Reviewer A

Comment 1: I had an opportunity to review the first revised version of this manuscript. This is a single-center cohort study to assess the influence of preoperative cerebral ischemia (CI) on the outcome of patients with acute type aortic dissection (aTAAD). This study includes relatively a large number of patients (total n=1175), and analyzed many variables how the presence of CI affected the outcomes. Overall this manuscript was very well written and presented with robust statistical data set, and the conclusion was clear. The messages derived from this study would be very informative with great value of evidence. I have nothing to add on.
Reply 1: Thanks for your comments.
**Change in the text:** No change.

Reviewer B
The authors present their data on acute type A aortic dissection with or without cerebral ischemia. Based on their findings, central repair was effective in patients with cerebral ischemia, while patients with coma resulted in poor outcomes. Suggestion was also made on the timing of the surgery in which reperfusion to the cerebral tissue should be performed before 12.75 hours after onset.

These could be important information. However, as the authors mentioned in their manuscript, prompt surgery for patients with aortic dissection, especially in those with cerebral ischemia, has been suggested in many previous reports. Before considering this manuscript for publication, the authors should reconsider their study design, especially the analysis. Present data and analysis may not support the authors' conclusion.

Comment 1: One of the important data in this paper is the ROC curve analysis. Transient ischemia and coma are totally different pathology. The authors should differentiate these 2 conditions in their ROC curve analysis.
Reply 1: Thanks for your comments. I have analyzed again in the separate transient ischemia and coma group, the results are as follows.

Neurological outcome--Transient ischemia
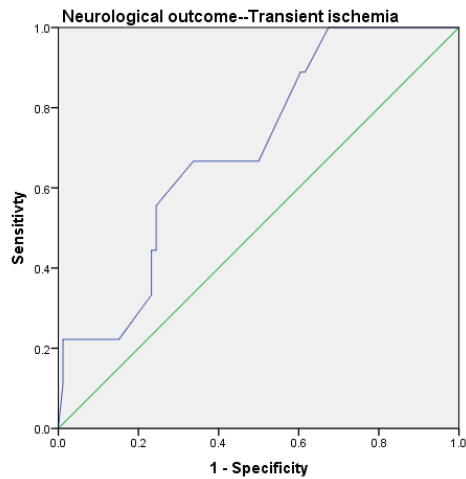
Area under curve	0.697
P value	0.053
Cut-off point	12.75hours
Sensitivity	66.7%
Specificity	33.7%

Neurological outcome-Coma group
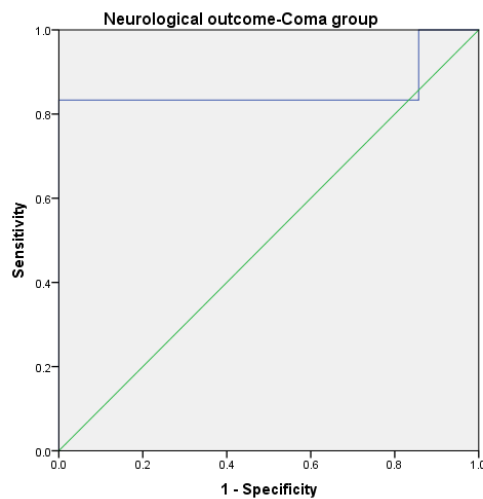
Area under curve	0.857
P value	0.032
Cut-off point	12.75hours
Sensitivity	83.3%
Specificity	0%

The results tend to be non-significant even with the same cut-off point, but the specificity is not good. The final results are just the same as the original, but as numbers in each group are not enough, which could influence the results, I have not changed into the results as the reviewer's suggestions.

Change in the text: I have revised the description of results about safe duration.

Comment 2: Were there any differences in the entry site and prevalence of re-entry

between patients with and without cerebral ischemia. What about patients with persistent ischemia and transient ischemia. Also, were there any differences in thrombosed and non-thrombosed false lumen between patients with and without cerebral ischemia.

Reply 2: Thanks for your comments. The results of the entry and re-entry site between cerebral ischemia and non-cerebral ischemia (P=0.10), and between persistent and transient ischemia (P=0.15) were not different, and the same as the differences in thrombosed lumen (P=0.1).

Change in the text: No change. The results could not support the conclusions from this research.

Comment 3: Although the timing of surgery is an important factor, surgical strategy is another important factor to treat patients with malperfusion. Central repair is probably the most effective and important treatment. However, this was not performed in some patients presented with CI. The authors should provide the reason for this.

