

## Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-23-990>

### Reviewer A

I appreciate author's efforts. The authors evaluated the surgical outcomes between the patients with coronary artery involvement (CAI) and non-CAI in acute type A aortic dissection. Surgical outcomes for acute type A aortic dissection with CAI are very poor compared to with non-CAI because of coronary artery malperfusion associated with devastated myocardial ischemia. The authors concluded that the patients with CAI had higher in-hospital mortality and morbidity compared to non-CAI, but short-term survival was comparable. However, this study required the major revisions as following reasons.

**Comment 1:** In the Introduction section, the authors stated that 'of note, this procedure has an inevitable tendency toward prolonging cardiopulmonary bypass and cross-clamp time, thereby adding myocardial ischemia duration correspondingly.' Did this include a meaning that the total arch replacement with frozen elephant trunk increases the cardiopulmonary bypass and cross-clamp time compared to conventional total arch replacement? I think that this information is wrong because many reports showed that the total arch replacement with frozen elephant trunk is comparable or superior compared to conventional total arch replacement, owing to distal anastomosis of zone 1 or 2 and inner reinforcement by open stent graft which led the less bleeding and decreasing operation time. Then, please revise the sentence. Moreover, the authors should describe the introduction more focusing on CAI and coronary artery malperfusion.

**Reply 1:** Thank you very much for bringing up this important question. We have described TAR with or without FET implantation as an "aggressive arch surgical technique" or "extended arch replacement", as opposed to ascending aortic or hemiarch replacement. What can be determined at present is that extended arch replacement is associated with prolonged cardiopulmonary bypass time and cross-clamp time<sup>1,2</sup>. It's apparent that our description in the manuscript has led to some misunderstandings, so we have made some modifications.

You mentioned that the application of FET may reduce intraoperative bleeding and operation time. Based on our clinical practice experience and previous literature reports, in terms of intraoperative conditions, when comparing TAR+FET to TAR alone, there is no significant difference in CPB time, cross-clamp time, or circulatory arrest time<sup>3</sup>. However, the use of FET covers the fragile anastomosis at the distal end of the arch affected by dissection, which indeed contributes to a reduction of intraoperative bleeding and hemostasis time<sup>4</sup>.

In addition, we may have included too much description of arch procedure in the Introduction section. In this revision, we have made some adjustments.

References

- (1) Larsen, M.; Trimarchi, S.; Patel, H. J.; Di Eusanio, M.; Greason, K. L.; Peterson, M. D.; Fattori, R.; Hutchison, S.; Desai, N. D.; Korach, A.; Montgomery, D. G.; Isselbacher, E. M.; Nienaber, C. A.; Eagle, K. A.; Bartnes, K.; Myrmet, T. Extended versus Limited Arch Replacement in Acute Type A Aortic Dissection. *Eur. J. Cardio-Thorac. Surg. Off. J. Eur. Assoc. Cardio-Thorac. Surg.* **2017**, *52* (6), 1104–1110. <https://doi.org/10.1093/ejcts/ezx214>.
- (2) Chen, S.-W.; Chen, Y.; Ma, W.-G.; Zhong, Y.-L.; Qiao, Z.-Y.; Ge, Y.-P.; Li, C.-N.; Zhu, J.-M.; Sun, L.-Z. Limited vs. Extended Repair for Acute Type I Aortic Dissection: Long-Term Outcomes over a Decade in Beijing Anzhen Hospital. *Chin. Med. J. (Engl.)* **2021**, *134* (8), 986–988. <https://doi.org/10.1097/CM9.0000000000001416>.
- (3) Poon, S. S.; Tian, D. H.; Yan, T.; Harrington, D.; Nawaytou, O.; Kuduvalli, M.; Haverich, A.; Ehrlich, M.; Ma, W.-G.; Sun, L.-Z.; Estrera, A. L.; Field, M.; International Aortic Arch Surgery Study Group. Frozen Elephant Trunk Does Not Increase Incidence of Paraplegia in Patients with Acute Type A Aortic Dissection. *J. Thorac. Cardiovasc. Surg.* **2020**, *159* (4), 1189-1196.e1. <https://doi.org/10.1016/j.jtcvs.2019.03.097>.
- (4) Uchida, N.; Shibamura, H.; Katayama, A.; Shimada, N.; Sutoh, M.; Ishihara, H. Operative Strategy for Acute Type a Aortic Dissection: Ascending Aortic or Hemiarch versus Total Arch Replacement with Frozen Elephant Trunk. *Ann. Thorac. Surg.* **2009**, *87* (3), 773–777. <https://doi.org/10.1016/j.athoracsur.2008.11.061>.

