Right Ventricular Outflow Tract Stenting in Tetralogy of Fallot Infants With Risk Factors for Early Primary Repair

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Background—Tetralogy of Fallot with cyanosis requiring surgical repair in early infancy reflects poor anatomy and is associated with more clinical instability and longer hospitalization than those who can be electively repaired later. We bridged symptomatic infants with risk factors for early primary repair by right ventricular outflow tract stenting (stent).

Methods and Results—Four groups of tetralogy of Fallot with confluent central pulmonary arteries were studied: stent group (n=42), primary repair (aged <3 months) with pulmonary stenosis (early-PS group; n=44), primary repair (aged <3 months) with pulmonary atresia (early-PA group; n=49), and primary repair between 3 and 11 months of age (surg>3mo group; n=45). Stent patients had the smallest pulmonary arteries with a median (95% credible intervals) Nakata index (mm²/m²) of 79 (66–85) compared with the early-PA 139 (129–154), early-PS 136 (121–153), and surg>3mo 167 (153–200) groups. Only stent infants required unifocalization of aortopulmonary collaterals (17%). Stent and early-PA infants had younger age and lower weight than early-PS infants. Stent infants had the most multiple comorbidities. Stenting allowed deferral of complete surgical repair to an age (6 months), weight (6.3 [5.8–7.0] kg), and Nakata index (147 [132–165]) similar to the low-risk surg>3mo group. The 3 early treatment groups had similar intensive care unit/hospital stays and high reintervention rates in the first 12 months after repair, compared with the surg>3mo group.

Conclusions—Right ventricular outflow tract stenting of symptomatic tetralogy of Fallot with poor anatomy (small pulmonary arteries) and adverse factors (multiple comorbidities, low weight) relieves cyanosis and defers surgical repair. This allowed pulmonary arterial and somatic growth with clinical results comparable to early surgical repair in more favorable patients. (Circ Cardiovasc Interv. 2016;9:e003979. DOI: 10.1161/CIRCINTERVENTIONS.116.003979.)

Key Words: cardiac catheterization ▪ cyanosis ▪ risk assessment ▪ stent ▪ tetralogy of Fallot

The majority of tetralogy of Fallot (TOF) patients with confluent good size pulmonary arteries undergo uneventful elective primary repair in the first year of life, with excellent results; however, acute postoperative course and survival are superior when surgery can be performed beyond the neonatal period. Infants who require early intervention are either prostaglandin dependent or severely cyanosed and have tenuous antegrade pulmonary blood flow that is a consequence of the poor anatomy of the right ventricular outflow tract (RVOT; infundibular or valvar stenosis) and/or pulmonary arterial tree (hypoplastic vessels and multiple aortopulmonary collateral arteries [MAPCAs]). Coexisting neonatal comorbidities may not have had time to resolve, for example, prematurity, low weight, infection, neurological injury, and other conditions requiring noncardiac surgery. These comorbidities increase the risk of, or may delay, primary cardiac repair. Some centers perform early repair, whereas others bridge to complete repair. The most common bridging option is an aortopulmonary shunt, but alternatives include arterial duct stenting and percutaneous or surgical RVOT augmentation. Risk factors for primary repair lie on a continuum with no sharp decision boundaries defined with respect to management. Centers with excellent outcomes for early infant repair have identified low weight, severe cyanosis, pulmonary atresia rather than stenosis, hypoplastic pulmonary arteries, and noncardiac comorbidities as risk factors for higher mortality and reintervention. Blalock–Taussig shunts (BTS) performed in infants with prematurity, low weight, and hypoplastic pulmonary arteries have increased complications, including pulmonary artery stenosis and pulmonary...
WHAT IS KNOWN

- Primary repair of tetralogy of Fallot with confluent central pulmonary arteries is the standard of care in many institutions with excellent outcomes.
- Some infants with prematurity, low weight, poor pulmonary artery anatomy, and noncardiac comorbidities have significant risk factors for whom bridging to complete repair still has a role.
- In higher risk infants, right ventricular outflow tract stenting is an alternative bridging option to aortopulmonary shunts or early complete repair.

WHAT THE STUDY ADDS

- It demonstrates that right ventricular outflow stenting is an effective bridging procedure allowing somatic and pulmonary artery growth.
- It provides our approach to the management of symptomatic tetralogy of Fallot in early infancy (n=180) and our selection criteria for bridging to complete repair by right ventricular outflow tract stenting.

Methods

Patient Population

This study was approved by the institutional ethics review board. Our cardiac surgical and catheterization databases were searched to identify all infants ≤1 year of age with TOF with pulmonary valve (PV) stenosis (TOF-PS) or pulmonary valve atresia (TOF-PA) with confluent central pulmonary arteries who underwent RVOT stent implantation and/or surgical repair between January 2000 and April 2015. This search included all infants who had assessment for or attempted RVOT stenting. Patients with TOF and double-outlet right ventricle (RV) subtype and/or an atrioventricular septal defect were included. Infants with an absent PV were excluded.

Noncardiac Comorbidities

Comorbidities deemed to increase risk for, or delay, primary repair were necrotizing enterocolitis, sepsis, cerebrovascular event, lung compromise, and conditions requiring neonatal surgery, which included tracheoesophageal fistula and gastrointestinal anomalies.

Institutional Management Approach

Elective TOF repair is performed at ≥6 months of age with earlier repair indicated by tenuous pulmonary blood flow. Risk factors for primary repair in our institution are defined as low weight (<2.5 kg), prematurity (<37 weeks gestational age), pulmonary artery hypoplasia (Z score <-2), and important noncardiac comorbidities. We sought to triage infants based on these risk factors for primary repair or RVOT stenting, recognizing that combining multiple risk factors is inherently a clinical judgment, and none of these were considered absolute contraindications to early primary repair. Potential for PV preservation was a major consideration in decision making and contraindicated RVOT stent implantation even if this prolonged the preoperative length of stay (LOS). During this period, RVOT stent implantation was the primary palliative procedure. Aortopulmonary shunts and ductal stents were reserved for infants in whom RVOT patency could not be established, that is, RVOT muscular atresia and unsuccessful RVOT intervention, or those with nonconfluent central pulmonary arteries.1,16

Patient Groups

Our past institutional experience has indicated that complete repair performed between 3 and 11 months of age was associated with the best survival and physiological outcomes.7

The 4 groups were as follows: RVOT stent (stent group), primary repair <3 months of age with TOF-PS (early-PS group), primary repair <3 months of age with TOF-PA (early-PA group), and primary repair between 3 and 11 months of age (surg>3mo group). Differentiation was made between TOF-PS and TOF-PA as the latter has been reported to be a risk factor for neonatal repair.1,12 The surg>3mo group acted as a reference group of lower-risk TOF infants operated at the optimal age1,5,7,13 to compare with infants requiring early intervention. Forty-five infants were randomly selected from 407 operated during this period (randomization details are given in the Data Supplement).

Procedural Details

Details of the technique for RVOT stenting have previously been described.13 RVOT surgery were the following: (1) valve sparing for infants deemed at the time of surgery to have an adequately sized pulmonary annulus, (2) transannular patch, and (3) RVOT conduit. Additional procedures included RVOT muscle bundle resection, pulmonary arterioplasties, and MAPCA unifocalization or ligation. The decision to close the atrial and ventricular septal defects (VSD) was made at the discretion of the surgeon based on intraoperative hemodynamics. A case example of RVOT stenting in a TOF-PS infant is available in Movies I and II in the Data Supplement.

Data Collection

Medical records, echocardiography, angiography, and hemodynamic data were reviewed. Pulmonary artery and valve measurements were obtained from echocardiographic studies that were performed before RVOT stenting, before TOF repair, and at last available follow-up. This allowed for uniform assessment of pulmonary artery and valve data used at the time of decision making. PV and proximal pulmonary artery diameters were adjusted to body surface area and reported as Z scores based on normal values established at our institution. The Nakata index was calculated as the sum of the distal left pulmonary artery (LPA) and right pulmonary artery (RPA) areas indexed to body surface area.

