

Peer Review File

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Reviewer A

Cai et al report their experience of complete repair of the spectrum of AVSDs in 150 patients who underwent surgery between 2013 and 2021. They observed an overall early mortality of 5.3%, with 11% early mortality in the complete AVSD group. They determined that pre-operative pulmonary hypertension and LAVV regurgitation within 24 hours of surgery were the risk factor for death on multivariable analysis. There is a modestly sized study, with medium term follow up. Overall the manuscript is reasonably well written although it would require English revision as some errors make the manuscript unclear.

Major:

Comment 1: The impact of pulmonary hypertension is an interesting aspect of the study. It is possible this has a bimodal distribution, ie highest in those under 3 months and beyond 12 months. It would be interesting if you could analyse this by 3 months intervals of age, for example.

Reply 1: Thanks for your suggestion. We analyze the impact of pulmonary hypertension by 3 months intervals of age and the results are listed in the new Table 6. We found that the proportion of patients with severe pulmonary hypertension before surgery was highest in patients under 3 months, which may be related to the large left-to-right shunt, LAVV severe regurgitation and physiological pulmonary hypertension. The number of patients who had severe pulmonary hypertension were mostly under 6 months and beyond 12 months, and were more likely to suffer from postoperative pulmonary hypertensive crisis and progress to death, compared with patients between 6-9 months and 9-12 months.

Changes in the text: We have modified our text as required, and the modifications are marked in red. (See new “Table 6”; See “Impact of pulmonary hypertension analyzed by 3 months intervals of age” in “Results”; See page 21, line 5-6 in “Discussion”; See paragraph “Impact of pulmonary hypertension on children of different intervals of age” in “Discussion”)

Comment 2: Following from this question, when do you aim to performed repair of complete AVSD? When patients need surgery under 3 months do you always perform complete repair? Do you ever use PA banding?

Reply 2: Thanks for your question. In our center, we prefer to perform CAVSD surgery at 3-6 months old. When patients under 3 months develop congestive heart failure (CHF) and severe LAVV regurgitation, complete repair is recommended. The PA banding is rarely used in our center and only applied in one patient (who was

under 3 months) before complete repair of CAVSD. Our view is similar to Goutallier et al at the Royal Children's Hospital, Melbourne on the surgical approach of severe CHF patients under 3 months (Reference: Repair of complete atrioventricular septal defect between 2 and 3.5 kilograms: Defining the limits of safe repair). Only for those patients who have CHD mostly due to large left to right shunt without severe LAVVR, initial PAB is recommended when their condition can not tolerate the complete repair.

Changes in the text: No changes in the text

Comment 3: How do you decide whether to use modified single patch or double patch? I suspect double patch is used for the patients with the deep VSD. I think the comparison between the two groups is best left out of the paper as there are too few patients with double patch, and the choice of double patch is probably dictated by anatomy.

Reply 3: Thanks for your question. In our center, double patch technique was usually used in patients with deep VSD. However, the use of modified single patch technique or double patch technique may depend on the surgeon's favorite .

As what you mention above that the comparison between the two groups is best left out of the paper as there are too few patients with double patch, we agree with you as this may cause statistical bias. So we deleted Table 6 and the related contents in "Results" and "Discussions" in our text.

Changes in the text: We deleted Table 6 and the related contents in "Results", "Discussions" and "Limitations" in our text.

Comment 4: The finding of LAVV regurgitation within 24 hours predicting poor outcomes is interesting. What is your suggestion? Early reoperation? Second bypass run if the initial result is imperfect.

Reply 4: Thanks for your question. In our study, \geq Moderate LAVV regurgitation within the first 24 hours after surgery predicts LAVV reoperation and indicates further aggravation during follow-up. For severe LAVV regurgitation within the first 24 hours after surgery, reoperation is required. For moderate LAVV regurgitation, regular echocardiography should be planned to trace the degree of LAVV regurgitation.

Changes in the text: No changes in the text

Minor

Comment 5: Background of the abstract: the first sentence emphasizes the incidence of LAVV regurgitation, however the aim of your study is broader than that. I would suggest changing it.

Reply 5: Thanks for your suggestion. We have changed the first sentence in the "Background" of the abstract.

Changes in the text: We have modified our text and the modifications are marked in red. (See "Background" of the Abstract)

Comment 6: Results of the abstract: include the % of early mortality in each group

Reply 6: Thanks for your suggestion. We add the early mortality in each group as required.

Changes in the text: We have modified our text as required, and the modifications are marked in red. (See “Results” of the Abstract)

Comment 7: Introduction, line 4 – 5: Do you mean early mortality? Most modern studies have a lower mortality than 10%. It is generally less than 3%.