**Changes in the text:** On page 4 line 5-7, line 9-12, and line 15-18, which now reads:

In our perspective, CAI demonstrates an unstable state, which may be confined to the coronary ostium without compromising blood flow or may progress to coronary artery malperfusion (CAM) at any time, causing myocardial ischemia or even catastrophic myocardial infarction.

Prompt surgical repair constitutes the primary life-saving approach for patients with ATAAD<sup>1</sup>. However, there is still some controversy regarding the optimal strategy for coronary revascularization, particularly the choice between coronary ostial repair (COR) and coronary artery bypass grafting (CABG).

Of note, as an aggressive arch surgical technique, compared to ascending aortic or hemiarch replacement, it has an inevitable tendency toward prolonging cardiopulmonary bypass (CPB) time and cross-clamp time<sup>2</sup>, thereby adding to the myocardial ischemia duration correspondingly.

## References

- (1) Isselbacher, E. M.; Preventza, O.; Black, J. H.; Augoustides, J. G.; Beck, A. W.; Bolen, M. A.; Braverman, A. C.; Bray, B. E.; Brown-Zimmerman, M. M.; Chen, E. P.; Collins, T. J.; DeAnda, A.; Fanola, C. L.; Girardi, L. N.; Hicks, C. W.; Hui, D. S.; Jones, W. S.; Kalahasti, V.; Kim, K. M.; Milewicz, D. M.; Oderich, G. S.; Ogbechie, L.; Promes, S. B.; Ross, E. G.; Schermerhorn, M. L.; Times, S. S.; Tseng, E. E.; Wang, G. J.; Woo, Y. J. 2022 ACC/AHA Guideline for the Diagnosis and Management of

Aortic Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation* **2022**. <https://doi.org/10.1161/CIR.0000000000001106>.

(2) Poon, S. S.; Theologou, T.; Harrington, D.; Kuduvalli, M.; Oo, A.; Field, M. Hemiarch versus Total Aortic Arch Replacement in Acute Type A Dissection: A Systematic Review and Meta-Analysis. *Ann. Cardiothorac. Surg.* **2016**, *5* (3), 156–173. <https://doi.org/10.21037/acs.2016.05.06>.

**Comment 2:** In the Operative techniques section, how did the authors reconstruct the left subclavian artery? Anatomical or anti-anatomical (bypass to the left axillary artery)?

**Reply 2:** Thank you so much for pointing out such a significant issue. For all patients included in the current study who underwent total arch replacement and frozen elephant trunk implantation, we performed anatomical reconstruction of the left subclavian artery. In rare cases where the left subclavian artery is too adherent to be dissociated or the wall of the vessel is too fragile to be sutured due to the dissection progression, we may choose to ligate the proximal end and perform an end-to-side anastomosis between the vascular graft and the left axillary artery for the purpose of reconstruction. In this revision, we have mentioned specific method to reconstruct.

**Changes in the text:** On page 7 line 11, which now reads:

Finally, the left subclavian artery and the innominate artery were anatomically reconstructed.

**Comment 3:** In the Operative techniques section, did the authors use the retrograde cardioplegia? If the patients had coronary artery malperfusion by acute type A aortic dissection, the retrograde cardioplegia is a better method owing to perfuse the coronary artery properly compared to antegrade cardioplegia.

