

Peer Review File

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Reviewer A

The authors have constructed a well thought study on a topic that has great interest for most cardiothoracic surgeons. The findings are very compelling.

Reply:

We feel grateful for the reviewer's warm comment.

Reviewer B

This paper demonstrated the prognosis of residual dissection in the descending aorta after surgical repair for acute type A aortic dissection.

So, I have some comment and question.

1. On page 4, lines 77 to 80, you describe the location of the intimal tear, but the name does not match the figure in FigureS1 and neither does the Legend. (Proximal/Middle/Lower or Upper thoracic/Lower thoracic/Abdomen?) Incidentally, the aorta of lower than the celiac artery is not a Lower descending aorta.

Reply:

Thank you for the reviewer's comment. We fully agree with this point. We revised as upper/lower thoracic and abdominal aorta.

Revision: (Page 7, Line 96-98)

1) Upper thoracic aorta (upper than the T7 spine), 2) Lower thoracic aorta (between the T7 and the celiac artery), or 3) Abdominal aorta (lower than the celiac artery).

2. For the graph in FigureS3, the order of the 3 colors in Legend and the order of the Bar are different. Also, the order of the three groups is different in Table1 and TableS1. If the order of the three groups is not standardized, readers may confuse the order of the three groups.

Reply:

We agree with the reviewer's comment. We revised to a single style (order) in the Tables and figures.

Revision: (Figure S4, Table 1, Supplementary tables)

3. It has previously been recognized that the IMH group has a lower expansion rate than the Classic and Retro groups and that the Retro group with remaining intimal tears has more aortic events than the IMH and Classic groups.

Reply:

Thank you for the advice. Regarding this issue, we expanded this issue in the Discussion and added reference.

Addition: (Discussion, Page 12 Line 231)

In particular, the tear near left subclavian artery is closely related to the distal aortic dilatation. (22)

Reviewer C

The authors present an interesting manuscript about the fate of the descending aorta after intervention for Acute type A aortic dissection.

I would like to congratulate the authors for the thorough analysis. I have some minor comments and questions for the authors.

What the authors mean by "total aortic arch replacement". Did you perform Elephant Trunk or Frozen ET procedure? In this case the proximal descending aorta would be treated at the time of the operation.

Reply:

Thank you very much for the reviewer's warm words. In the present study, "total arch replacement" indicates replacement of the arch with 3-branch vessels (Innominate, Lt carotid & subclavian) and the corresponding arch. The ET or FET were eliminated in the cohort. For more clarification, we expanded our explanation.

Addition: (Methods, Page 6, Line 88)

Among these, 134 (29.3%) patients who received simultaneous procedures on the descending aorta such as elephant trunk or stent insertions at the time of AD repair and 24 (5.3%) patients who were revealed as having genetic aortopathy were excluded.

What about the penetrating aortic ulcer? Why didn't you consider it as a separate entity? Why didn't patients with retrograde lesions have more extensive surgery at the time of their first operation?

Reply:

Penetrating aortic ulcer was regarded as same as one of the separated entry tears (Line 95). For the second question, we fully agree with the reviewer's point. The cohort, however, includes 10-years of our experiences, and there has been several modifications during the follow-up. In addition, it is regrettable that the use of FET graft has been only available from 2022 depending on our reimbursement system. As the reviewer commented, we are now more aggressive to perform extensive surgery for the Retro-type A AD, but it is true we have been conservative for those patients in the previous time.

In the classic group a distinction should be made between DeBakey type I or II dissection. Patients with retrograde dissection already have descending aortic disease unlike classic type I.

Reply:

All these patients are DeBakey type I. For more clarification, we listed this in the Method section.

Addition: (Methods, Page 6, Line 87)

From January 2009 to December 2018, 457 adult patients (aged >17 years) visited our center for acute TAAD (DeBakey type II were excluded).

Reviewer D

Thank you for presenting this retrospective observational study on residual dissection in the descending aorta following surgical repair of acute type A dissections at a single center. My primary concern pertains to the methodology employed for aortic measurements, as this constitutes a critical aspect of the study. Equally important are the confounding factors that might have impacted the results, potentially influencing the generalizability of the study findings.