Data Analysis

The data for each variable is summarized as a median and range (continuous variables) or as a proportion (binary variables) in Tables 1 and 2 and in Tables I through III in the Data Supplement. These tables also show the difference between the median or proportion of the stent group and that of the other groups. If the stent group is similar to another group for some variable, the difference between the medians or proportions of the 2 groups will be close to zero, and zero will lie within the 95% credible interval for this difference in medians or proportions. All of these credible intervals are 95% highest posterior density credible intervals obtained from a Bayesian hierarchical model (Data Supplement). Vague/
Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stent-Baseline (n=42)</th>
<th>Stent-Preoperative (n=37)</th>
<th>Early-PA (n=49)</th>
<th>Early-PS (n=44)</th>
<th>Surg&gt;3mo (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
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<tr>
<td>Median (range)</td>
<td>2.8 (1.4 to 8.0)</td>
<td>6.3 (4.0 to 10.7)</td>
<td>3.0 (2.2 to 4.4)</td>
<td>3.9 (2.4 to 6.9)</td>
<td>6.7 (4.2 to 10.0)</td>
</tr>
<tr>
<td>CI</td>
<td>1.6 to 4.4</td>
<td>2.7 to 7.0</td>
<td>1.7 to 4.3</td>
<td>2.0 to 6.0</td>
<td>3.3 to 9.2</td>
</tr>
<tr>
<td>Difference in group median</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>With stent-baseline (CI)</td>
<td>2.6 (2.0 to 3.0)*</td>
<td>0.03 (−0.3 to 0.3)</td>
<td>0.8 (0.5 to 1.2)*</td>
<td>2.9 (2.4 to 3.4) *</td>
<td></td>
</tr>
<tr>
<td>With stent-preoperative (CI)</td>
<td>−2.6 (−3.1 to −2.0)*</td>
<td>−1.7 (−2.4 to −1.1)*</td>
<td>0.3 (−0.4 to 1.0)</td>
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<td>Age, d</td>
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<tr>
<td>Median (range)</td>
<td>21 (1 to 303)</td>
<td>181 (45 to 464)</td>
<td>13 (4 to 82)</td>
<td>51 (2 to 90)</td>
<td>183 (94 to 299)</td>
</tr>
<tr>
<td>CI</td>
<td>12 to 29</td>
<td>156 to 213</td>
<td>13 to 20</td>
<td>31 to 51</td>
<td>166 to 195</td>
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<tr>
<td>Difference in group median</td>
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<tr>
<td>With stent-baseline (CI)</td>
<td>164 (137 to 196)*</td>
<td>−3 (−13 to 5)</td>
<td>21 (8 to 34)*</td>
<td>161 (145 to 178)*</td>
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</tr>
<tr>
<td>With stent-preoperative (CI)</td>
<td>−167 (−198 to −140)*</td>
<td>−144 (−176 to −115)*</td>
<td>−3 (−37 to 27)</td>
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<td>Saturation, %</td>
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<tr>
<td>Median (range)</td>
<td>75 (60 to 85)</td>
<td>86 (60 to 92)</td>
<td>86 (75 to 93)</td>
<td>85 (60 to 96)</td>
<td>86 (70 to 94)</td>
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<tr>
<td>CI</td>
<td>73 to 77</td>
<td>83 to 87</td>
<td>85 to 87</td>
<td>81 to 85</td>
<td>84 to 87</td>
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<td>Difference in group median</td>
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<tr>
<td>With stent-baseline (CI)</td>
<td>6 (−32 to 42)</td>
<td>6 (−31 to 41)</td>
<td>9 (−26 to 43)</td>
<td>8 (−28 to 42)</td>
<td></td>
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<tr>
<td>With stent-preoperative (CI)</td>
<td>0 (−35 to 35)</td>
<td>3 (−30 to 37)</td>
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<tr>
<td>PGE dependent</td>
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<tr>
<td>n</td>
<td>24</td>
<td>49</td>
<td>12</td>
<td>0</td>
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<tr>
<td>Proportion (CI)</td>
<td>0.57 (0.41 to 0.71)</td>
<td>1.0 (0.99 to 1.0)</td>
<td>0.27 (0.15 to 0.40)</td>
<td>0 (0 to 0)</td>
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<tr>
<td>Difference in proportions with stent-baseline (CI)</td>
<td>0.43 (0.28 to 0.6)*</td>
<td>−0.3 (−0.5 to −0.1)*</td>
<td>−0.57 (−0.72 to −0.42)*</td>
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<tr>
<td>Comorbidities</td>
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<td>Maximum in 1 patient</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>0</td>
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<tr>
<td>n with ≥1</td>
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<td>16</td>
<td>7</td>
<td>0</td>
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<tr>
<td>Proportion with ≥1 (CI)</td>
<td>0.38 (0.23 to 0.52)</td>
<td>0.33 (0.2 to 0.46)</td>
<td>0.16 (0.06 to 0.27)</td>
<td>0 (0 to 0.04)</td>
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<tr>
<td>Difference in proportion ≥1 with stent-baseline (CI)</td>
<td>−0.08 (−0.28 to 0.11)</td>
<td>−0.25 (−0.43 to −0.06)*</td>
<td>−0.4 (−0.56 to −0.25)*</td>
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<tr>
<td>Prematurity</td>
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<td>n</td>
<td>11</td>
<td>11</td>
<td>4</td>
<td>9</td>
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<tr>
<td>Proportion (CI)</td>
<td>0.26 (0.13 to 0.35)</td>
<td>0.22 (0.12 to 0.32)</td>
<td>0.13 (0.04 to 0.22)</td>
<td>0.20 (0.1 to 0.29)</td>
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<tr>
<td>Difference in proportions with stent-baseline (CI)</td>
<td>−0.01 (−0.17 to 0.11)</td>
<td>−0.09 (−0.27 to 0.02)</td>
<td>−0.03 (−0.2 to 0.09)</td>
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<td>NEC</td>
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<td>n</td>
<td>1</td>
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<td>Sepsis</td>
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<td>n</td>
<td>2</td>
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<td>GI surgery</td>
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<td>0</td>
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</table>

(Continued)
very weakly informative priors were used. Tables IV through VI in the Data Supplement includes bootstrap 95% confidence intervals of the trimmed means or proportions and for the difference between the trimmed mean or proportion of the stent group and that of other groups. Our focus is on the behavior of the stent group, and all possible pairwise comparisons are not discussed within the text. Similar conclusions about the stent group are reached by these different methods of analysis. The probability of PV preservation was estimated by logistic regression with very weakly informative priors. Reinterventions are displayed as Kaplan–Meier curves. Analyses were performed with R-3.3.1 and JAGS 4.2.0.

Table 1. Continued

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stent-Baseline (n=42)</th>
<th>Stent-Preoperative (n=37)</th>
<th>Early-PA (n=49)</th>
<th>Early-PS (n=44)</th>
<th>Surg&gt;3mo (n=45)</th>
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<tbody>
<tr>
<td>Genetic syndrome</td>
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<td>n</td>
<td>13</td>
<td>10</td>
<td>6</td>
<td>7</td>
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<tr>
<td>Proportion (CI)</td>
<td>0.24 (0.15 to 0.4)</td>
<td>0.20 (0.11 to 0.30)</td>
<td>0.14 (0.07 to 0.25)</td>
<td>0.17 (0.08 to 0.27)</td>
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<tr>
<td>Difference in proportions</td>
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<tr>
<td>with stent-baseline (CI)</td>
<td>−0.05 (−0.23 to 0.06)</td>
<td>−0.09 (−0.28 to 0.03)</td>
<td>−0.08 (−0.27 to 0.04)</td>
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<td>MAPCAs</td>
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<tr>
<td>n</td>
<td>13</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Proportion (CI)</td>
<td>0.31 (0.16 to 0.43)</td>
<td>0.06 (0 to 0.13)</td>
<td>0.02 (0 to 0.08)</td>
<td>0.04 (0 to 0.11)</td>
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<tr>
<td>Difference in proportions</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>with stent-baseline (CI)</td>
<td>−0.23 (−0.39 to −0.06)*</td>
<td>−0.26 (−0.41 to −0.11)*</td>
<td>−0.24 (−0.4 to 0.1)*</td>
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</tbody>
</table>

Continuous variables are presented as their median and range, categorical variables as a proportion. 95% CI are derived from a Bayesian hierarchical model. Group comparisons are facilitated by examining the difference between a group’s median or proportion and that of the stent group. The 2 groups differ, if the 95% CI for this difference in medians (or proportions) does not include 0 (*). CI indicates credible interval; GI, gastrointestinal; MAPCAs, multiple aortopulmonary collateral arteries; NEC, necrotizing enterocolitis; PA, pulmonary atresia; PGE, prostaglandin; and PS, pulmonary stenosis.

Results

The primary surgical repair groups were early-PS (n=44), early-PA (n=49), and surg>3mo (n=45). Forty-two infants (TOF-PS, n=33 and TOF-PA, n=9) had successful RVOT stenting. Three stent infants were >3 months old, presenting late (4, 7, and 10 months old) with severe cyanosis, hypoplastic pulmonary arteries, and MAPCAs. Early intervention (<3 months old) was performed in 24% of the studied TOF population. RVOT stenting was 100% successful in

Figure 1. Distribution of noncardiac comorbidities. The stent group has a preponderance of low weight patients with small pulmonary arteries and multiple comorbidities. Each infant is represented by a number that indicates his/her number of comorbidities. The pulmonary arteries of the stent patient with 5 comorbidities were too small to measure accurately by echocardiography. PA indicates pulmonary atresia; and PS, pulmonary stenosis.
of Right Ventricular Outflow Tract Stenting

the TOF-PS patients. In the TOF-PA infants with true valvar atresia (n=12), radiofrequency perforation of the PV was successful in 75% (9/12), and all of these were successfully stented (9/9) (Figure I in the Data Supplement). Additional patient and RVOT stenting details are available in the Data Supplement.

In 5 infants, RVOT stenting was preceded by a separate procedure with radiofrequency perforation of the PV (n=2), PV balloon dilation (n=2), and pulmonary artery stenting (n=1). One early-PS infant underwent PV dilation before repair.

There were 3 infants with TOF-atrioventricular septal defect (stent, n=2 and early-PS, n=1) and 12 infants with TOF double-outlet RV (stent, n=5; early-PA, n=2; early-PS, n=4; and surg>3mo, n=1).

Clinical Characteristics at the Time of Stenting or Primary Surgical Repair

Clinical characteristics are summarized in Table 1.