**Reply 3:** Your precious comment is gratefully appreciated and we will clarify this point in the context of our center. In fact, acceptable myocardial protection can be achieved with either antegrade cardioplegia<sup>1,2</sup> or retrograde cardioplegia<sup>3,4</sup>. As we described in the “Operative techniques” section, antegrade cardioplegia was used in all patients, considering it to be a simple and rapid way to induce cardiac arrest. Our antegrade perfusion strategy included two approaches. Firstly, for patients with less severe CAI, we delivered cardioplegia through the ostia of both the left and right coronary arteries. Secondly, in cases of severe CAI with elevated direct antegrade perfusion pressure, we prioritized CABG and achieved myocardial protection by perfusing through the bypass graft.

In patients with severe CAI, retrograde cardioplegia also serves as an alternative option that avoids damage to the coronary ostia and saves time compared to CABG. However, there are also some challenges, such as myocardial edema and inadequate right ventricular myocardial protection<sup>5</sup>. In our future practices, we intend to explore the use of retrograde cardioplegia in certain patients as well.

## Reference

- (1) Qin, W.; Fan, R.; Wang, J.; Li, J.; Huang, F.; Chen, X. Outcomes of Surgical Treatment on Type A Acute Aortic Dissection Accompanied with Coronary Artery Involvement. *Front. Surg.* **2022**, *9*, 950264. <https://doi.org/10.3389/fsurg.2022.950264>.
- (2) Kreibich, M.; Bavaria, J. E.; Branchetti, E.; Brown, C. R.; Chen, Z.; Khurshan, F.; Siki, M.; Vallabhajosyula, P.; Szeto, W. Y.; Desai, N. D. Management of Patients With Coronary Artery Malperfusion Secondary to Type A Aortic Dissection. *Ann. Thorac. Surg.* **2019**, *107* (4), 1174–1180. <https://doi.org/10.1016/j.athoracsur.2018.09.065>.
- (3) Kayali, F.; Jubouri, M.; Al-Tawil, M.; Tan, S. Z. C. P.; Williams, I. M.; Mohammed, I.; Velayudhan, B.; Bashir, M. Coronary Artery Involvement in Type A Aortic Dissection: Fate of the Coronaries. *J. Card. Surg.* **2022**. <https://doi.org/10.1111/jocs.16981>.
- (4) Kawahito, K.; Adachi, H.; Murata, S.; Yamaguchi, A.; Ino, T. Coronary Malperfusion Due to Type A Aortic Dissection: Mechanism and Surgical Management. *Ann. Thorac. Surg.* **2003**, *76* (5), 1471–1476; discussion 1476. [https://doi.org/10.1016/s0003-4975\(03\)00899-3](https://doi.org/10.1016/s0003-4975(03)00899-3).
- (5) Whittaker, A.; Aboughdir, M.; Mahbub, S.; Ahmed, A.; Harky, A. Myocardial Protection in Cardiac Surgery: How Limited Are the Options? A Comprehensive Literature Review. *Perfusion* **2021**, *36* (4), 338–351. <https://doi.org/10.1177/0267659120942656>.

**Comment 4:** Recent data analysis mainly uses the expression of median [interquartile range] rather than mean±SD because common data is not consisted of normal distribution. In this study, the authors used both median and mean expressions. Therefore, the expression of data, including table, should be unified as median.

**Reply 4:** Thank you for your valuable comments on the article. In this revision, we have modified the tables as well as the expression of data in the article as suggested.

**Changes in the text:** On page 7 line 15-16, which now reads:

Continuous variables are denoted as medians (interquartile ranges), and were compared by Mann-Whitney U test.

On page 8 line 3-5, which now reads:

In our cohort of 204 patients, 67 (32.8%) with a median age of 53.0 years were eventually diagnosed with CAI, among whom 56 (83.6%) were men. Patients in the CAI group appeared to have higher creatinine levels (87.6 [72.4, 111.9] vs. 77.9 [65.0, 97.1],  $P=0.02$ ).