Reply:

Thank you for the reviewer's comment. We will do our best to revise our manuscript.

Here are specific comments for your consideration:

1. Please consider rephrasing the conclusion sentence in the abstract to succinctly encapsulate the study's findings.

Revision: (Abstract, Page 3, Line 50)

The descending aorta growth was faster in Retro and Classic than IMH and related with the tear location.

2. Page 2, line 31: I recommend choosing either the term "endpoint" or "outcome" and maintaining consistency throughout the manuscript.

Reply:

We replaced “outcome” instead of “endpoint”.

3. Expound upon the surgical technique in more detail on page 4, line 87. It would be helpful to include specific tips or considerations for each type of acute dissection, as well as information on heparinization patterns, activated clotting time during procedures, and the types of grafts used. These aspects might have potentially influenced the results and should be addressed.

Reply:

Thank you for the advice, and we added this in the Method. For the type of grafts used, we don't have any specific preferences.

Addition: (Method, Page 7, Line 110)

After sternotomy, we give 200 unit/kg of heparin. During cardiopulmonary bypass, occasional 50~100 unit/kg of heparin are added to target 400 sec of activated clotting time.

4. The central concern that necessitates addressing is the methodology employed for aortic measurements. Was a core-lab utilized for this purpose? Please specify the detailed protocol in the methods section and discuss potential risks related to inter- and intra-observer reliability. Additionally, provide information on how discrepancies in inter-observer measurements were managed.

Reply:

We fully agree with the reviewer's point. We discussed this issue a lot with radiologists in the setting of initial design of study and performed several efforts to reduce potential confounders. We set measurement protocol as a diameter of external layer of the maximal size of descending aorta (Line 119-120). To get a perpendicular diameter measurement, we used a reconstructed CT image regarding the vectors of central route of the descending aorta.

For inter-observer reliability issue, all the measurements were performed by one author, and the other author measured it again. If there was a significant gap between two measurements, we consulted special radiologists to be confirmed. For intra-observer reliability issue, we performed mixed effect model to regard fixed and random effects. As the measurements were continuous variables, we conducted the linear mixed model (Line 138). For more clarification, we expanded our measurement protocols.

Addition: (Method, Page 8, Line 128)

Our measurement protocols for descending aorta are as follows. The maximal external aortic diameter was measured in the perpendicular axis of aortic course using the enhanced planar CT images. To obtain perpendicular axis, CT images were reconstructed parallel to the vectors of central route of the descending aorta. The reconstructed images were generated by a computer program (Zetta PACS, TaeYoung Soft, Anyang-si, Korea) under the supervision of radiologists. To reduce inter-observer gap in the measurement, all the measurements were performed by one author, and the other measured it again. If there was a significant difference between two measurements, we consulted to a special radiologist to be confirmed.

Addition: (Limitation, Page 14, Line 280)

Despite our efforts to reduce bias in the aortic measurements, there could be remaining inter- and intra-observer diversity in the measurement.

5. Kindly mention the imaging program used for the measurements. Were the measurements conducted on contrast-enhanced planar reconstructions or on 3D reconstructions?

Reply:

We used Zetta PACS (TaeYoung Soft, Anyang-si), and the measurement were conducted on planar images.

Addition: (Method, Page 8, Line 131)

The reconstructed images were generated by a computer program (Zetta PACS, TaeYoung Soft, Anyang-si, Korea) under the supervision of radiologists.

6. Reflect upon the validity of assuming the fair nature of this assessment, as stated in lines 105-106 on page 4. Could there be any cross-validation with autopsy data?

Reply:

As we conducted retrospective and observational study, it is regretful that there is no cross-validation of autopsy data.

7. An important addition would be Kaplan-Meier curves, illustrating both overall survival and aneurysm-related deaths.

Reply:

Thank you for the reviewer's valuable point, but this may be out of scope in the present study (descending aorta change). We will add KM-plot in the following study regarding survival or any clinical issues.

8. It's intriguing that the results reveal no difference between classic and intramural hematoma acute dissections concerning aortic growth and secondary interventions. This observation might suggest that they represent distinct entities from retrograde dissections. I recommend discussing this point in the discussion section.

Reply:

This is exactly same point to our understanding through the present evaluation. We further expanded this issue in the discussion.

