Establishment of right ventricle-pulmonary artery continuity as the first-stage palliation in older infants with pulmonary atresia with ventricular septal defect may be preferable to use of an arterial shunt

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Abstract

OBJECTIVES: Right ventricle-pulmonary artery (RV-PA) conduit and systemic-to-pulmonary artery (S-PA) shunt in younger infants for the first-stage palliation with pulmonary atresia with ventricular septal defect (PAVSD) obtained good results. However, the pulmonary arteries (PA) grow slow in older infants undergoing an S-PA shunt. We compared the clinical outcomes of the two procedures in older infants with PAVSD.

METHODS: A total of 48 patients with PAVSD underwent the first-stage palliative procedure between January 2010 and July 2012. Patients were divided into the RV-PA group and the S-PA group based on whether they had an RV-PA conduit (n = 24) or an S-PA shunt (n = 24). The early and late outcomes were compared between groups.

RESULTS: There was no significant difference in in-hospital mortality, mechanical ventilation time, paediatric intensive care unit stay and hospital stay between groups (all P > 0.05). The RV-PA conduits were associated with better PA growth compared with the S-PA shunts (P < 0.001). The RV-PA group had a higher rate of second-stage biventricular surgery compared with the S-PA group (P = 0.03). The early outcomes among different conduits of the RV-PA conduit were not different (all P > 0.05). A positive correlation was found between the size of conduits and body weight (R² = 0.684, P < 0.001).

CONCLUSIONS: In older infants with PAVSD who underwent the first-stage palliative procedure, early outcomes showed no difference between the RV-PA conduit group and the S-PA shunt group. The RV-PA conduits were associated with better growth of the PA and higher rates of second-stage biventricular repair. Autologous pericardium is a good choice for RV-PA conduits, and there is a correlation between body weight and size of conduit.

Keywords: Congenital heart diseases • Pulmonary arteries • Septal defect • Shunts

INTRODUCTION

Pulmonary atresia with ventricular septal defect (PAVSD) is a complex congenital heart disease characterized by heterogeneous and frequently severe anomalies of pulmonary blood supply. Various traditional palliative surgeries have been applied to restore the best possible pulmonary circulation to these patients. Systemic-to-pulmonary artery (S-PA) shunt, such as the modified Blalock-Taussig (mBT) shunt, was designed to increase blood flow to the pulmonary arteries (PAs) in an effort to alleviate cyanosis and stimulate growth. However, the S-PA shunt is often associated with an unstable haemodynamic status due to excessive or insufficient pulmonary blood flow after surgery, higher perioperative mortality and significant diastolic runoff from the coronary circulation [1–4]. Additionally, the PAs grow slow in older children undergoing an S-PA shunt, especially in patients older than 1 year [5–7].

Right ventricle to pulmonary vein (RV-PA) conduit for the first-stage palliation of hypoplastic left heart syndrome (HLHS) was first reported by Kishimoto et al. [8] in 1999. The RV-PA conduit provided a stable systemic circulation as well as adequate pulmonary blood flow and was associated with lower inter-stage mortality in patients with HLHS [9–11]. Pruett et al. [7] found that the Norwood procedure with an RV-PA conduit promotes better distal left PA growth than mBT shunt. In 2008, Bradley et al. [12] first assessed the outcomes of using an RV-PA conduit as a single, controlled source of pulmonary blood flow in patients with biventricular hearts such as tetralogy of Fallot with pulmonary atresia. They found that the RV-PA conduit provided successful palliation in biventricular heart disease and allowed significant growth with
protection of oxygen saturation prior to complete repair, which compared favourably with those of an mBT shunt. However, there were only 10 patients included in this study, and all of the children were younger with a median age of 9 days and a median weight of 3 kg. In developing countries, such as China, most infants with PAVSD undergoing surgery are older. For these older infants, the outcomes of S-PA shunt were not satisfactory, and the results of the RV-PA conduits still not clear.

Herein, we compare the clinical outcomes of an RV-PA conduit with an S-PA shunt for older infants with PAVSD, and describe our initial experience in selection of RV-PA conduits.