Table 1(partial). Demographics and preoperative characteristics

Variable	CAI group (n=67)	Non-CAI group (n=137)	<i>P-value</i>
----------	---------------------	--------------------------	----------------

Age(y)	53.0 (44.0, 58.0)	50.0 (40.0, 57.0)	0.08
BMI(kg/m <sup>2</sup> )	25.3 (23.5, 28.4)	26.4 (24.2, 29.4)	0.07
Creatinine(μmol/L)	87.6 (72.4, 111.9)	77.9 (65.0, 97.1)	0.02*
Echocardiography			
LVEF(%)	62.0 (60.0, 65.0)	63.0 (60.0, 65.0)	0.64
LVEDD(mm)	49.0 (45.0, 54.0)	48.0 (44.0, 52.0)	0.29

Values are presented as n (%), mean±SD, or medians (interquartile ranges).

**Table 2(partial). Operative characteristics**

Variable	CAI group (n=67)	Non-CAI group (n=137)	P- value
Rectal temperature(°C)	25.4 (24.7, 26.3)	25.4 (24.5, 26.7)	0.67
Nasopharyngeal temperature(°C)	24.6 (24.2, 25.0)	24.6 (24.0, 25.2)	0.82

Values are presented as n (%), mean±SD, or medians (interquartile ranges).

**Comment 5:** Was this study verified by statistician? Please receive the verification of statistician.

**Reply 5:** Thank you for your valuable suggestions. Prior to this revision, we sought advice from a professional statistician, who raised certain concerns regarding our multivariable logistic regression analysis. Given our limited sample size and small number of positive outcome events, it would be inappropriate to include all variables related to CAI in the multivariable analysis. Therefore, in this revision, we conducted a multivariable analysis by separately incorporating the variables associated with CAI, aiming to obtain the corresponding OR values, 95% CIs, and P-values. We adjusted for variables based on univariable analysis with P<0.05 and established risk factors from previous studies.

**Changes in the text:** On page 7 line xx-xx, which now reads:

Univariable analysis was performed first to select clinically relevant variables (P<0.05), which were then included along with previously reported risk factors in the multivariable analysis for adjustment to ascertain independent risk factors (P<0.05) for operative mortality.

On page x line xx-xx, which now reads:

After multivariable adjustment for male sex, age, BMI, amylase, AAR, CPB time, and cross-clamp time, CAM was identified as an independent risk factor for operative mortality (OR, 12.221; 95% CI, 3.047-49.040; P<0.001), as shown in Table 5.

**Table 5. Univariable and multivariable analyses for in-hospital mortality**

Variable	Univariable analysis		Multivariable analysis <sup>†</sup>	
	OR (95%CI)	P- value	OR (95%CI)	P- value

CAI	2.771 (1.130-6.794)	0.026	<u>1.379 (0.566-4.457)</u>	<u>0.379</u>
Neri classification				
A	0.876 (0.182-4.214)	0.869	<u>0.565 (0.105-3.036)</u>	<u>0.505</u>
B	4.618 (1.642-12.988)	0.046	<u>3.160 (0.914-10.927)</u>	<u>0.499</u>
C	6.350 (1.034-39.009)		<u>2.372 (0.193-29.113)</u>	
CAI side				
Isolated left	NA	NA	<u>NA</u>	<u>NA</u>
Isolated right	1.814 (0.582-5.655)	0.304	<u>1.047 (0.284-3.860)</u>	<u>0.944</u>
Bilateral	4.939 (1.669-14.612)	0.004	<u>3.251 (0.787-13.438)</u>	<u>0.103</u>
CAM	12.955 (4.591-36.552)	<0.001	<u>12.223 (3.047-49.040)</u>	<u>&lt;0.001</u>
Management				
COR	2.174 (0.808-5.846)	0.124	<u>1.675 (0.564-4.980)</u>	<u>0.353</u>
CABG	4.875 (1.631-14.569)	0.005	<u>1.050 (0.173-6.362)</u>	<u>0.958</u>
Salvage CABG	7.867 (1.937-31.944)	0.004	<u>2.649 (0.357-19.661)</u>	<u>0.341</u>

†Adjusted for male sex, age, BMI, amylase, AAR, CPB time, and cross-clamp time.

OR, odds ratio; CI, confidence interval.