Surgical repair or RVOT stenting was required earlier at a median of 13 days in the early-PA and 21 days in the stent infants compared with 51 days in the early-PS group. Baseline saturations in the stent group increased acutely from a median of 75% to 94% after stenting and 86% preoperatively. The stent and early-PA infants had similar low weights that were ≈0.8 kg less than the early-PS infants. No surg>3mo infant had a noncardiac comorbidity. Stent infants had more concurrence of weight <2.5 kg, Nakata index <100 mm²/m², and multiple comorbidities compared with the other 3 groups (Figure 1). Clinical course flow diagrams are provided in Figures II and III in the Data Supplement.

PV and Pulmonary Arteries

PV and artery dimension Z scores are in Table 2 and Figures 2 and 3. The stent group and the few early-PA neonates with a measurable PV (11/49) had similar small PV dimensions, which were smaller than the early-PS and surg>3mo groups.

The stent group had the smallest pulmonary arteries whether measured in absolute terms (LPA and RPA diameter in mm), Z score (LPA and RPA), or Nakata index (Table 2; Figure 3; Table I in the Data Supplement). During a median 5.7-month interval from stenting to surgical repair, both

<table>
<thead>
<tr>
<th>Table 2. Pulmonary Valve and Artery Dimensions</th>
</tr>
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<tbody>
<tr>
<td>Variable</td>
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<tr>
<td></td>
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<tr>
<td>PV Z score</td>
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<tr>
<td>Median (range)</td>
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<tr>
<td>Stent-Baseline (n=42)</td>
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<tr>
<td>−6.6 (−13.9 to −3.2)</td>
</tr>
<tr>
<td>Stent-Preoperative (n=37)</td>
</tr>
<tr>
<td>−6.3 (−13.8 to −0.9)</td>
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<tr>
<td>Early-PA (n=49)</td>
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<tr>
<td>−4.4 (−12.0 to −0.7)</td>
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<tr>
<td>Early-PS (n=44)</td>
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<td>−2.7 (−5.9 to 2.5)</td>
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<td>Surg&gt;3mo (n=45)</td>
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<tr>
<td>−2.7 (−5.9 to 2.5)</td>
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<tr>
<td>CI</td>
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<td>−7.7 to −6.3</td>
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<tr>
<td>Difference in group median</td>
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<tr>
<td>With stent-baseline (CI)</td>
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<td>−0.6 (−3.4 to 2.2)</td>
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<td>2.3 (1.3 to 3.3)*</td>
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<td>4.6 (3.6 to 5.5)*</td>
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<td>LPA Z score</td>
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<td>Median (range)</td>
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<td>Stent-Baseline (n=42)</td>
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<td>−3.9 (−8.4 to 0.1)</td>
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<td>Stent-Preoperative (n=37)</td>
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<td>−1.4 (−12.0 to 2.9)</td>
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<td>Early-PA (n=49)</td>
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<td>−1.7 (−6.8 to 3.10)</td>
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<td>Early-PS (n=44)</td>
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<td>−2.3 (−7.8 to 2.70)</td>
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<td>Surg&gt;3mo (n=45)</td>
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<td>−0.68 (−4.10 to 3.40)</td>
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<td>−4.4 to −3.1</td>
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<tr>
<td>Difference in group median</td>
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<tr>
<td>With stent-baseline (CI)</td>
</tr>
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<td>1.9 (0.8 to 2.9)*</td>
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<tr>
<td>1.9 (1.1 to 2.8)*</td>
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<tr>
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Continuous variables are presented as their median and range, categorical variables as a proportion. 95% CI are derived from a Bayesian hierarchical model. Group comparisons are facilitated by examining the difference between a group’s median or proportion and that of the stent group. The 2 groups differ, if the 95% CI for this difference in medians (or proportions) does not include 0 (*). Absolute dimensions (mm) for PV, LPA, and RPA are available in the Data Supplement. CI indicates credible interval; LPA, left pulmonary artery; PA, pulmonary atresia; PS, pulmonary stenosis; PV, pulmonary valve; and RPA, right pulmonary artery.
branch pulmonary arteries grew in absolute terms (LPA and RPA both x1.6), by Z score (LPA x2.8, RPA x2.5) and Nakata index (x1.8; Figure 3). Hence, the stent group underwent complete repair with pulmonary artery dimensions similar to the surg>3mo patients. The Nakata index was <100 mm²/m² in 83% of stent infants at the time of RVOT stenting compared with 10% to 25% in the other groups, whereas by the time of surgery, only 16% of stent infants had a Nakata index <100 mm²/m².

The stent group had the highest number of infants with MAPCAs (n=13, 31%; Table 1). Only stent infants had clinically important MAPCAs that warranted intervention: preoperative embolization (n=4) and intraoperative unifocalization (n=6) or ligation (n=5).

Figure 2. Left: Pulmonary valves (PV) are smaller in the early treatment groups compared with surg>3mo group. Right: Probability of PV preservation is predicted by preoperative Z score. Assigning a patient to the stent group (black) commits them to a transannular patch and is based on an echocardiogram rather than an intraoperative assessment. The curve based only on the surgeon’s intraoperative decision (early-PS, surg>3mo; red) is similar to the one that also includes the stent group (black). The 2 curves have overlapping 95% credible intervals (broken lines), suggesting consistency. PA indicates pulmonary atresia; and PS, pulmonary stenosis.

Figure 3. A, Angiography. Left: initial right ventricular outflow tract (RVOT) stent palliation at 29 d of age. Right: cardiac catheterization 4 mo later demonstrating increase in pulmonary artery size. B, The stent group had the smallest pulmonary arteries (LPA; RPA; Nakata index) that grow into the range of the surg>3mo group by the time of surgical repair. LPA indicates left pulmonary artery; PA, pulmonary atresia; PS, pulmonary stenosis; and RPA, right pulmonary artery.
After RVOT stenting, additional catheterizations were required for RVOT obstruction (repeat dilation of a stent once \([n=7]\) or twice \([n=1]\); implantation of a second \([n=9]\) or third \([n=1]\) stent), pulmonary artery dilation \((n=1)\) or embolization of MAPCAs \((n=2)\) before surgery (Table II in the Data Supplement). The additional RVOT stents were required for obstruction proximal \((n=7)\) or distal to \((n=1)\) or within the existing stent \((n=2)\).

The stent group underwent complete repair at \(\approx 6\) months and \(\approx 6.3\) kg, similar to the surg\(>3\)mo group. Three stent infants await elective surgical repair. In 2 stent infants, further cardiac treatment was not sought because of severe comorbidities. Further perioperative data are available in Table III in the Data Supplement.

Branch pulmonary artery repair was often (33% to 62%) required in all the groups. The PV was preserved most frequently in 69% of the surg\(>3\)mo group compared with 41% in the early-PS and none of the stent or early-PA patients. The stents were completely retrieved in 35 infants (95%). The probability of PV preservation decreased with smaller PV diameter: 0.46, 0.33, and 0.23 for PV \(Z\) scores of \(-4\), \(-5\) and \(-6\), respectively (Figure 5). Cardiopulmonary bypass (CPB) time was the longest in the stent group. Postrepair median RV pressure was \(\approx 50\) mmHg systemic in all groups. The VSD was left open or fenestrated in 6 patients, all with a Nakata index <100 mm²/m² (stent, \(n=5\); early-PS, \(n=1\)). Two of the stent group have subsequently had VSD closure 2.4 and 3.2 years postoperatively. Delayed chest closure was not required in the surg\(>3\)mo patients and was less frequent in the stent group (17%) compared with the early-PA and early-PS groups. Six infants required postoperative extracorporeal membrane oxygenation (stent, \(n=4\); early-PA, \(n=2\)) and in 5 of these the Nakata index was <100 mm²/m². Cerebral stroke or hemorrhage occurred in 3 infants who underwent primary surgical repair at 8, 44, and 74 days. There were 4 early deaths in the stent and early-PA groups \((n=2\) each). There were 2 late deaths at 3 (early-PS, septicemia) and 1.3 years (early-PA, sudden death) after repair.

Length of Stay
Three LOS time periods are reported (Table III and Figure IV in the Data Supplement): (1) presurgical, the total time before surgical repair; (2) postsurgical, time from repair to hospital discharge; and (3) the cumulative stay, the sum of presurgical and postsurgical stay. The distribution of cumulative stay was right skewed with a long tail and a median of \(\approx 1\) month for the early-PA \((28\) days) and stent \((25\) days) groups, which was considerably longer than the early-PS \((16\) days) and surg\(>3\)mo \((7\) days) groups. Preoperative stay was a major component of cumulative stay for the 2 groups with the longest stay (early-PA: median 49% and maximum 81% of total stay; stent: median 47% and maximum 87% of total stay) but was much less important in the other 2 groups (early-PS: median 14% and maximum 75% of total stay; surg\(>3\)mo: median 0% and maximum 18% of total stay). The postoperative LOS was shortest for the surg\(>3\)mo \((7\) days) with the other 3 groups having similar long values (stent 11 days; early-PA 14 days; and early-PS 13 days). Postoperative intensive care unit stay was shortest for the surg\(>3\)mo \((2\) days) and 2.5 to 3.5 times longer for the other groups (stent 5 days; early-PS 6 days; and early-PA 7 days).

