 pre-intubation and 93 non-intubation). There were no statistically significant differences in intra- and postoperative data after matching. Authors conclude by saying that preemptive intubation may benefit high-risk patients.

Some comments.

Comment 1: *Methods. The section has to be reorganized. The first subheading must be “Study design” where authors describe in detail the type of study they present the readership and not “Patients”.*

Reply 1: Thanks very much for your comments. We have made changes in the article.

Changes in the text: we have modified our text as advised (see Page 4, line 73)".

Comment 2: *The ethical aspects of the study must be clearly highlighted under separate subheading “Ethics”.*

Reply 2: Thanks very much for your comments. We have made changes in the article.

Changes in the text: we have modified our text as advised (see Page 5, line 91)".

Comment 3: *Data collection. Apparently and as described in the methods section, authors collected a number of variables such as age, BMI, comorbidities, LVEF, shock, pericardial effusion, etc. However, it does not look like they have collected an important parameter such as the time between the onset of symptoms and the time of the initiation of the operation. This is always a critical factor to understand outcomes.*

Reply 3: Thank you very much for your suggestion.

Changes in the text: We have added this important parameter according to your suggestion, as shown in Table 1

Comment 4: *Although this may sound clear for the authors, it may not for the readership, especially those who are not fully familiar with the topic. Then, authors should define what “preemptive” intubation is.*

Reply 4: Thank you very much for your suggestion.

Changes in the text: We have added this definition according to your suggestion (see Page 4, line 80-81)".

Comment 5: *It is interesting that authors consider (lines 92-93) patients who “were at risk of dissection rupture”. By definition, ALL patients with type A dissection ARE AT RISK of RUPTURE. This is why they have to be operated. Elaborate.*

Reply 5: Thank you very much for your suggestion. What you said is very professional. It is imperative to note that all patients diagnosed with dissections inherently face a heightened risk of rupture. However, we acknowledge that our current statement inaccurately portrays this risk and should instead emphasize a higher risk of rupture.

Changes in the text: we have modified our text as advised (see Page 4, line 85)".

Comment 6: *What is “long transfer”? Define.*

Reply 6: Thank you very much for your suggestion. We express our sincere gratitude for your valuable suggestion. It is worth noting that the distribution of medical resources in China exhibits significant disparities, particularly in the context of aortic dissection repair surgeries being performed in smaller hospitals without the necessary capacity for comprehensive treatment. Consequently, patients necessitate subsequent transfer to higher-level hospitals, a process that often entails prolonged waiting times for ambulance commanders.

Changes in the text: we have modified our text as advised (see Page 4, line 86-88)".

Comment 7: *What is “massive” pericardial effusion? Define.*

Reply 7: Thank you very much for your suggestion. We mainly evaluate the amount of pericardial effusion through echocardiography, when ultrasound shows a pericardial effusion thickness of 10-20mm and a volume of approximately 300-1000ml.

Changes in the text: not applicable.

Comment 8: *Results. Authors refer to those patients who “were excluded according to the exclusion criteria”. This is fine; however, there are no “inclusion/exclusion criteria” in the methods section. One only knows those patients who were intubated. Elaborate.*

Reply 8: Thank you very much for your suggestion.

Changes in the text: We have added this definition according to your suggestion (see Page 4-5, line 88-90)".

Comment 9: *If one uses the authors’ terms such as “massive” pericardial effusion, why those with “massive” were intubated and those with a “submassive” not?*

Reply 9: Thank you very much for your questions. In clinical practice, it has been observed that patients presenting with a significant volume of pericardial effusion are

at an increased risk of experiencing dissection rupture. This risk may be exacerbated by adverse factors such as cough and pain, rendering them more susceptible to rupture. Additionally, in cases where patients are diagnosed with sub-massive pericardial effusion and exhibit restlessness or difficulty in alleviating pain, the feasibility of pre-tracheal intubation is also recommended.

Changes in the text: not applicable.

Comment 10: *The rate of massive effusion in the intubation group was just a trend ($p=0.049$), namely marginal significance, if any.*

Reply 10: Thank you very much for your questions. Though the rate of massive effusion in the intubation group was just a trend ($p=0.049$), namely marginal significance, but, the rate between two groups was 28% vs 10.8%, We believe that the difference in pericardial effusion between the two groups is still statistically significant.