Addition: (Discussion, Page 12, Line 237)

This observation might suggest that the Retro type of AD has a distinct entity from Classic or IMH.

9. Another notable limitation is the absence of data on key confounding factors such as blood pressure (systolic and diastolic), heart rate, smoking habits, and medication usage.
10. Could you please provide information about the post-surgery prescription of antiplatelet or anticoagulation therapies? Additionally, specify any other medications administered, such as statins, antihypertensive agents, and beta-blockers.

Reply:

This is added in the limitation. For anticoagulation or antiplatelet therapy, regrettably we are not recognizable for these as it may be prescribed by another center. We have no specific protocol to give anticoagulation for these patients.

Addition: (Limitation, Page 14, Line 273)

The absence of data on blood pressure, heart rate, and medication usage may be a hidden confounders for the study outcomes.

Reviewer E

The objective of the study under review is pertinent and timely as it aims to address the residual descending aortic dissection (AD) following acute type A AD (TAAD) repair, a topic that hasn't been widely reported. Since the sample size was resonable, I believe this paper is substantially worth spreading.

Reply:

Thank you for the reviewer's comment.

Comments and Suggestions:

Title:

Though the title clearly reflects the content of the study, I think that the title lacking in assertiveness. I recommend the title of this paper is "Fate of Descending Aorta after Acute Type A Aortic Dissection Repair" alternatively.

Reply:

We agree with this recommendation. We modified the title.

Revision: (Title)

Fate of Descending Aorta after Acute Type A Aortic Dissection Repair

Inclusion Criteria Clarification:

Your classification is based on dissection subtypes, but it remains unclear if cases where the dissection can be completely replaced with an artificial vessel post-initial treatment are incorporated. For clarity and transparency, please explicitly state this in your inclusion criteria.

Intervention Details:

It's mentioned that patients who underwent concomitant procedures on the descending aorta were excluded, but it would be beneficial to clarify whether interventions like the Frozen Elephant Trunk (FET) technique are part of these. The use of FETs in TAR for TAAD is a common treatment method and should not be excluded.

Reply:

We think these two comments are on the same issue. We modified Method section for more clarification.

Revision: (Method, Page 6, Line 87)

From January 2009 to December 2018, 457 adult patients (aged >17 years) visited our center for acute TAAAD (DeBakey type II were excluded). Among these, 134 (29.3%) patients who received simultaneous procedures on the descending aorta such as elephant trunk or stent insertions at the time of AD repair and 24 (5.3%) patients who were revealed as having genetic aortopathy were excluded.

Figures:

Based on the abstract, the significance of Figure 1A isn't immediately clear. If this figure isn't pivotal to the study's conclusions, consider eliminating it to streamline the presentation. Instead, prioritize Figure 1B and Figure 2.

Reply:

We agree with the reviewer's point. However, as every individual measurement of aorta (previous Figure 1A) was included in the linear mixed model, we transferred this figure to supplementary.

Transfer: (Figure S2)

Additional Data Points:

It would enrich the study's depth if information about the thrombosis of the false lumen, the location of the reentry, and any instances of malperfusion were incorporated. These details can provide a comprehensive picture of the patient's condition and potential complications.

Reply:

We understood the reviewer's point. These variables, however, are substantially diverse for every patient, and which are unavailable to categorize into few groups. In this regard, many prior publications with retrospective observational data regard primary entry tear as a risk factor rather than secondary or tertiary entries (For instance, *Circulation* 2012;125:3133-41. *Eur J Cardiothorac Surg* 2012;42:571-6. Etc...). In addition, some tiny entry tears are only recognizable in fine-sliced CT scan which is not used in previous time.

Mortality Details:

The provided abstract does not specify the number of cases that resulted in premature deaths. Considering the findings from the *JAMA Cardiology* article, which reported a mortality rate of 5.8% for patients with TAAAD in the first 48 hours[1], it would be essential for the study to include this detail for comparison and context.

Reply:

The reviewer is right. We expanded this issue in the revised manuscript. However, this is not included in the abstract due to the word number limitation.