Reintervention After TOF Complete Repair
No patient was lost to follow-up. Reintervention after complete repair occurred in 2 phases: (1) the initial 15 months
during which 25% of the stent, early-PS, and early-PA had at least 1 intervention, whereas only 4% of the surg≥3mo group had an intervention during this period and (2) a late phase with a similar slower reintervention rate in all 4 groups, with the surg≥3mo group starting from a lower base (Figure 4). The majority of these procedures were catheterizations. Pulmonary artery procedures predominated in the early phase and were more frequent in those with a small Nakata index (Figure VA in the Data Supplement). Interventions on the RVOT increased slowly in all groups, and by 4 years were as numerous as the pulmonary artery interventions in the early-PA and surg≥3mo groups but remained less common in the stent and early-PS groups. Reintervention graphs are provided in Figure V in the Data Supplement.

Discussion

RVOT stenting has previously been described in isolation, with case series focusing on technique and acute results.15,19,20,22,28 In this study, data on 180 patients who underwent RVOT stenting, early primary repair, and standard risk repair put our selection criteria for RVOT stenting and early primary repair into perspective. We demonstrate efficacy and safety of RVOT-stenting in a subset of TOF infants who were symptomatic and were selected by their multiple adverse clinical factors that we estimated would cumulatively increase the risk of primary repair. These infants had good outcomes relative to infants with lower risk who underwent primary repair.

The optimal timing for TOF repair has evolved to balance the benefits of early repair with the risks related to the technical and physiological challenges of neonatal surgery.1,2,7,10,13,14,21,22 Most (88%) of our early intervention (early-PA, early-PS, and stent) groups required treatment before 60 days of age and thus would be considered as higher risk groups in many centers. Infants <3 months of age selected for primary repair (early-PS and early-PA) had excellent survival rates, similar to other reports of neonatal or early infant TOF-PS and TOF-PA repair (1-year survival of 94–95.4%).12,15,16,19 All 3 postoperative neurological events occurred in the early repair patients, reinforcing the risks of cardiac surgery to the infant brain.19

A Nakata index ≤100 mm²/m² (Figure 3) captures ≥95% of the stent group’s distribution and confirms that we identified patients for RVOT stenting based on small pulmonary arteries. TOF patients with severely hypoplastic central pulmonary arteries (Nakata index <100 mm²/m²) are at risk of suprasystemic RV pressures and RV failure after primary repair.4–6 In these infants, there are merits to staging and avoiding rescue VSD fenestration.5 Strategies have included surgically created RVOT augmentation with the VSD left open and aortopulmonary shunts. Many of our stent infants had diminutive central pulmonary arteries and had outcomes better than historical reports.4–6 Our institutional preference is to avoid BTS,16 but we recognize that others have reported success with this approach, albeit with difficulty in small, premature neonates with hypoplastic pulmonary arteries.11,22–26

Separating patients by PV diameter was more difficult, with overlap between the stent and early-PS groups (Table 2; Table III in the Data Supplement; Figure 2) and to a lesser extent surg≥3mo group. Potential for PV preservation excluded RVOT stent implantation in our approach. However, we were overly optimistic in our ability to preserve PV based on the preoperative echocardiogram, as they were only salvaged in 41% of the early-PS group. A reasonable cutoff maybe a PV Z score of −5 to −6 (Figure 2), which corresponds to a probability of PV preservation of 0.33 and 0.23, respectively. This would increase the number of early-PS patients referred for RVOT-stenting, but with only a small increase in the number of transannular patches.

Early primary repair results in a high incidence (80% to 100%) of transannular patch repair.2,3,12–14,21 PV preservation rates range between 32% and 60% after BTS palliation.11,23 In the report by Stewart et al,24 primary repair infants had a mean PV diameter of 9.1±1.5 mm, Z score −1.7±1.2 with PV preservation in 80% but even the transannular patch infants had a larger mean PV of 6.4±1.1 mm and Z score −4.8±1.7. Stent implantation wholly below the valve provides the potential for preservation of the PV annulus at the time of TOF repair but is not applicable to all patients.19

RVOT Stenting and Technical Considerations

This series includes successful percutaneous RVOT stenting in the TOF-PA subgroup. Stumper et al17 did not include TOF-PA in their series and had a similar high success rate of 95% for TOF-PS infants. Others have described a hybrid approach of perventricular RVOT stenting for TOF-PA infants with hypoplastic pulmonary arteries.24 The high frequency of inadvertent perforation and pericardial effusion did not preclude RVOT stenting in the TOF-PA subgroup, if the PV was successfully perforated (Data Supplement). This series includes our learning curve, and our current reintervention rate for residual obstruction after RVOT stenting has decreased, as we more extensively covered the majority/all of the RVOT.7,15 Complete intraoperative stent retrieval was achieved in 95% in this study and in 44% in the study by Barron et al.19 CPB times were longest in the stent group. Barron et al19 comment that stent removal increased the length of the procedure but also noted there was no difference in CPB time between repairs after RVOT stenting compared with transannular patch repairs in unstented infants. Similarly, Castleberry et al22 report that CPB time was not different between repair after initial BTS and RVOT stenting. RVOT reconstruction (including stent removal) and complex pulmonary artery anatomy seem to have important contributions to CPB time.

Length of Stay

Postoperative outcome data consistently demonstrate shorter LOS when TOF repair is performed beyond the neonatal period.12,13,19,29 Postoperative inotropic, intensive care unit, and hospital stay days as reported by Pigula et al13 for infants undergoing primary repair <3 months of age were similar to our 3 early intervention groups but longer than our surg≥3mo group. Early-PS infants were older than the early-PA infants, and LOS was shorter both postoperatively and cumulatively. The younger age of TOF-PA infants provides some explanation of the higher morbidity reported in the literature.
for this subgroup compared with TOF-PS infants. All the early intervention groups had long preoperative LOS, which was often the major component of their cumulative hospital stay. Some of this is unavoidable (prematurity, noncardiac surgery). There was a trend for the stent group to have the shortest postoperative intensive care unit stay of all the early intervention groups (Table III in the Data Supplement). Kanter et al reported shorter LOS after BTS palliation compared with primary TOF repair with equalization of cumulative LOS after subsequent repair.

Limitations

Our 3-month cutoff is an institutional criterion. Each center can identify, although the exact criteria and thresholds will vary, a higher risk group of TOF infants that require earlier than usual treatment for cyanosis.

The 4 groups are not identical by design. Our focus in this study has been on the worst end of this early treatment group who were bridged to complete repair at 6 months by RVOT stenting. Hence, we provide comparative data to demonstrate that the stent group had worse anatomy and more medical problems than the other early treatment groups.

We do not explore an alternative bridging strategy, for example, BTS. Based on our current criteria, only a quarter of our patients require a bridging procedure, and there were insufficient patients to explore 2 bridging procedures concurrently. In our institution, BTS historically have had suboptimal outcomes.

This study demonstrates the efficacy and safety of RVOT stenting as a bridging procedure, but a randomized trial is required to identify the optimal management among RVOT stenting, BTS, or primary repair for infants with similar risk profiles. To date, a randomized trial of early primary repair versus staged repair with a BTS has not been attempted, despite it being feasible for several decades. A trial comparing strategies may choose a Nakata index ≤100 mm²/m² and PVZ score <-5 as appropriate anatomical thresholds for patient selection.

Conclusions

In an era of primary TOF repair, some young infants possess significant risk factors, most notably small pulmonary arteries, MAPCAs, and comorbidities in whom a bridging procedure still has a role. RVOT stenting resulted in relief of cyanosis, somatic and pulmonary artery growth, and resolution of noncardiac comorbidities. This translated to good clinical outcomes, comparable to those with initially more favorable clinical features.

Disclosures

None.

References


Right Ventricular Outflow Tract Stenting in Tetralogy of Fallot Infants With Risk Factors for Early Primary Repair
Juan Pablo Sandoval, Rajiv R. Chaturvedi, Lee Benson, Gareth Morgan, Glen Van Arsdell, Osami Honjo, Christopher Caldarone and Kyong-Jin Lee

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SUPPLEMENTAL MATERIAL

Right ventricular outflow tract-stenting in tetralogy of Fallot infants with risk factors for early primary repair

Supplement Methods

The first part of the Supplement provides additional clinical data as referenced in the main manuscript.

The second part of the Supplement includes additional statistical analyses. Bayesian hierarchical models were used to ascertain 95% highest posterior density credible intervals for the median of measured variables in the four (Stent, early-PA, early-PS, Surg>3mo) or five (Stent(baseline), Stent(pre-op), early-PA, early-PS, Surg>3mo) clinical groups. Identical conclusions are reached from an analysis of trimmed means and their 95% bootstrap confidence intervals.

Study patient selection criteria

A. Inclusion criteria for entry into the study were:
   1) TOF-PS or TOF-PA with confluent pulmonary arteries. TOF with DORV or TOF with AVSD included.
   2) < 1 year old at presentation

B. Exclusion criteria for entry into the study:
   1) TOF with absent pulmonary valve syndrome

C. Criteria for RVOT stenting:
1) All infants had duct-dependent pulmonary blood flow or significant cyanosis requiring treatment prior to hospital discharge.

2) All infants were assessed as having a pulmonary valve that had a very low chance of being salvaged at the time of surgery.