MATERIALS AND METHODS

Patient population

Between January 2010 and July 2012, 48 patients with PAVSD underwent palliative operation at Fuwai Hospital, Beijing, China. All patients were diagnosed with PAVSD combined atrial septal defect or patent ductus arteriosus in which a palliative surgery was needed to encourage the growth of PAs, and a subsequent two-ventricle repair was planned. Among the 48 patients, 24 patients received an RV-PA conduit (RV-PA group) and the other 24 patients underwent an S-PA shunt (S-PA group). The inclusion criteria for an RV-PA conduit included patients uneven development of both sides PA, stenosis of the joint part of both sides PA and PA branch stenosis, poor development of PA, need for pulmonary arterioplasty and other vascular anatomical variations (right-side aortic arch and right-side descending aorta, subclavian artery malformation). In patients with even development of both sides PA, a relative better fusion of left and right PA was assigned to S-PA shunt. Furthermore, indications for the two procedures also included that patient has an intrinsic pulmonary artery trunk with a Nakata index of <120 mm²/m². Diagnosis of PAVSD was established by echocardiographic analysis in all cases. All patients underwent computed tomography scanning, and angiographies analysis was performed on indication. The Institutional Review Board approved the study, and informed consent was obtained from all patients.

Surgical techniques

Surgery was performed under general anaesthesia with an endotracheal tube for ventilation. Through a midline sternotomy, the thymus gland was excised. In the RV-PA group, we followed the technique that has been previously reported [9, 12]. Cardiopulmonary bypass was established through the ascending aorta and the right atrium. After the aorta was clamped, a non-valved conduit from the right ventricular outflow tract to the central PAs was placed. The type of conduit included autologous pericardium conduit, bovine jugular veins and polytetrafluoroethylene (PTFE) blood vessels (Gore-Tex, Gore & Associates, Flagstaff, AZ, USA). Autologous pericardium constitutes most of the anterior wall of a conduit when the main PA was partly developed. When the main PA was severely undeveloped, autologous pericardium, bovine jugular veins or PTFE blood vessels acted as the whole conduit. In summary, the size of conduit used in the RV-PA group was 6.0–12.0 mm. According to our experience, conduit diameter was 6–8 mm in patients weighing from 5 to 10 kg, one-half to two-thirds of normal PA in patients weighing >10 kg and part of the conduit was clipped using titanium clips according to arterial oxygen saturation after cardiopulmonary bypass. In the S-PA group, the mBT shunt was performed in 20 patients and central shunt operation was performed in 4 patients. All 24 patients received a PTFE blood vessel as S-PA shunt. The diameter of the PTFE shunt was 3.0–6.0 mm depending on patient’s weight, vessel size and preoperative physiology. Seven patients in the RV-PA group and 5 patients in the S-PA group underwent concomitant transcatheter aortopulmonary collateral artery embolization in hybrid operating theatre. Postoperative treatment was the same as that for children who underwent other types of operation. Second-stage biventricular surgery included removal of the RV-PA conduit, placement of an RV-PA valved conduit and complete intracardiac repair.

Follow-up

All patients were followed biannually by the referring paediatric cardiologist in Fuwai Hospital and obtained a clinical assessment, an X-ray film and an echocardiogram. Cardiac angiography and computed tomography were performed when indicated. PA growth was evaluated using the Nakata index [13], which was calculated angiographically by the formula: Nakata index (mm²/m²) = (right PA area + left PA area)/body surface area.

Statistical analysis

Statistical analyses were performed with the SPSS 13.0 software (SPSS, Inc., Chicago, IL, USA). Continuous variables are expressed as medians with ranges or means with standard deviations and compared using Student’s t-test or the non-parametric test. Categorical data are expressed as percentages and compared using a χ² test or Fisher’s exact test. Kaplan–Meier analysis was used for survival, with the log-rank test used to determine significant differences. Multivariate analyses of variables were performed using Cox proportional hazards regression models. A linear regression analysis was used to analyse the relationship between the size of the RV-PA conduit and body weight. To examine the reliability of the regression line, we calculated predicted value and 95% confidence intervals (CIs) of RV-PA conduit size for each individual according to the regression formula. Then all patients in the RV-PA group were divided into two subgroups, matching group and mismatching group, according to whether the actual conduit size was included in 95% CI of predicted size. A probability value of <0.05 was considered statistically significant.

RESULTS

Baseline patient characteristics and early results

The baseline characteristics and early results are given in Table 1. Patients in both groups were of similar age, sex, body weight, Nakata index, blood pressure and oxygen saturation before surgery. After surgery, there were three deaths in the S-PA group. One died of inability to maintain adequate oxygen saturation despite a large shunt. Another 2 patients died of low cardiac output syndrome. Three patients underwent second admission to the paediatric intensive care unit (PICU) in the RV-PA group because of high central venous pressure and right pleural effusion.
and 2 in the S-PA group because of respiratory dysfunction and unstable systemic circulation. In the S-PA group 3 patients required re-exploration, 2 for adjusting the size of PTFE blood vessel and 1 for PTFE blood vessel thrombosis. There was no significant difference in mechanical ventilation time, PICU stay, hospital stay and hospital mortality between groups (all $P > 0.05$). Subgroup analysis indicated that baseline patient characteristics and early results were not different between patients with an S-PA shunt ($n = 24$) and patients undergoing an RV-PA procedure with autologous pericardium conduits ($n = 17$; Table 2).