CAI, coronary artery involvement; CAM, coronary artery malperfusion; COR, coronary ostium repair; CABG, coronary artery bypass grafting.

**Comment 6:** In the Results section, treatment of CAI is unclear and confused. The authors should describe the coronary artery repair techniques each type of Neri classification clearly.

**Reply 6:** We apologize for not stating this paragraph clearly. In this revision, we tried to describe our surgical management based on Neri classifications.

**Changes in the text:** On page 9 line 1-7, which now reads:

Among the 67 patients in the CAI group (Table 3), isolated right CAI (40/67, 59.7%) was the most common, followed by bilateral CAI (25/67, 37.3%), while left CAI alone (2/67, 3.0%) was relatively rare. For all patients with type A lesions (31/67, 46.3%), we repaired the coronary ostium and two of them underwent salvage CABG procedure. For patients with type B lesions (30/67, 44.8%), most of them underwent repair (29/30, 96.7%), except for one patient who underwent direct CABG due to severe destruction of the coronary ostium. In addition, five patients underwent a salvage CABG procedure. For the patients with type C lesions (6/67, 8.9%), we performed direct CABG in all cases.

**Comment 7:** Why did the author perform CABG in non-CAI group. Did preoperative coronary CT angiography reveal the ischemic heart disease?

**Reply 7:** Thank you very much for your precious comments. In the non-CAI group, a total of 3 patients underwent normal CABG. These three patients received coronary CT angiography examination at external hospitals due to acute chest pain and were subsequently transferred to our hospital for surgical treatment. We describe the findings and revascularization approaches for the three patients as follows.

The first patient was a 52-year-old male. Coronary CTA revealed moderate luminal narrowing in the proximal left anterior descending (LAD) artery. Consequently, he underwent LSCA-SVG-LAD grafting during the surgery.

The second patient, a 50-year-old male, had severe narrowing in the mid-segment of the LAD and moderate narrowing in the left circumflex (LCX) artery. He underwent AO-SVG-LAD and AO-SVG-OM grafting procedures.

The third patient, also a 50-year-old male, had moderate stenosis in both the right coronary artery (RCA) and LAD. Therefore, he underwent IA-SVG-RCA and LSCA-SVG-LAD grafting.

**Comment 8:** Cause of mortality should be described separately between CAI and non-CAI group. Moreover, in-hospital mortality each Neri classification, and CAI side should be described.

**Reply 8:** Thank you for your valuable suggestions. In the revised manuscript, we have elucidated the cause of mortality according to the presence or absence of CAI in the “In-hospital morbidity and mortality” section to provide a more organized and concise representation. Moreover, we attempted to describe in-hospital mortality in the CAI group including Neri classification, CAI side, and surgical management from a text format to a table format.

**Changes in the text:** On page 9 line xx-xx, which now reads:

Early mortality occurred in 12 (17.9%) patients in the CAI group, including respiratory failure in four patients, stroke and multiple organ dysfunction syndrome in three patients each, malignant arrhythmia in one patient, and distal aortic dissection rupture in one patient. In the non-CAI group, in-hospital mortality occurred among 10 (7.3%) patients, including stroke and multiple organ dysfunction syndrome in four patients each, respiratory failure in one patient, and myocardial infraction in one patient. Compared to the non-CAI group, patients in the CAI group experienced a higher postoperative mortality rate ( $P=0.02$ ).

Table S1. Details of in-hospital mortality in the CAI group.

No.	Sex	Age	CAI side	Neri classification†	Management‡	Salvage CABG	Graft site	Cause of death
1	M	48	Bilateral	A/C	Repair/CABG	N	AO-SVG-RCA	Stroke
2	M	58	Bilateral	B/B	Repair/Repair	Y	LSCA-	Respiratory