3) One or more of the following:
   a) Small pulmonary arteries (z-score < -2)
   b) Prematurity (< 37 weeks)
   c) Significant non-cardiac comorbidities e.g. necrotizing enterocolitis, sepsis, cerebral vascular event, lung compromise, neonatal surgery required e.g. tracheoesophageal fistula and gastrointestinal anomalies

4) Coronary artery anatomy did not influence the decision to proceed to stenting.

D. Randomization of Surg>3 mo group. The Stent group data was collected over a 15 year period, thus we identified all 407 consecutive TOF-PS patients with confluent pulmonary arteries that were repaired during that period. These consecutive patients were numbered sequentially 1 to 407. We used a uniform random number generator to provide 45 integers between 1 and 407, inclusively. These 45 integers were used to identify the corresponding patient.

Additional patient characteristics – age of Stent infants

Five infants were >90 days old at the time of RVOT-stenting: 2 premature with TOF-PA (born at 27 and 29 weeks; stented at 39 weeks and 43 days corrected respectively; their weight increased
from a birthweight of 1 and 0.98 kg to 3.1 and 2.4 kg respectively, at the time of stenting) and 3 late presenting TOF-PS infants (4, 7, 10 months old) with severe cyanosis, hypoplastic pulmonary arteries and MAPCAs.

**RVOT stent implantation data and discussion**

RVOT angiography delineated the anatomy and the presence of antegrade blood flow (Supplement Figure 1). All infants with TOF-PA required PV radiofrequency energy perforation prior to RVOT stenting. Balloon dilation of the PV was given first consideration and RVOT stent implantation was performed if the obstruction extended along a muscular outflow tract. All stents were implanted through a percutaneous venous route. Coronary stents (single or multiple) were utilized in all infants.

All TOF-PS patients (n=28) referred for RVOT-stenting were successfully stented. An additional 5 patients were diagnosed as valvar pulmonary atresia by echocardiography, but at the time of RVOT angiography were found to have antegrade blood flow across their pulmonary valve (Supplement Videos AB). These 5 patients were given their correct diagnosis of TOF-PS in this study. This makes a total of 33 TOF-PS patients all of whom were successfully stented.

Echocardiography had suggested valvar atresia in 19 patients, but 5/19 were found to have antegrade flow across their pulmonary valve by angiography and 2/19 were found to have muscular atresia. One of these muscular atresia patients had a mistaken attempt at RF
perforation. Hence there were 12/19 true valvar pulmonary atresia patients (Supplement Figure 2).

RVOT-stenting of TOF with valvar pulmonary atresia is a 2 step procedure:

a) radiofrequency perforation of the pulmonary valve (successfully performed in 9/12), followed by

b) stenting of the pulmonary valve and RVOT (successfully performed in 9/9).

Hence, failure to stent a TOF-PA patient (5/14) occurred because we were unable to perforate the pulmonary valve (n=5). Failure to perforate the pulmonary valve, occurred because of technical factors (n=3) or because there was muscular rather than valvar atresia (n=2).

Success of RVOT stenting depends on whether the denominator includes the total number of TOF-PA infants in whom radiofrequency perforation had any chance of success (valvar atresia =12; n=33+12=45; success=42/45, 93%) or in the total number of TOF-PA infants in whom radiofrequency perforation was attempted (valvar atresia =12, muscular atresia=1; n=33+ 13=46; success= 42/46, 91%). In summary, RVOT-stenting was 100% successful in the TOF-PS patients (33/33). In the TOF-PA infants with true valvar atresia (n=12), radiofrequency perforation of the pulmonary valve was successful in 75% (9/12) and all of these were successfully stented (9/9; Supplement Figure 1).
Inadvertent perforation did not preclude subsequent successful RVOT-stenting and occurred in 6 infants with pericardiocentesis required in 2. Three infants, who had valvar atresia RVOT anatomy, had unsuccessful RVOT-stenting attempt, one of whom had inadvertent perforation followed by a failed attempt at ductal stenting. This infant proceeded to a surgical shunt 4 days later which required 3 revisions and was complicated by intra-operative cerebral injury and seizures 6 days later, with subsequent complete repair at 5.5 months of age. The other 2 infants underwent complete repair with transannular patch at 7 and 12 days of age which was 4 and 9 days respectively after failed RVOT-stenting attempt.

Discussion of RF perforation technique: PV-RF complication occurred frequently but occurred in small infants with small PV size with significant risks for surgery as demonstrated by the infant who experienced significant technical issues during subsequent BTS placement complicated by stroke. Reciprocally, RVOT-stenting has been performed after unsuccessful aorto-pulmonary shunt procedures\(^1\). We have previously reported successful PV-RF procedures in 75% of infants with a more heterogenous population of PA with VSD conditions\(^2\) and 93% of infants with pulmonary atresia with an intact ventricular septum\(^3\) the latter indicating that RVOT anatomy influences technical success. In the RVOT stent experience reported by Stumper et al., pulmonary atresia patients were excluded\(^4\). Others have described a hybrid approach of perventricular RVOT-stenting for infants with TOF-PA and hypoplastic pulmonary arteries\(^5\). Lack of antegrade flow by echocardiography or right ventriculography should not be regarded as definitive and a direct RVOT angiogram is recommended given there was 100% procedural success if the anatomy was TOF-PS.
Post-operative deaths

There were 4 early post-operative deaths in the Stent and early-PA groups (n=2 each) (Supplement Figure 2). Both Stent infants required post-operative ECMO, one had an open VSD (died at 10 days) and the other with a closed VSD weaned off ECMO after 3 days and died from non-cardiac causes. In the early-PA group, 2 infants died at 54 and 55 days post-operatively, one requiring ECMO support, both with RV failure.

Follow-up

No patient was lost to follow-up. Median (range) follow-up times were: Stent 3.2 years (0.3, 12.1 years), early-PS 5.0 years (0.1, 14.0 years), early-PA 7.8 years (0.2, 13.8 years) and Surg>3mo 5.0 years (0.02, 12.4 years).

Pulmonary artery missing data

Supplement Table 1 displays the number of data points for pulmonary artery and valve measurements for all groups. In the Stent (baseline) group, both the RPA and LPA were too small to be measured in 1 infant. In the early-PA group, we were unable to find the echocardiogram videotape in 2 infants for LPA measurements and the LPA was not adequately visualized in 1 infant. In the early-PS group, the videotape was not available in 1 infant
Supplement Table 1. Pulmonary valve and artery absolute dimensions (Bayesian hierarchical model)

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<td>[6.8, 8.0]</td>
<td></td>
</tr>
<tr>
<td>Difference in group median with Stent (baseline)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>0 [-1.1,1.1]</td>
<td>1.4 [0.9, 1.9]</td>
<td>3.7 [3.1,4.4]</td>
<td></td>
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<tr>
<td>LPA Z-score</td>
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<tr>
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<td>n=47</td>
<td>n=44</td>
<td>n=45</td>
</tr>
<tr>
<td>median (range)</td>
<td>-3.9 (-8.4, 0.1)</td>
<td>-1.4 (-12.0, 2.9)</td>
<td>-1.7 (-6.8, 3.10)</td>
<td>-2.3 (-7.8, 2.70)</td>
<td>-0.68 (-4.10, 3.40)</td>
</tr>
<tr>
<td>[CI]</td>
<td>[-4.4, -3.1]</td>
<td>[-2.6, -0.9]</td>
<td>[-2.2, -1.1]</td>
<td>[-3.0, -1.8]</td>
<td>[-1.2, 0]</td>
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<tr>
<td>LPA (mm)</td>
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<td>n=37</td>
<td>n=47</td>
<td>n=44</td>
<td>n=45</td>
</tr>
<tr>
<td>median (range)</td>
<td>3.0 (1.2, 5.8)</td>
<td>4.9 (1.2, 8.0)</td>
<td>4.0 (1.9, 7.1)</td>
<td>3.8 (1.9, 6.6)</td>
<td>5.7 (3.3, 9.0)</td>
</tr>
<tr>
<td>[CI]</td>
<td>[2.7, 3.3]</td>
<td>[4.3, 5.4]</td>
<td>[3.6, 4.2]</td>
<td>[3.5, 4.0]</td>
<td>[5.3, 6.1]</td>
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<tr>
<td>Difference in group median with Stent (baseline)</td>
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</tr>
<tr>
<td></td>
<td>1.8 [1.2,2.4]</td>
<td>0.9 [0.5,1.2]</td>
<td>0.7 [0.4,1.1]</td>
<td>2.6 [2.0,3.1]</td>
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</tr>
<tr>
<td></td>
<td>1.1 [-1.7,-0.5]</td>
<td>-0.9 [-1.6,-0.4]</td>
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<tr>
<td>RPA Z-score</td>
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<td>n=37</td>
<td>n=49</td>
<td>n=44</td>
<td>n=45</td>
</tr>
<tr>
<td>median (range)</td>
<td>-4.05 (-9.6, 1.32)</td>
<td>-1.6 (-6.6, 1.5)</td>
<td>-1.0 (-8.4, 2.3)</td>
<td>-1.75 (-4.70, 2.50)</td>
<td>-0.5 (-4.1, 3.5)</td>
</tr>
<tr>
<td>[CI]</td>
<td>[-4.7, -3.3]</td>
<td>[-2.2, -0.8]</td>
<td>[-1.7, -0.8]</td>
<td>[-2.2, -1.3]</td>
<td>[-1.2, -0.1]</td>
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</tbody>
</table>
### RPA (mm)