Reply 7: Thanks for your question. The 10% in introduction (line 4-5) does not mean early mortality, it means mortality in a long-time follow-up (around 20 years). We found that the mortality showed in reference 3 “Contemporary outcomes of complete atrioventricular septal defect repair: analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database” means in-hospital mortality, and it causes misunderstanding. We changed it and adds a new reference here.

Changes in the text: We use new reference 3 “Repair of complete atrioventricular septal defect between 2 and 3.5 kilograms: Defining the limits of safe repair.” to replace the original reference 3. The information of the new reference is marked in red in section “References”.

Comment 8&9: Introduction line 7: Down syndrome is generally a protective factor, as you demonstrate later in the article. Predictors of LAVV reoperation” on page 15: it states that Down syndrome is a risk factor for reoperation, but it is actually protective.

Reply 8&9: Thanks for your question. As it is showed in Table 5, Down syndrome is not a risk factor for LAVV reoperation in univariable analysis(P=0.397). The statement that Down syndrome is a risk factor for LAVV reoperation in the paragraph is actually a writing error, and it is deleted from the paragraph.

Changes in the text: The statement that Down syndrome is a risk factor for LAVV reoperation is deleted from the paragraph “Predictors of LAVV reoperation”.

10. For the Kaplan Meier curves, I would suggest excluding the curves with the combined CAVSD / TAVSD / PAVSD group, and instead only include the separated graphs. Also confidence intervals should be included

Reply 10: Thanks for your suggestion. We exclude the curves with the combined CAVSD / TAVSD / PAVSD group, and only include the separated graphs. In order to include the confidence intervals, we use GraphPad Prism 8 to redraw Figure 1 to Figure 6.

Changes in the text: The use of GraphPad Prism 8 was added to the paragraph “Statistical analysis”. More accurate P values and their corresponding Figure order are marked in red. The new Figures are submitted. (See page 10, line 8; See page 15, line 6-7; See page 18, line 8; See page 19, line 2; See page 23, line 3; See page 24, line 2; See page 24, line 8; See page 26, line 6-8)

Comment 11: You could consider including two further references in your discussion of early cAVSD repair:

a. Buratto E, Hu T, Lui A, Wu DM, d'Udekem Y, Brizard CP, Konstantinov IE. Early repair of complete atrioventricular septal defect has better survival than staged repair after pulmonary artery banding: A propensity score-matched study. *J Thorac Cardiovasc Surg.* 2021;161:1594-1601.

b. Goutallier CS, Buratto E, Schulz A, Hu T, Lui A, Davies B, Konstantinov IE, Brizard CP. Repair of complete atrioventricular septal defect between 2 and 3.5 kilograms: Defining the limits of safe repair. *J Thorac Cardiovasc Surg.* 2022 (in press)

Reply 11: Thanks for your suggestion. We have included the two references in our discussion of early cAVSD repair.

Changes in the text: We have added the follow-up results of these two references in our text to support our views and the modifications are marked in red. (See “Mortality” in the “Discussion” paragraph, Page 22, line 8-10)

Reviewer B

The authors make a single-centre analysis of AVSD outcome including all types of AVSD. Although I am convinced that the anatomical and hemodynamic complexity of complete AVSD should not be compared to that of partial AVSD, I appreciate the comprehensive analysis of the authors.

I have two questions:

Comment 1: Was the preoperative moderate or severe pulmonary hypertension medically treated? If not: why the patients were not treated before the operation in order to reduce the risk of severe postoperative hypertensive crises?

Reply 1: Thanks for your question. For younger patients, we rarely use drugs to decrease the pulmonary pressure before surgery because it has high risk to increase left-to-right shunts and progress CHD. For older children, we prefer to perform cardiac catheterization to assess pulmonary resistance to decide whether they require medical treatment.

Changes in the text: No changes in the text

Comment 2: table 3: in-hospital mortality. Patient 2 had moderate LAVV regurgitation before the re-operation and the same moderate degree after the re-operation. Patient 6 had moderate LAVV regurgitation before the re-operation and a severe LAVV regurgitation after the re-operation. In these 2 cases it was not feasible to improve the LAVV function with a repair, can the authors explain why is this result accepted and a valve replacement has not been considered? Although I realize that the results of LAVV replacement in this setting are quite disappointing.

Reply 2: Thanks for your question. For these small babies, mechanical valve implantation is hard to perform. If do, the smallest mechanical valve is probably put

to the left atrium, which will have high risk of low cardiac function, arrhythmia, anticoagulation related complication and further reoperation. Although ROSS II procedure was reported to be another way for these patients, it was still high risk and had other problems in the future.

Changes in the text: No changes in the text