Addition (Result, Page 10, Line 179)

Immediate (<48 hours) and early (<30 days) deaths occurred in 7 (2.3%) and 24 (8.0%) patients, respectively. Of these, 4 (1.3%) had the first postoperative CT scans.

Conclusions:

While the conclusion establishes the significance of monitoring the descending aorta based on subtypes, it lacks recommendations for clinical application. A stronger conclusion would provide guidance on how this data might be used in patient management, surgical decisions, or prognosis.

Reply:

Thank you for the reviewer's advice. We added conclusion below the discussion section.

Addition (Conclusion, Page 13, Line 267)

The descending aorta growth was faster in Retro and Classic than IMH and related with the tear location. Careful assessment on the tear locations in descending aorta is warranted for the initial acute type A AD repair plan as well as the postoperative follow-up.

Concluding Remarks:

This study offers valuable insights into the behavior of the descending aorta post TAAD repair. Addressing the aforementioned comments can further enhance the paper's clarity and its clinical applicability. The authors are encouraged to consider these suggestions for the betterment of the final manuscript.

I hope this review helps improve the quality of your research. If there are further queries or clarifications needed, please don't hesitate to reach out.

Reply:

Thank you for the reviewer's encouragement.

Reviewer F

This paper evaluates the long-term imaging course of residual dissection after initial surgery for acute aortic dissection by anatomically dividing the descending aorta into

three locations. Furthermore, I think it is an interesting paper that evaluates as follows: 1) Classic, 2) Retro, and 3) IMH as a classification of dissection.

1. We understand that residual intimal tear in the proximal descending aorta are the factor of aortic events after the first surgery, but we believe that it is natural that the retro group increases in the form of dissection.

Reply:

Thank you for the reviewer's comment. We started this study in the same suggestion of the reviewers. we expanded this in the discussion.

Addition (Discussion, Page 12, Line235)

In the present study, the proximal entry tear in the remaining descending aorta (above T7 spine level) were observed in 19.5%, 14.3% and 77.3% of the patients with Classic, IMH and Retro types of AD, respectively. This observation might suggest that the Retro type of AD has a distinct entity from Classic or IMH. We carefully surmise that this gap may be a principal inducer of the gradually stratified growth of descending aorta depending on the types of AD (Retro>Classic>IMH).

2. The author referred to the problem of the long-term, including the reentry of type B dissociation, in his discussion, but I think that if that is the case, it would be quite biased to consider IMH as an evaluation item equally.

Reply:

This issue has been debated over a decade as some investigators argue that the IMH is a different type of disease from AD (J Cardiol. 2014 Sep;64(3):153-61.). Nevertheless, it is more common that IMH is also one of the types of AD because the current clinical guidelines do not regard IMH separately from other types of Ads (Circulation. 2022;146:e334–e482). In addition, we regarded ulcerations in IMH as an entry tear in our cohort which often we find as a trigger to progress to the dissection during follow-up.

3. Do you use a conventional elephant trunk or frozen elephant trunk during total arch replacement? Please add it to the details of the surgical procedure if possible. (P4 line 87)

Reply:

The ET or FET were eliminated in the cohort. For more clarification, we expanded our explanation.

Addition: (Methods, Page 6, Line 87)

Among these, 134 (29.3%) patients who received simultaneous procedures on the descending aorta such as elephant trunk or stent insertions at the time of AD repair and 24 (5.3%) patients who were revealed as having genetic aortopathy were excluded.

4. Based on the results of this study, please consider whether you considered changing the surgical strategy based on the preoperative image evaluation at the time of the first surgery.

Reply:

Thank you for the reviewer's comment. As we listed in the manuscript "Given recent advance in the vascular graft materials, we have many options to cover the descending aorta through the sternotomy approach such as the concomitant frozen elephant trunk insertion during the upstream aorta repair." (Discussion, Line 259, Page13), we have more aggressive plan to cover when the tear exists in proximal descending aorta. Recent development of distally stented surgical graft for total arch replacement with FET gives us many advantages to treat these patients. We expanded this in the Conclusion.

Addition (Conclusion, Page 13, Line 267)

The descending aorta growth was faster in Retro and Classic than IMH and related with the tear location. Careful assessment on the tear locations in descending aorta is warranted for the initial acute type A AD repair plan as well as the postoperative follow-up.