<table>
<thead>
<tr>
<th></th>
<th>Median (Range)</th>
<th>CI</th>
<th>Median (Range)</th>
<th>CI</th>
<th>Median (Range)</th>
<th>CI</th>
<th>Median (Range)</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.0 (1.2, 6.0)</td>
<td>[2.8, 3.3]</td>
<td>4.8 (2.6, 7.8)</td>
<td>[4.5, 5.4]</td>
<td>4.3 (1.6, 6.5)</td>
<td>[4.0, 4.5]</td>
<td>4.0 (3.0, 7.5)</td>
<td>[4.0, 4.6]</td>
</tr>
<tr>
<td>Difference in group median with Stent (baseline) [CI]</td>
<td>1.9 [1.4, 2.5]</td>
<td>-0.7 [-1.2, -0.2]</td>
<td>4.3 (1.6, 6.5)</td>
<td>[4.0, 4.5]</td>
<td>1.2 [0.8, 1.6]</td>
<td>-0.7 [-1.3, -0.2]</td>
<td>2.6 [2, 3.1]</td>
<td>0.6 [0, 1.2]</td>
</tr>
</tbody>
</table>

### Nakata index (mm²/m²)

<table>
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<tr>
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<th>n=41</th>
<th>n=37</th>
<th>n=46</th>
<th>n=43</th>
<th>n=45</th>
</tr>
</thead>
<tbody>
<tr>
<td>median (range)</td>
<td>79 (18, 214)</td>
<td>147 (57, 299)</td>
<td>139 (80, 324)</td>
<td>136 (64, 313)</td>
<td>167 (51, 466)</td>
</tr>
<tr>
<td>[CI]</td>
<td>[65.6, 87.4]</td>
<td>[134.9, 168.2]</td>
<td>(131.4, 159.6)</td>
<td>[124.6, 157.4]</td>
<td>[159.8, 210.5]</td>
</tr>
</tbody>
</table>

Difference in medians for LPA, RPA, PV z-scores are in Table 2 in the main paper.

Continuous variables are presented as their median and range, binary variables as a proportion. 95% credible intervals [CI] are derived from a Bayesian hierarchical model. Group comparisons are facilitated by examining the difference between a group’s median or proportion, and that of the Stent group. The two groups differ, if the 95% credible interval for this difference in medians (or proportions) does not include 0 (bold).

Abbreviations: LPA, left pulmonary artery; PV, pulmonary valve; RPA, right pulmonary artery.
Supplement Table 2. Time interval between index catheterization and re-intervention

<table>
<thead>
<tr>
<th>Patient</th>
<th>Days to re-intervention 1 (from initial RVOT stent)</th>
<th>Days to re-intervention 2 (from initial RVOT stent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>109 (additional stent)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>44 (additional stent)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>64 (additional stent)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>111 (APC coil)</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>151 (APC coil, dilate stent)</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>58 (dilate stent)</td>
<td>188 (dilate stent)</td>
</tr>
<tr>
<td>18</td>
<td>15 (additional stent)</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>8 (additional stent)</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>90 (dilate stent)</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>118 (APC coil)</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>31 (additional stent)</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>18 (additional stent)</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>28 (additional stent)</td>
<td>103 (additional stent)</td>
</tr>
<tr>
<td>38</td>
<td>9 (additional stent)</td>
<td></td>
</tr>
<tr>
<td>39</td>
<td>24 (dilate stent)</td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>149 (LPA dilation, APC coil)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: APC, aortopulmonary collateral; LPA, left pulmonary artery; RVOT, right ventricular outflow tract
Supplement Table 3. Peri-operative data (Bayesian hierarchical model)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stent</th>
<th>early-PA</th>
<th>early-PS</th>
<th>Surg&gt;3mo</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n=37</td>
<td>n=49</td>
<td>n=44</td>
<td>n=45</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (range)</td>
<td>139 (67, 310)</td>
<td>117 (70, 230)</td>
<td>107 (65, 251)</td>
<td>99 (57, 208)</td>
</tr>
<tr>
<td>[CI]</td>
<td>[123, 158]</td>
<td>[110, 123]</td>
<td>[102, 123]</td>
<td>[94, 113]</td>
</tr>
<tr>
<td>Cross clamp time (min)</td>
<td>85 (26, 187)</td>
<td>80 (33, 180)</td>
<td>83 (40, 173)</td>
<td>67 (32, 156)</td>
</tr>
<tr>
<td>[CI]</td>
<td>[74, 98]</td>
<td>[69, 83]</td>
<td>[74, 90]</td>
<td>[62, 77]</td>
</tr>
<tr>
<td>PV preserved</td>
<td>0</td>
<td>0</td>
<td>18</td>
<td>31</td>
</tr>
<tr>
<td>n</td>
<td></td>
<td></td>
<td>0.41 [0.27, 0.55]</td>
<td>0.69 [0.56, 0.82]</td>
</tr>
<tr>
<td>proportion [CI]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>comparison with Stent group, difference in proportions [CI]</td>
<td>0 [-0.01, 0]</td>
<td>0.4 [0.3, 0.6]</td>
<td>0.7 [0.5, 0.8]</td>
<td></td>
</tr>
<tr>
<td>Transannular patch</td>
<td>29</td>
<td>21</td>
<td>26</td>
<td>14</td>
</tr>
<tr>
<td>n</td>
<td></td>
<td></td>
<td>0.59 [0.44, 0.72]</td>
<td>0.31 [0.2, 0.47]</td>
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<tr>
<td>proportion [CI]</td>
<td>0.78 [0.57, 0.86]</td>
<td>0.43 [0.3, 0.57]</td>
<td>0.59 [0.44, 0.72]</td>
<td>0.31 [0.2, 0.47]</td>
</tr>
<tr>
<td>comparison with Stent group, difference in proportions [CI]</td>
<td>-0.3 [-0.51, -0.11]</td>
<td>-0.17 [-0.36, 0.02]</td>
<td>-0.43 [-0.62, -0.21]</td>
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<tr>
<td>Conduit</td>
<td>8</td>
<td>28</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>n</td>
<td></td>
<td></td>
<td>0.57 [0.43, 0.7]</td>
<td>0.31 [0.2, 0.47]</td>
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<tr>
<td>proportion [CI]</td>
<td>0.21 [0.11, 0.36]</td>
<td>0.57 [0.43, 0.7]</td>
<td>0.33 [0.13, 0.52]</td>
<td>0.31 [0.2, 0.47]</td>
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<tr>
<td>comparison with Stent group, difference in proportions [CI]</td>
<td></td>
<td></td>
<td>0.33 [0.13, 0.52]</td>
<td>0.31 [0.2, 0.47]</td>
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<tr>
<td></td>
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<td>-0.24 [-0.39, -0.12]</td>
<td>-0.24 [-0.39, -0.12]</td>
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<tr>
<td></td>
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<td>-0.24 [-0.39, -0.12]</td>
<td>-0.24 [-0.39, -0.12]</td>
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### Pulmonary artery repair

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Proportion [CI]</th>
<th>Comparison with Stent group, difference in proportions [CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>23</td>
<td>0.62 [0.38, 0.69]</td>
<td>-0.11 [-0.32, 0.05]</td>
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<tr>
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<td>22</td>
<td>0.45 [0.32, 0.56]</td>
<td>-0.14 [-0.36, 0.04]</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>0.41 [0.3, 0.54]</td>
<td>-0.19 [-0.43, 0.01]</td>
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<tr>
<td></td>
<td>15</td>
<td>0.33 [0.24, 0.5]</td>
<td>-0.14 [-0.36, 0.04]</td>
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</table>

### MAPCA unifocalization

<table>
<thead>
<tr>
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<th>Proportion [CI]</th>
<th>Comparison with Stent group, difference in proportions [CI]</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>0.19 [0.07, 0.3]</td>
<td>-0.18 [-0.33, -0.08]</td>
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<td>0</td>
<td>0</td>
<td>-0.18 [-0.33, -0.08]</td>
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<td>0</td>
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<td>-0.18 [-0.33, -0.08]</td>
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### VSD open

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<th>Comparison with Stent group, difference in proportions [CI]</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>0.14 [0.03, 0.24]</td>
<td>-0.12 [-0.26, -0.04]</td>
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<td>0</td>
<td>0</td>
<td>-0.10 [-0.24, -0.01]</td>
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<tr>
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<td>1</td>
<td>0.02 [0, 0.07]</td>
<td>-0.12 [-0.26, -0.04]</td>
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</table>

### RV/Ao pressure

<table>
<thead>
<tr>
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<th>Median (Range) [CI]</th>
<th>Comparison with Stent group, difference in medians [CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.48 (0.22, 0.9) [0.44, 0.55]</td>
<td>-0.03 [-0.1, 0.04]</td>
</tr>
<tr>
<td></td>
<td>0.5 (0.29, 0.8) [0.48, 0.54]</td>
<td>0.01 [-0.06, 0.09]</td>
</tr>
<tr>
<td></td>
<td>0.51 (0.26, 0.77) [0.47, 0.54]</td>
<td>0.03 [-0.04, 0.1]</td>
</tr>
<tr>
<td></td>
<td>0.47 (0.28, 0.67) [0.43, 0.49]</td>
<td>0.02 [0, 0.07]</td>
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</table>