### Table 1: Patient characteristics, perioperative and follow-up results

<table>
<thead>
<tr>
<th>Variables</th>
<th>RV-PA conduit, $n = 24$</th>
<th>S-P shunt, $n = 24$</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, months</td>
<td>26.6 (2–72)</td>
<td>31.6 (2–98)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>11 (45.8%)</td>
<td>13 (54.2%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>10.2 ± 4.4</td>
<td>11.1 ± 4.3</td>
<td>0.24</td>
</tr>
<tr>
<td>Nakata index, mm²/m²</td>
<td>96.6 ± 50.2</td>
<td>89.9 ± 48.2</td>
<td>0.32</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>90.4 ± 8.7</td>
<td>88.2 ± 9.6</td>
<td>0.20</td>
</tr>
<tr>
<td>Preoperative $O_2$ sat (%)</td>
<td>75.1 ± 9.7</td>
<td>77.0 ± 8.9</td>
<td>0.24</td>
</tr>
<tr>
<td>PDA, n (%)</td>
<td>17 (70.8%)</td>
<td>19 (79.2%)</td>
<td>1.0</td>
</tr>
<tr>
<td>MAPCAs, n (%)</td>
<td>7 (29.2%)</td>
<td>5 (20.8%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Normal PA arborization</td>
<td>18 (75%)</td>
<td>22 (91.7%)</td>
<td>0.25</td>
</tr>
<tr>
<td>CPB time, min</td>
<td>80 ± 29</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Aortic cross clamp, n (%)</td>
<td>1 (4.2%)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Material of conduit, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous pericardium</td>
<td>17 (70.8%)</td>
<td>0 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gore-Tex blood vessel</td>
<td>5 (8.4%)</td>
<td>24 (100%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bovine jugular vein</td>
<td>2 (20.8%)</td>
<td>0 (0%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Concomitant procedure, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary arterioplasty</td>
<td>6 (25%)</td>
<td>2 (8.4%)</td>
<td>0.25</td>
</tr>
<tr>
<td>MAPCAs embolization</td>
<td>7 (29.2%)</td>
<td>5 (20.8%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Mechanical ventilation time, h</td>
<td>40 (10–106)</td>
<td>46 (14–120)</td>
<td>0.43</td>
</tr>
<tr>
<td>Re-intubation, n (%)</td>
<td>0 (0%)</td>
<td>2 (8.4%)</td>
<td>0.47</td>
</tr>
<tr>
<td>PICU stay, h</td>
<td>85 ± 42</td>
<td>88 ± 77.1</td>
<td>0.43</td>
</tr>
<tr>
<td>Reexploration after initial procedure, n (%)</td>
<td>0 (0%)</td>
<td>3 (12.5%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Second admission to PICU, n (%)</td>
<td>4 (2.8%)</td>
<td>2 (8.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
<td>0 (0%)</td>
<td>3 (12.5%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Hospital stay, days</td>
<td>21.7 ± 8.4</td>
<td>22 ± 9.7</td>
<td>0.45</td>
</tr>
<tr>
<td>Qp:Qs</td>
<td>1.12 ± 0.54</td>
<td>1.20 ± 0.66</td>
<td>0.32</td>
</tr>
</tbody>
</table>