Reply 3: Thanks for your comments. I agree with you. In this cohort, total 131 patients with preoperative cerebral ischemia had been included in this research. 108 patients in the 131 received surgical repair, while the other 23 patients refused surgery. The main reasons for refusing surgery were preoperative rupture, family refusing and comorbidity diseases (I have mentioned in Line 94-95).

Change in the text: No change.

Comment 4: The authors should provide more information on how they performed the surgery. (ex. CPB plan, cannulation strategy, temperature management, cerebral protection strategy). How did the authors monitor cerebral perfusion during surgery? What was the reperfusion strategy for cerebral ischemia? (ex. was perfusion to the axillary artery or carotid artery performed prior to central repair?)

Reply 4: Thanks for your comments! But we have not tried to apply reperfusion methods before central repair in this cohort.

Change in the text: I have revised from Line 104-109.

Comment 5: Reperfusion injury to the ischemic brain tissue is sometimes observed in patients with severe cerebral ischemia which may result in cerebral edema or cerebral hemorrhage requiring craniotomy. What is the authors' strategy for reperfusion? Is the brain re-perfused totally in all the cases?

Reply 5: Thanks for your comments! 15 patients with CC after surgery were all thought to be induced by ischemic reperfusion brain injury, two of them received craniotomy. I'm so sorry we don't have any new points about the strategy for reperfusion except conventional brain dehydration treatment.

Change in the text: No change.

Comment 6: The authors defined cerebral complication as "positive finding on CT/MRI or physical findings." What about patients who have no symptoms but may have positive findings on CT, which are often observed in clinical practice.

Reply 6: Thanks for your comments! Cranial CT/MRI is not a regular check after aTAAD surgical repair, thus we don't do this without positive symptoms. But thanks for your questions, I think it's important that we have to regularly check cranial CT or MRI after operation.
Change in the text: No change.

Comment 7: Line 265-267: Thrombolysis using intravenous tissue plasminogen activator is not a traditional method in patients with aortic dissection, and for those patients who may need surgery.
Reply 7: Thanks for your comments! I agree with you. Just as I mentioned in the discussion part, tPA therapy was an option for thrombolysis for patients with acute cerebral infarction, but maybe not suitable for aTAAD patients concomitant with cerebral ischemia, endovascular treatment is the first line choice.
Change in the text: No change.

Comment 8: (Line 209) "Patients with CI had been considered as contraindications for open central repair." If this is true, the authors should provide a reference. Many papers suggest early surgery for patients with cerebral ischemia. Again, the authors should distinguish transient type ischemia from persistent type.
Reply 8: Thanks for your comments! I agree with you. This sentence is not exact.
Change in the text: I have deleted this one.

Comment 9: The authors concluded that reperfusion strategy for cerebral ischemia should be performed in patients with coma. However, the authors only showed data on 3 patients who performed stent treatment. Only 1 survived, which does not support their conclusion.
Reply 9: Thanks for your comments! I agree with you. Actually, we have treated more patients with cerebral reperfusion first in 2020, and the results were excellent. But just like your opinion, the data in this manuscript could not reflect the conclusion that coma patients are suitable for receiving cerebral reperfusion first strategy. I have explained in the manuscript that coma patients could not reached our hospital within 15 hours and the outcomes of central repair were not so good that we have to have a relative safe duration.
Change in the text: No change.

Comment 10: If this study was performed following treatment strategy shown in figure 6, then the authors may present this figure. However, due to retrospective aspect of the paper and with small sample size, there are not enough data to present this figure as a statement.
Reply 10: Thanks for your comments!
Change in the text: I have deleted Figure 6 to avoid misunderstanding.

Comment 11: The authors concluded that patients with persistent type or those with coma should have their brain reperfused before 12.75 hours. Again, I believe ROC

curve analysis included patients with transient type. Generally thinking, 12 hours seems to be too long for patients in coma.

Reply 11: Thanks for your comments! I agree with you. 12 hours may be a safe duration with a weak association, but according to the previously reports and the experiences from neurology, and of course we have to realize the reality in China, which is we can't transfer patients to the central hospital as quickly as possible. So, we have raised a 'longer' safe duration.

Change in the text: No Change.

Comment 12: There are grammatical errors throughout the whole manuscript which makes it hard to follow.

Reply 12: Thanks for your comments!

Change in the text: I have sent the revised manuscript to an assisting language checker, some grammatical errors had been revised.