### ECMO

<table>
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<tr>
<th>Group</th>
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<th>Proportion [CI]</th>
<th>Comparison with Stent group, difference in proportions [CI]</th>
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<tbody>
<tr>
<td></td>
<td>4</td>
<td>0.11 [0.02, 0.2]</td>
<td>-0.06 [-0.19, 0.04]</td>
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<tr>
<td></td>
<td>2</td>
<td>0.04 [0, 0.09]</td>
<td>-0.1 [-0.22, 0.02]</td>
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<tr>
<td></td>
<td>0</td>
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<td>-0.1 [-0.22, 0.02]</td>
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### Delayed chest closure

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<tr>
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<th>Comparison with Stent group, difference in proportions [CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>0.19 [0.07, 0.31]</td>
<td>0.34 [0.14, 0.52]</td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>0.53 [0.39, 0.66]</td>
<td>0.22 [0.02, 0.40]</td>
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<tr>
<td></td>
<td>18</td>
<td>0.41 [0.27, 0.55]</td>
<td>-0.18 [-0.32, -0.07]</td>
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<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>-0.18 [-0.32, -0.07]</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td></td>
<td></td>
</tr>
<tr>
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<tr>
<td><strong>Arrhythmia</strong></td>
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<tr>
<td>n proportion [CI]</td>
<td>9</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>0.24 [0.14, 0.36]</td>
<td>0.33 [0.18, 0.41]</td>
<td>0.25 [0.15, 0.36]</td>
</tr>
<tr>
<td>comparison with Stent group, difference in proportions [CI]</td>
<td>0.03 [-0.09, 0.21]</td>
<td>0 [-0.14, 0.15]</td>
<td>-0.03 [-0.21, 0.07]</td>
</tr>
<tr>
<td><strong>Chylothorax</strong></td>
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<td></td>
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<tr>
<td>n proportion [CI]</td>
<td>9</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>0.24 [0.15, 0.35]</td>
<td>0.29 [0.18, 0.37]</td>
<td>0.27 [0.17, 0.36]</td>
</tr>
<tr>
<td>comparison with Stent group, difference in proportions [CI]</td>
<td>0.01 [-0.1, 0.15]</td>
<td>0 [-0.11, 0.14]</td>
<td>0 [-0.14, 0.1]</td>
</tr>
<tr>
<td><strong>LOS cumulative (days)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (range) [CI]</td>
<td>25 (8, 155) [22, 36]</td>
<td>28 (14, 238) [27, 37]</td>
<td>16 (5, 98) [14, 21]</td>
</tr>
<tr>
<td>comparison with Stent group, difference in medians [CI]</td>
<td>4 [-6, 12]</td>
<td>-11 [-20, -4]</td>
<td>-20 [-29, -14]</td>
</tr>
<tr>
<td><strong>LOS pre-op (days)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (range) [CI]</td>
<td>10 (1, 126) [5.4, 16.8]</td>
<td>11 (1, 63) [10.0, 15.4]</td>
<td>2 (0, 51) [1.2, 3.4]</td>
</tr>
<tr>
<td>comparison with Stent group, difference in medians [CI]</td>
<td>2 [-4, 7]</td>
<td>-8 [-14, -4]</td>
<td>-10 [-16, -7]</td>
</tr>
<tr>
<td><strong>LOS post-op (days)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (range) [CI]</td>
<td>11 (4, 70) [9.8, 16.9]</td>
<td>14 (7, 231) [13.5, 19.8]</td>
<td>12.5 (5.0, 96.0) [10.3, 15.5]</td>
</tr>
<tr>
<td>comparison with Stent group, difference in medians [CI]</td>
<td>3.5 [-1.4, 8.1]</td>
<td>-0.3 [-4.8, 4]</td>
<td>-5.4 [-9.5, -2.1]</td>
</tr>
<tr>
<td><strong>LOS ICU cumulative (days)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (range) [CI]</td>
<td>10 (1, 132) [7.1, 15.5]</td>
<td>10 (4, 161) [10.4, 16.5]</td>
<td>6 (1, 59) [5.1, 8.5]</td>
</tr>
<tr>
<td>comparison with Stent group, difference in medians [CI]</td>
<td>2.6 [-3.1, 7.4]</td>
<td>-3.9 [-9.1, 0.05]</td>
<td>-8.3 [-13.3, -4.9]</td>
</tr>
<tr>
<td>LOS ICU post-op (days)</td>
<td>median (range)</td>
<td>comparison with Stent group, difference in medians [CI]</td>
<td></td>
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<tr>
<td>------------------------</td>
<td>---------------</td>
<td>-----------------------------------------------------</td>
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<tr>
<td></td>
<td>5 (1, 42)</td>
<td>3.6 [1.1, 6.1]</td>
<td></td>
</tr>
<tr>
<td>[CI]</td>
<td>[3.4, 6.7]</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>7 (3, 160)</td>
<td>0.9 [-1.3, 2.9]</td>
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</tr>
<tr>
<td>[CI]</td>
<td>[6.7, 10.5]</td>
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<tr>
<td></td>
<td>6 (1, 26)</td>
<td>-2.5 [-4.5, -1.1]</td>
<td></td>
</tr>
<tr>
<td>[CI]</td>
<td>[4.5, 7.1]</td>
<td></td>
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<tr>
<td></td>
<td>2 (1, 10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[CI]</td>
<td>[1.9, 2.7]</td>
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<td></td>
</tr>
</tbody>
</table>

Continuous variables are presented as their median and range, binary variables as a proportion. 95% credible intervals [CI] are derived from a Bayesian hierarchical model. Group comparisons are facilitated by examining the difference between a group’s median or proportion, and that of the Stent group. The two groups differ, if the 95% credible interval for this difference in medians (or proportions) does not include 0 (bold).

Abbreviations: Ao, aorta; CPB, cardiopulmonary bypass; ECMO, extracorporeal oxygenation; ICU, intensive care unit; LOS, length of stay; MAPCA, multiple aortopulmonary collateral arteries; min, minutes; RV, right ventricle; VSD, ventricular septal defect.
Supplement Figure 4a

**Pre-op hospital stay**

- Surg >3mo
- early PS
- early PA
- Stent

**Post-op hospital stay**

- Surg >3mo
- early PS
- early PA
- Stent

**Total hospital stay**

- Surg >3mo
- early PS
- early PA
- Stent

**Pre-op ICU stay**

- Surg >3mo
- early PS
- early PA
- Stent

**Post-op ICU stay**

- Surg >3mo
- early PS
- early PA
- Stent

**Total ICU stay**

- Surg >3mo
- early PS
- early PA
- Stent
**Supplement Figure Legend**

Figure 1.

Details of technical success of RVOT-stenting in TOF-PS and TOF-PA subgroups.

Figure 2.

Clinical outcomes. Abbreviations: ECMO, extracorporeal membrane oxygenation; PA, pulmonary artery; PV, pulmonary valve; recath, recatheterization; unifocalization (of aortopulmonary collaterals); VSD, ventriculoseptal defect.

Figure 3.

Distribution of non-cardiac co-morbidities.

Figure 4ab.

The early treatment groups have much longer length of stay (LOS), often due to prolonged pre-operative stays which were up to 80-90% of total LOS in some infants. Breakdown of length of stay (LOS) in intensive care unit (ICU) and hospital by pre-operative, post-operative and total days (a). The shortest length of stay in hospital and ICU occurred in the Surg>$3mo group. The early treatment groups have much longer LOS, often due to prolonged pre-operative stays which were up to 80-90% of total LOS in some infants (b).
Figures 5abc.

PA interventions were more frequent in those with small PAs (Nakata index) (a), occurred frequently than right ventricular outflow tract (RVOT) procedures (b). Catheter interventions predominate in all groups (c).
Supplement References


SUPPLEMENTAL MATERIAL: STATISTICAL ANALYSIS

Models

Bayesian hierarchical models were used to ascertain 95% highest posterior density credible intervals for the median of measured variables in the four (Stent, early-PA, early-PS, Surg>3mo) or five (Stent(baseline), Stent(pre-op), early-PA, early-PS, Surg>3mo) clinical groups. These are reported in Supplement Tables 3, 4, 5. All priors were vague with high variances. There were many different sensitivity analyses used for the Bayesian hierarchical models, including varying the form of the likelihood and priors, and varying the priors from being completely diffuse to increasingly informative. In addition to MCMC based methods, for some variables results were checked by conjugate models or by using numerical integration (package R-INLA)\(^1\). Our results were reassuringly stable to these approaches.

For length of stay variables, maximum likelihood estimates were also obtained for Lognormal, Weibull and Gamma distribution fits to the data, by using the fitdistr function from the package MASS\(^2\). The parameter values by maximum likelihood and Bayesian methods were quite similar.

Scripts were adapted from example model files in Lunn\(^3\) for:

a) A binomial variable (with a Normal prior on logit theta, with theta the probability of a positive response; Example 10.1.1):

```r
for (i in 1:N){
    y[i] ~ dbin(theta[i], n[i])
    logit(theta[i]) <- logit.theta[i]
```
logit.theta[i] ~ dnorm(mu, inv.omega.squared)

}

inv.omega.squared <- 1/pow(omega, 2)

omega ~ dunif(0,1000)

mu ~ dunif(-100,100)

N, the number of observations; y, the response variable.