							SVG- LAD	failure
3	M	67	Right	C	CABG	N	AO- SVG- RCA	MODs
4	M	65	Right	B	Repair	N	-	MODs
5	M	68	Bilateral	B/B	Repair/Repair	N	-	Respiratory failure
6	M	55	Bilateral	B/B	Repair/Repair	N	-	Stroke
7	M	47	Right	B	Repair	N	-	MODs
8	M	38	Bilateral	B/B	Repair/Repair	N	-	Stroke
9	M	40	Bilateral	B/B	Repair/Repair	N	-	Malignant arrhythmia
10	M	55	Bilateral	A/A	Repair/Repair	Y	LSCA- SVG- RCA	Distal aortic rupture
11	F	43	Right	A	Repair	N	-	Respiratory failure
12	F	58	Right	B	Repair	Y	LCCA- SVG- PDA	Respiratory failure

† The Neri classification for left CAI is indicated before the "/" and the Neri classification for right CAI is indicated after the "/".

‡ The management approach for the left coronary artery is presented before the "/" and the management approach for the right coronary artery is presented after the "/".

Abbreviations: CAI, coronary artery involvement; CABG, coronary artery bypass grafting; AO, aorta; LSCA, left subclavian artery; LCCA, left common carotid artery; SVG, saphenous vein graft; RCA, right coronary artery; LAD, left anterior descending artery; PDA, posterior descending artery; MODs, multiple organ dysfunction syndrome.

**Comment 9:** In the risk factors for perioperative death, did Neri classification affect outcomes? Was there any differentiation of perioperative mortality and morbidity each Neri classification? Because the multivariate analysis did not show the odds ratio and P value about Neri classification. Moreover, the methods of multivariate analysis for in-hospital mortality may be inappropriate. Please reverify the statistical methods by consulting the statistician.

**Reply 9:** Your precious comment is gratefully appreciated. We have consulted a professional statistician and tried to response logically. In this revision, we re-conducted a multivariable analysis and made adjustments for variables including male gender, age, BMI, amylase levels, AAR, CPB time, and cross-clamp time, as demonstrated in "Comment 5". Even after the adjustments, variables such as Neri classification, CAI side, and surgical management showed no correlation with



postoperative mortality. However, CAM still remains an independent risk factor. We have to acknowledge that due to limited sample size and small number of positive outcome events, the model's stability may be affected. We have also added a discussion on the relationship between CAI and CAM, and have revised our final conclusions.

**Changes in the text:** On page 13 line 2-4, line 7-9, and line 12-16, which now reads:

In our study, the CAI group had an elevated rate of in-hospital morbidity and mortality, which may have resulted from additional CA-related procedures that complicated the surgery, increasing CPB time and cross-clamp time.

Wang et al. <sup>1</sup> found that acute coronary involvement increased short-term operative mortality among patients even without myocardial ischemia. CAI is an unstable condition, and CAM may occur at any time due to the dissection process, even during intraoperative hemodynamic changes <sup>2</sup>.

After multivariable adjustment, CAM was also identified as an independent risk factor for in-hospital mortality (OR, 12.221; 95% CI, 3.047-49.040; P<0.001). Since CAI is more likely to manifest as malperfusion compared to the involvement of other organ vessels, and has an adverse impact on patient prognosis <sup>3</sup>, it is necessary to pay sufficient attention to concomitant CAI and to treat the involved CA in a timely manner for better outcomes.

#### Reference

- (1) Wang, M.; Fan, R.; Gu, T.; Zou, C.; Zhang, Z.; Liu, Z.; Qiao, C.; Sun, L.; Gong, M.; Li, H.; Zhang, H. Short-Term Outcomes of Acute Coronary Involvement in Type A Aortic Dissection without Myocardial Ischemia: A Multiple Center Retrospective Cohort Study. *J. Cardiothorac. Surg.* **2021**, *16* (1), 107. <https://doi.org/10.1186/s13019-021-01469-z>.
- (2) Uchida, K.; Karube, N.; Minami, T.; Cho, T.; Matsuki, Y.; Nemoto, H.; Yabu, N.; Yasuda, S.; Suzuki, S.; Masuda, M. Treatment of Coronary Malperfusion in Type A Acute Aortic Dissection. *Gen. Thorac. Cardiovasc. Surg.* **2018**, *66* (11), 621–625. <https://doi.org/10.1007/s11748-018-1014-y>.
- (3) Hashimoto, O.; Saito, Y.; Nakayama, T.; Okino, S.; Sakai, Y.; Nakamura, Y.; Fukuzawa, S.; Himi, T.; Ishibashi, I.; Kobayashi, Y. Prognostic Impact of Branch Vessel Involvement on Computed Tomography versus Clinical Presentation of Malperfusion in Patients With Type a Acute Aortic Dissection. *Am. J. Cardiol.* **2021**, *152*, 158–163. <https://doi.org/10.1016/j.amjcard.2021.05.005>.

