Author’s response to reviews

Title: Two-stage correction of type IV total anomalous pulmonary venous connection

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Dear Editor:

We thank you and the reviewers for reviewing our manuscript entitled “Two-stage correction of type IV total anomalous pulmonary venous connection (JCTS-D-16-00346).” The reviewer’s comments are excellent and constructive. Our point-by-point responses to each of the comments are as follows.

Point-by-point responses

[Reviewer #1’s Comment]

1. The sample is too small;

[Our Response]

The review’s comment is correct. The sample size is indeed small. Owing to the rarity of type IV TAPVC (The incidence of TAPVC is 0.7%–1.5% among all congenital heart defects. Further, among all types of TAPVCs, type IV is especially rare, with an incidence of 5%–13 %.), obtaining a large sample of type IV TAPVC in a single center would be difficult. (Emory group identified only 19 patients, including 2 patients with heterodoxy syndrome, in their 30 years of experience [1], and St. Louis et al. identified only 159 patients with type IV TAPVC from a large database of the Pediatric Cardiac Care Consortium, which was collected from multiple institutes from 1982 to 2007 [2]). However, as Reviewer #2 mentioned, although this is a small series, our results provide a technical option to treat this disease, confirming the practice of delaying complete repair to reduce postoperative pulmonary obstruction. We believe that it would provide reassurance for safety after the delayed stage operation.
2. Postoperative and especially medium or long term follow up data are lacking;

[Our Response]

We presented the postoperative outcome in the results, showing that neither turbulent nor continuous flow was observed in any of the patients on postoperative echocardiography. In addition, we mentioned that there was no significant obstruction on outpatient follow-up echocardiography, and cardiac function was NYHA functional class 1 in all 7 patients. However, we did not present the follow-up duration. We have added the follow-up period of individual patients in Results and in Table 2. We also added the echocardiographic data from the last follow-up echocardiography. The measured median Vmax across the LSPV anastomosis site was identical on pre-discharge and at the last follow-up echocardiography (1.0 m/s), indicating no flow disturbance.

[Reviewer #2’s Comment]

Although this is a small series, it confirms a practice of delaying complete repair in order to mitigate the problematic complication of pulmonary venous obstruction, seen in up to 25 % of patients that undergo repair for TAPVC during the neonatal period. The work should be published and I provide the following comments for the authors review and consideration.

[Our Response]

We thank the reviewer for his comment so eloquently put. This is exactly the message that we are trying to convey to the readers but we just weren’t able to lay it out as eloquently as did the reviewer. And if the Reviewer #2 allows, we would like to add the reviewer’s sentence in our discussion section.

1) Sentence one of Introduction: should be revised to " is a cyanotic defect in which all pulmonary…

[Our Response]

We have changed “congenital cyanotic defect that drains” to “cyanotic defect in which,” as suggested.

2) Sentence two of introduction: delete rate

[Our Response]

We have changed “incidence rate” to “incidence,” as suggested.

3) The authors excluded all functional single ventricular anatomy for their review. This is a difficult population to deal with, especially the heterotaxy population, in which the incidence of
mixed type TAPVC in high. Where there patients in the authors series that had this type of anatomy. If so, these authors should consider including these patients in this descriptive analysis.

(Summary) Include the patients with single ventricle physiology if there are.

[Our Response]

We completely agree that TAPVC with a single ventricle is difficult to manage. (This is confirmed again by a recently published research by St. Louis et al. [2]). We speculated that to confirm the efficacy of our strategy, which comprised delayed correction of small isolated pulmonary veins after incorporating the major confluent pulmonary veins, we had to exclude the possible confounding factors that could affect the surgical strategy and outcomes. A single ventricle possesses hemodynamic complexity. Such patients frequently require emergent palliative procedures in addition to correction of the abnormal pulmonary venous connection. We felt that including patients with single ventricle physiology might make our results more confusing, affecting the efficacy of delayed correction. Hence, we excluded all patients with single ventricle physiology when we sorted the data from all TAPVC cases. We checked our database again after receiving Reviewer #2’s comment. Of a total of 133 patients with TAPVC, 30 patients (22.6%) had single ventricular physiology. This proportion is similar to or a little lesser than that observed in other published series. Unfortunately, there was no patient with single ventricle physiology among the patients who were enrolled in the staged operation for type IV B TAPVC. We hope to analyze such patients in a large-sample study in future.