### Follow-up results

Except for 3 early deaths, the clinical follow-up was complete in all 45 patients, with a median follow-up of 23 months (9–38 months). PA growth was angiographically evaluated in 16 patients with an RV-PA conduit and in 8 patients with an S-PA shunt. Both the RV-PA conduits (Nakata index 289.8 ± 53.9 vs 96.6 ± 50.2 mm²/m², $P < 0.001$) and S-PA shunts (Nakata index 191.9 ± 49.9 vs 89.9 ± 48.2 mm²/m², $P < 0.001$) significantly promoted growth of the PA. The RV-PA conduits were associated with better PA growth compared with the S-PA shunts (Nakata index 289.8 ± 53.9 vs 191.9 ± 49.9, $P < 0.001$; Fig. 1). During the follow-up, there were no deaths in either group. In crude comparison, patients with an RV-PA conduit had higher rates of biventricular surgery (15 vs 6 patients, $P = 0.023$). Kaplan–Meier analysis showed a higher rate of biventricular repair in the RV-PA group ($P = 0.019$, Fig. 2). In Cox regression models, the RV-PA group showed a higher rate of second-stage biventricular surgery compared with the S-PA group (hazard ratio: 2.97, 95% CI: 1.11–7.89, $P = 0.03$). Compared with the RV-PA group, the mean time interval from the initial procedure to biventricular repair was significantly longer in patients with an S-PA shunt (23.8 ± 13.9 vs 15.2 ± 7.9 months, $P = 0.043$). The RV-PA procedure with an autologous pericardium conduit ($n = 13$) was also associated with a better PA growth than S-PA shunt ($n = 18$; Nakata index 276.4 ± 47 vs 191.9 ± 49.9, $P < 0.001$). Therefore, patients with RV-PA surgery using an autologous pericardium conduit had higher rates of biventricular surgery (11 vs 6 patients, $P = 0.003$; Table 2) and shorter time interval from initial surgery (14.8 ± 7 vs 23.8 ± 13.9 months, $P = 0.03$; Table 2) than patients with an S-PA shunt.

### Materials of conduit

For the 24 patients with an RV-PA conduit, 17 autologous pericardium, 5 PTFE blood vessels and 2 bovine jugular veins served as conduit respectively. No significant differences were seen among these conduits in respect of cardiopulmonary bypass time (86 ± 26 min, 83 ± 37 min, 93 ± 40 min, all $P > 0.05$), mechanical ventilation time, PICU stay (85 ± 55.6 h, 86 ± 67.5 h, 68 ± 2.8 h, all $P > 0.05$) and hospital stay (20 ± 11 days, 29.5 ± 9.7 days, 17 ± 4 days, all $P > 0.05$).

### Relation between size of conduit and body weight

A positive significant correlation was found between the size of conduits and body weight with a Spearman’s correlation.
A linear regression analysis also showed a positive relationship between the size of conduits and body weight ($r = 0.827$, $R^2 = 0.684$, $P < 0.001$). Based on our aim of deriving a practical and simple formula for routine care, the following regression formula was employed: size of conduits (mm) = $0.325 \times$ body weight (kg) + $4.629$. To examine the reliability of regression formula, differences between the matching group ($n = 13$) and the mismatching group ($n = 11$) were compared. The mismatching group was associated with longer mechanical ventilation time (median 56 vs 23 h; $P = 0.026$; Table 3) and longer PICU stay (114 ± 56 vs 58 ± 37 h, $P = 0.019$; Table 3) compared with the matching group. Compared with the mismatching group, the matching group was also associated with better PA growth, shorter time interval between surgery and higher rate of biventricular repair (Table 3). Other perioperative and follow-up data are detailed in Table 3.

### DISCUSSION

In the present study, we report our initial experience with a palliative RV-PA conduit in older infants with PAVSD, and compare the early and follow-up outcomes between the RV-PA conduit and the S-PA shunt. The main findings include: (i) RV-PA conduit provided better PA growth, higher rate of second-stage biventricular surgery and shorter time interval from initial palliative surgery to biventricular repair; (ii) the early results showed no significant difference between the RV-PA conduit and the S-PA shunt; (iii) there was a positive significant correlation between size of conduits and body weight, and we developed a practical and simple formula for routine care.

PAVSD is a complex congenital heart disease, which comprises 1–2% of congenital heart defects [14]. Patients with confluent, good-sized PAs and a pulmonary trunk are suitable for a...
Fallot-like repair using a transannular patch. Patients with good-sized PAs but without a pulmonary trunk should undergo repair with an RV–PA conduit. Patients with confluent but hypoplastic PAs often need an arterial shunt or reconstruction of the right ventricle outflow tract, which may enhance PA growth. Studies indicated that PAs grow slow in older children undergoing S-PA shunt, especially in patients more than 1 year old [5–7]. The RV-PA conduit was first reported by Kishimoto et al. [8] for the first-stage palliation of HLHS. The RV-PA conduit as stage I palliation for PAVSD was first introduced in 2008 [12]. Though the pulmonary anatomy and physiology are different between HLHS and PAVSD, we consider that it is technically possible to perform surgery in patients with PAVSD as reported by Bradley et al. [12]. In the study by Bradley et al. [12], the RV-PA conduit provided a successful palliation in younger and lower weight infants with PAVSD. However, in developing countries such as China, most infants with PAVSD undergoing palliative surgery are older. The outcomes of S-PA shunt were not satisfactory, and the results of RV-PA conduit still not clear.