On page 14 line 3-4, which now reads:

CAM secondary to CAI was identified as an independent risk factor for postoperative mortality.

**Comment 10:** How many patients undergone preoperative PCI owing to coronary artery malperfusion?

**Reply 10:** We thank the reviewer for bringing up this important issue. According to our definition, in the CAI group, a total of 20 (29.9%) patients were identified

to have preoperative coronary artery malperfusion. Among them, 2 patients received coronary stent implantation at external hospitals and were subsequently transferred to our hospital for further surgical repair. Fortunately, both of these patients survived until discharge. We have also presented our data in the Discussion section to enhance the credibility.

**Changes in the text:** On page 12 line 15-16, which now reads:

In our study, two patients with CAM were prioritized for PCI treatment, and both were successfully discharged following subsequent surgery.

**Comment 11:** In the Table 5, isolated left of CAI side is overlapping.

**Reply 11:** We appreciate your warm work and apologize for our oversight. We have corrected the error in the Table 5.

**Changes in the text:**

Table 5 (partial). Univariable and multivariable analyses for in-hospital mortality

Variable	Univariable analysis		Multivariable analysis <sup>†</sup>	
	OR (95%CI)	P-value	OR (95%CI)	P-value
CAI side				
Isolated left				
<u>Isolated right</u>				
Bilateral				

### Reviewer B

**Comment 1.** Please provide the number of IRB approval.

**Reply 1.** We have provided the number of IRB approval.

**Comment 2.** Add the units for the following values in the main text.

203 in the CAI group appeared to have higher creatinine levels [87.6 (72.4, 111.90 vs.  
204 77.9 (65.0, 97.1),  $P=0.02$ ]. Elevated myocardial injury markers, including troponin

205 I, creatine kinase-MB, and myoglobin, were more commonly seen in patients  
206 complicated by CAI [49.3% vs. 14.6%,  $P<0.001$ ; 2.1 (1.2, 6.7) vs. 1.3 (0.8, 2.0),  
207  $P<0.001$ ; and 40.8 (25.2, 124.0) vs. 31.8 (17.5, 54.2),  $P=0.002$ ]. Another underlying

223  $P<0.001$ ). Moreover, the CAI group had a longer duration of CPB [207.0 (188.0,  
224 238.0) vs. 189.0 (170.0, 206.0),  $P<0.001$ ] and cross-clamp [116.0 (99.0, 144.0) vs.  
225 99.0 (87.0, 111.0),  $P<0.001$ ]. Nonetheless, there were no notable differences in

242 Patients with CAI experienced longer mechanical ventilation time [41.5 (14.5,  
243 111.5) vs. 17.3 (13.5, 42.5),  $P=0.004$ ] and correspondingly prolonged intensive  
244 care unit stays [103.2 (46.1, 205.9) vs. 55.5 (22.4, 107.7),  $P=0.009$ ], but there was

**Comment 3.** This number in the main text does not match with that in Table 5.

257 and cross-clamp time, CAM was identified as an independent risk factor for  
258 operative mortality (OR, 12.221; 95% CI, 3.047-49.040;  $P < 0.001$ ), as shown in  
259 Table 5. ↵

**Comment 4.** Add the age unit in Table S1.

**Comment 5.** MODs should be changed to MODS in Table S1.

**Comment 6.** Indicate the full name of the abbreviations that are marked yellow in the attached manuscript.

**Reply 2-6:** We have made changes to units, letter capitalization, numerical values, and abbreviations, with corresponding marks, which we hope will help you find them quickly.