Changes in the text: not applicable.

Comment 11: *Why “28-day mortality”? This is not the internationally accepted period which is “30 day mortality”. Did authors consider patients who died beyond day 28 without being discharged? Furthermore, inter-hospital transfers do not count as discharges. This is important. Elaborate.*

Reply 11: Thank you for your questions. Both the 28 days and 30 days mortality rates are generally considered the most appropriate and meaningful endpoint, and it is widely used in clinical trials. We are considering using the 28 days mortality rate, mainly in weeks (4 weeks). If the patient dies after more than 28 days, we can consider more whether the patient is caused by infection or other factors, which is unlikely to be related to the variable factors studied. Therefore, we should consider more about the 28 days mortality rate.

Changes in the text: not applicable.

Comment 12: *Were there patients coming from other institutions already intubated?*

Reply 12: Yes, when the first hospital patients visited unconditionally undergo aortic dissection repair surgery, while it is necessary to transfer to our hospital for treatment, but at high risk of rupture through remote assessment, we will recommend preemptive intubation, deep sedation and analgesia, and then transfer to our hospital.

Changes in the text: not applicable.

Comment 13: *In lines 167-168 one can read “...patients were timely transferred to the operating room for surgical intervention...”. What is “timely”? As said, this timings are not shown in this submission.*

Reply 13: Thank you for your suggestion, “timely” here mainly refers to after the

preparation of relevant preoperative examinations, such as blood tests, drug sensitivity tests, and surgical personnel such as cardiac surgeons, anesthesiologists, and extracorporeal circulation specialists are ready to proceed, then sent to the operating room.

Changes in the text: not applicable.

Comment 14: *Limitations. Why do authors state “The clinical data may not be comprehensive enough”? What does this actually mean. Unclear. Elaborate.*

Reply 14: Thank you for your suggestion. Our study is a retrospective study, mainly focusing on some data such as preoperative blood gas analysis data loss or too many missing items.

Changes in the text: not applicable.

Comment 15: *Figures. Authors must confirm the time units in the KM curves.*

Reply 15: Thank you for your suggestion.

Changes in the text: We have modified our KM curves according to your suggestion (see figure 2 and 3)".

Comment 16: *The limitations are quite strong and render the submission in the weak side.*

Reply 16: Thank you very much for your suggestions, which have great help to our research. We will continue to improve our follow-up study, thank you again.

Changes in the text: not applicable.

Reviewer B

Overall, the authors should be commended for a rigorous study design and good data quality. The manuscript is written well, with only minor grammatical/syntax changes required.

Abstract - nil concerns.

Introduction - nil concerns.

Methods - all methodology appears valid, nil concerns.

Results - appropriately reported, nil concerns. Issues with outcomes as denoted below.

Comment 1: Discussion/outcomes/limitations - the principal issue with this study is the lack of generalisability of the data, in that not many variables yielded statistical significance. Additionally, as denoted by the KM curves, the 95% CI had substantial overlap - the authors rightly note that only a general trend can be appreciated. Given the lack of significance/generalisability, I would like the authors to provide more

detailed analysis in their discussion as to why this was not able to be reached, despite a number of statistical techniques/PSM. There does not appear to be any marked heterogeneity of the two cohorts, and the sample size at 136 is not too small - what do the authors therefore think accounts for this issue? This needs to be a focal point of the discussion section, if the article is to proceed to publication. The rationale for pre-emptive intubation is theoretically sound, but not supported by the findings.

Reply 1: We express our gratitude for your proposal. According to our expectations, we want to enter a more refined stage of management for aortic dissection patients through pre-emptive intubation. Reducing the pre-operative rupture rate is the main consideration of our study. There is indeed a difference in the pre-operative rupture rate between the two groups, but unfortunately, there is no significant difference in statistics

($p>0.05$). Perhaps we need a larger sample size and more cardiac centers to participate, and there may be a better research result. As for other clinical outcome, there are many factors that affect the outcome, and preoperative intubation may not affect the postoperative mortality rate and related complications.

Changes in the text: not applicable.