To our knowledge, our study is the first study comparing the clinical results of the RV-PA conduit and the S-PA shunt in older infants with PAVSD. RV-PA conduits are theoretically associated with a more stable postoperative course, increased coronary arterial flow because of the lack of aortic diastolic runoff and lower mortality [15]. In our study, we found that there was more hospital death, reexploration and second admission to PICU, longer mechanical ventilation time, PICU stay and hospital stay in patients with the S-PA shunt, but all of these did not achieve statistical significance. These results are consistent with previous studies [11, 16–19]. A recent multicentre randomized controlled trial which compared the RV-PA conduit and mBT shunt in younger infants with HLHS [4] found that transplantation-free survival at 12 months was higher with the RV-PA conduit. However, no significant difference in transplantation-free survival between groups was found during a median follow-up period of 32 months. And the rate of non-fatal adverse events was similar in the two groups.

Previous studies [4, 12, 20, 21] showed that palliative surgery could promote PA growth in younger (ages ranging from a few days to weeks) patients with PAVSD. Nevertheless, our data proved that the RV-PA conduit is associated with better PAs growth than the S-PA shunt in both younger and older infants. Rumball et al. [20] found that the Norwood procedure with RV-PA conduit is associated with better and more evenly distributed central pulmonary artery growth than mBT shunt using angiography. The speed of PA growth may affect the rate of second-stage biventricular repair and interval between the procedures. The following reasons may account for rapid PAs growth in the RV-PA group. First, pulsatile blood flow from the right ventricle to the PA may better facilitate PA growth [22]. Second, in our patients, the diameter of the S-PA shunt was 3.0–6.0 mm, which was smaller than the diameter of the RV-PA conduit (6.0–8.0 mm). Thinner conduits in the S-PA group may not effectively facilitate PA growth. Finally, more evenly balanced distribution of flow to the central PA was likely to result in improved central PA growth. Compared with RV-PA conduits, the blood flow in an S-PA shunt is in a more rightward orientation, which may be bad for PA growth.

The choice of conduit was affected by several factors, such as material of conduit, body weight, doctors’ preference and patient’s condition during operation. In our hospital, the largest size of Gore-Tex conduit is 8 mm. A larger PTFE conduit used in cavopulmonary vein anastomosis, obviously, is too large for S-PA shunt or RV-PA procedure. Furthermore, bleeding often occurs in the anastomosis of a Gore-Tex conduit and the pulmonary artery. The smallest size of the bovine jugular vein is 12 mm, so the use of bovine jugular vein is also limited. However, conduits made by autologous pericardium have a wide range of sizes. Therefore, the use of pericardium in an RV-PA procedure is frequent. Certainly, it is a little bit time-consuming to make a conduit with pericardium. We revealed that the RV-PA conduit with an autologous pericardium conduit achieved clinical outcomes similar to the other two conduits. A previous study indicated that autologous pericardial conduits for right ventricular outflow tract reconstruction showed superb properties [23]. Furthermore, autologous pericardium may be the most commonly used material in surgery for right ventricular outflow tract reconstruction, which is characterized by convenient acquisition, simple procedure, high patency rate and low cost.

Figure 2: Cumulative incidence curve of biventricular surgery for patients who underwent palliative conduit surgery with either an RV-PA or an S-PA shunt.

Figure 3: A positive significant correlation was found between size of conduits and body weight.
As we know, appropriate conduit size is important for early and late outcomes. Body weight is usually also important for determining the size of conduits. In our study, we found that a positive relationship exists between the size of conduits and body weight, and we developed a formula for calculating the size of conduit. The first advantage of the formula is its simplicity, which can make daily practice easier. Second, the subgroup analysis proved that it had better reliability.

Our study has several limitations. First, the retrospective nature of this study and relatively small study population may produce bias and be underpowered to detect a difference between groups. Second, we did not evaluate the function of the right ventricle prior to second-stage biventricular surgery. RV-PA conduit without valved conduit leads to PA regurgitation, which may impair the function of the right ventricle. Furthermore, the formula was generated using data from a small population in a single centre, which may limit its application in other populations. In the future, large-scale prospective studies are needed to establish more reliable and accurate formulas for calculating the size of conduits.

CONCLUSIONS

In conclusion, in this single-centre retrospective, non-randomized study, early outcomes were not different between the RV-PA conduit and the S-PA shunt for patients undergoing stage I palliation for PAVSD. The RV-PA conduit was associated with better growth of the PA and a higher rate of second-stage biventricular repair in older infants with PAVSD. Autologous pericardium is a good choice for an RV-PA conduit, and there is a correlation between body weight and the size of conduit.

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