4)When describing the anatomy of this subtype, the authors should utilized the classification system created by Chowdhury et al (1) and confirmed in a large series by St. Louis et al (2). These classification system breaks Type IV TAPVC in three types depending on the pattern of drainage. The respective outcomes have been published. This would allow for the audience to better correlate the authors outcomes to the published standards.

(Summary) Utilized the classification system created by Chowdhury et al./confirmed by St. Louis et al.

[Our Response]

We totally agree with the reviewer’s comment. We have modified our manuscript according to Chowdhury et al. and St. Louis et al.’s classification. In addition, we changed the term “mixed-type TAPVR” to “type IV TAPVC”.

According to Chowdhury et al.’s classification, all of our patients who underwent staged operation belonged to type IV B (“3+1” pattern) TAPVC. The detailed anatomic configurations have been described in Methods (study population and subtype variants).

Interestingly, in the report by St. Louis et al., the most common anatomic configuration for type IV TAPVC B consisted of all the right pulmonary veins and the left lower pulmonary vein
returning to the coronary sinus, while the left superior pulmonary vein drained to the innominate vein. Our cases had the same dominancy in anatomic configuration.

5) When describing the follow-up following the second stage, the authors should present the median follow-up period. It is clear that post-operative pulmonary venous obstruction most frequently within the first 24 months of repair. Some idea of the follow-up period would be helpful.

(Summary) Add follow-up period after 2nd operation

[Our Response]

Thank you for pointing this out. The follow-up period ranged from 7 to 59 months, while the median echocardiographic follow-up period was 22 months. This information has been added to Results and in Table 2. Echocardiographic data at the last follow-up has also been added in Results. The measured median Vmax across the LSPV anastomosis site was identical on pre-discharge and at the last follow-up echocardiography (1.0 m/s), which means that there was no pulmonary venous obstruction at pre-discharge and at the last follow-up.

6) I would comment in greater depth on the decision of determining the timing on the second stage. He authors waited on average of three years. What is the thought process for this period.. Please explain. Perhaps providing recommendation, this would contribute to the practice.

(Summary) Provide decision making process for 2nd operation time.

[Our Response]

Patients were monitored via echocardiography for volume overload every time they visited the outpatient clinic before the second operation. We have had regular conferences with pediatric cardiologists with regard to the results. If the echocardiography showed serial increase of volume, the second operation was planned. In addition, we had planned to perform the second operation if the patients would present any symptoms, since their activity would increase over time, although no patient presented symptoms of heart failure until the second operation. As an exception, a second operation was planned for patients who showed ostial narrowing of the pulmonary vein after first operation, regardless of volume loading or symptoms (Patient 2 and Patient 4). We did not intend to wait for an average of three years; however, our results at least confirmed that three years is a sufficient time for the growth of the left superior pulmonary vein in patients with type IV B TAPVC. We have added the above point in Methods and Discussion.

In addition, we found an error in the original manuscript.

We had originally stated in Discussion that the median size of the LSPV during the second operation was 9.0 mm. The correct size is 9.8 mm. The error has now been corrected.

An additional minor change was made to ensure consistency in the representation of the results between the main text and the abstract. In the original manuscript, the results were represented as
the median (range) in the abstract, whereas in the main text, the results were represented as the range (median). We have now changed the main text representation as median (range).

The institutional address has been updated to the new address, since the Korean government changed the address system.

The revised sentences/phrases are blue in color and have been underlined.

We feel fortunate to have had the reviewer’s expertise and the constructive comments that helped to improve our manuscript. Thank you very much.

Sincerely,

Tae-Gook Jun