This was used for variables in Table 1 (PGE-dependent, co-morbidities (1 or more), PGE-dependence, genetic syndrome, presence of MAPCAs) and Supplement Table 3 (PV preserved, transannular patch, conduit, pulmonary artery repair, MAPCA unifocalization, VSD open, ECMO, delayed chest closure, arrhythmia, chylothorax).

b) A relatively symmetric continuous variable (e.g. pulmonary artery dimensions). The likelihood was a Student’s t-distribution whose degrees of freedom was determined by the data, with priors specifying a vague mean and\( \alpha \); the prior for the Normal mean was initially a t-distribution, prior for the precision a Gamma distribution.

for(i in 1:Nobs){
  y[i] ~ dt(theta[group[i]],tau1[group[i]],k)
}

for(j in 1:N){
  theta[j] ~ dnorm(mu, tau2)
  tau1[j] ~ dgamma(0.0001,0.0001)
  sigma1[j] <- 1/tau1[j]
\[
\scriptsize
mu \sim \text{dnorm}(0, 0.000001) \\
\tau_2 \sim \text{dgamma}(0.0001, 0.0001) \\
\sigma_2 <- 1/\tau_2 \\
k \sim \text{dunif}(2, 100)
\]

Nobs, the number of observations; N, the number of groups; k, the degrees of freedom of the t-distribution.

This was used for variables in Table 1 (saturation) and Table 2 (PV z-score, LPA z-score, RPA z-score, Nakata index). Student t-distribution based estimates are presented.

c) A right-skewed continuous variable constrained to be positive (Lognormal, with a Normal prior for the mean and a half-cauchy prior for the variance.

\[
\text{for}(i \text{ in } 1:\text{Nobs})\{}
\text{y}[i] \sim \text{dlnorm}(\text{theta[group[i]],tau[group[i]]})
\}\n\]

\[
\text{for}(j \text{ in } 1:\text{N})\{}
\text{theta}[j] \sim \text{dnorm}(0,0.00001)
\text{etheta}[j] <- \text{exp(theta[j])} \# \text{median of lognormal distribution}
\text{tau}[j] <- \text{pow(sigma1[j],-2)}
\text{sigma}[j] \sim \text{dhalfcauchy}(25)
\}\n\]

Nobs, the number of observations; N, the number of groups
This was used in Table 1 (weight, age) and for duration times in Table 3 (cross-clamp, cardio-pulmonary bypass, length of stay). The estimates were similar whether the Lognormal or Weibull likelihood (Example 11.1.1) was used, with similar graphical fits of the densities with data histograms. DIC values were lower with the Lognormal, and this was used.

Three different chains were used and convergence was confirmed by trace plots, and resulted in unimodal densities for each variable. Nested indexing was used to specify the group to which each observation belonged. Initial values for location parameters were chosen to cover a ~100 fold range across realistic values, based on clinical experience and data published from our own centre. The packages JAGS-4.2.0, coda-0.18-1, rjags-4.6, runjags-2.0.4-2 were used. When applicable, the half Cauchy distribution provided by runjags was used to check the sensitivity of the analysis to specification of variance components as Gamma or Uniform on the log scale.

This confirmed there were only minor numerical differences.

As an additional evaluation of the robustness of the Bayesian hierarchical model estimates, a bootstrap analysis was also performed. Note that the bootstrap confidence intervals do not adjust for multiple comparisons. Davison and Hinkley suggest that bootstrapping the median may be feasible for at least moderate size, non-pathological data sets and both the median and trimmed mean were calculated. The mean was trimmed by a fraction of 0.2 from each end to make it more robust and was very close to the empirical median. Although their interpretation is different, the Bayesian 95% credible intervals for medians and proportions were numerically very similar to the bootstrap 95% confidence intervals for the trimmed mean or proportion. The estimates for the trimmed mean are presented in Supplementary Tables 4, 5, 6. All calculations were done in R-3.3.1.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Stent (baseline)</th>
<th>Stent (pre-op)</th>
<th>early-PA</th>
<th>early-PS</th>
<th>Surg&gt;3mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>n=42</strong></td>
<td><strong>n=37</strong></td>
<td><strong>n=49</strong></td>
<td><strong>n=44</strong></td>
<td><strong>n=45</strong></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>bhm median (CI)</td>
<td>2.8 (1.6, 4.4)</td>
<td>6.4 (2.7, 7.0)</td>
<td>2.9 (1.7, 4.3)</td>
<td>4.0 (2.0, 6.0)</td>
</tr>
<tr>
<td></td>
<td>boot trim mean (CI)</td>
<td>3.1 (2.9, 3.4)</td>
<td>6.5 (5.8, 7.2)</td>
<td>3.0 (2.8, 3.2)</td>
<td>4.0 (3.6, 4.6)</td>
</tr>
<tr>
<td></td>
<td>difference in trimmed means with Stent (baseline) [CI]</td>
<td>2.47 [1.86, 3.15]</td>
<td>-0.03 [-0.33, 0.25]</td>
<td>0.71 [0.31, 1.13]</td>
<td>3.02 [2.52, 3.51]</td>
</tr>
<tr>
<td></td>
<td>with Stent (pre-op) [CI]</td>
<td>-2.5 [-3.16, -1.95]</td>
<td>-1.76 [-2.49, -1.11]</td>
<td>-0.03 [-0.33, 0.25]</td>
<td>0.71 [0.31, 1.13]</td>
</tr>
<tr>
<td>Age (days)</td>
<td>bhm median (CI)</td>
<td>19 (12, 29)</td>
<td>183 (156, 213)</td>
<td>16 (13, 20)</td>
<td>39 (31, 51)</td>
</tr>
<tr>
<td></td>
<td>boot trim mean (CI)</td>
<td>24 (15, 39)</td>
<td>188 (161,220)</td>
<td>16 (12,22)</td>
<td>50 (40,60)</td>
</tr>
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<td></td>
<td>difference in trimmed means with Stent (baseline) [CI]</td>
<td>125 [106,147]</td>
<td>-5 [-14,0]</td>
<td>23 [10,34]</td>
<td>125 [106,140]</td>
</tr>
<tr>
<td></td>
<td>with Stent (pre-op) [CI]</td>
<td>-130 [-151, -114]</td>
<td>-103 [-126,-83]</td>
<td>-5 [-14,0]</td>
<td>23 [10,34]</td>
</tr>
<tr>
<td>Saturation (%)</td>
<td>bhm median (CI)</td>
<td>75 (73, 77)</td>
<td>85 (83, 87)</td>
<td>86 (85, 87)</td>
<td>83 (81, 85)</td>
</tr>
<tr>
<td></td>
<td>boot trim mean (CI)</td>
<td>75(73, 77)</td>
<td>85 (83, 87)</td>
<td>86 (85, 87)</td>
<td>83 (81, 85)</td>
</tr>
<tr>
<td></td>
<td>with Stent (pre-op) [CI]</td>
<td>1[-1,3]</td>
<td>1[-1,3]</td>
<td>1[-1,3]</td>
<td>1[-1,3]</td>
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<tr>
<td></td>
<td>bhm proportion (CI)</td>
<td>boot proportion (CI)</td>
<td>difference in trimmed means with Stent (baseline) [CI]</td>
<td></td>
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<td>------------------</td>
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<td>-------------------------------------------------------</td>
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<tr>
<td><strong>PGE-dependent</strong></td>
<td>0.56 (0.41, 0.71)</td>
<td>1 (0.99, 1.0)</td>
<td>0 (0, 0)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>0.57 (0.43, 0.71)</td>
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<td></td>
<td>1.0</td>
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<td></td>
<td></td>
<td></td>
<td>0.27 (0.16, 0.41)</td>
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<td></td>
<td></td>
<td>0</td>
<td></td>
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<tr>
<td></td>
<td><strong>Co-morbidities</strong></td>
<td><strong>0.43 [0.29,0.57]</strong></td>
<td><strong>-0.3 [-0.49,-0.11]</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>-0.57 [-0.71,-0.43]</strong></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>bhm proportion with ≥1 (CI)</td>
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<td>0.32 (0.2, 0.46)</td>
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<td>0.15 (0.06, 0.27)</td>
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<td></td>
<td>0 (0, 0.04)</td>
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<tr>
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<td>bhm proportion with ≥1 (CI)</td>
<td>0.38 (0.24,0.52)</td>
<td>0.33 (0.20,0.38)</td>
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<td></td>
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<td></td>
<td>0.16 (0.07,0.27)</td>
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<td>0</td>
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<tr>
<td></td>
<td>difference in trimmed means with Stent (baseline) [CI]</td>
<td>-0.06 [-0.17,0.06]</td>
<td>-0.07 [-0.19,0.04]</td>
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<td></td>
<td></td>
<td><strong>-0.12 [-0.21,-0.02]</strong></td>
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<td></td>
<td><strong>Prematurity</strong></td>
<td><strong>-0.06 [-0.21,0.14]</strong></td>
<td><strong>-0.17 [-0.33,-0.01]</strong></td>
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<td><strong>-0.06 [-0.24,0.12]</strong></td>
<td></td>
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<tr>
<td></td>
<td>bhm proportion (CI)</td>
<td>0.23 (0.13, 0.35)</td>
<td>0.21 (0.12, 0.32)</td>
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<td></td>
<td></td>
<td></td>
<td>0.13 (0.04, 0.22)</td>
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<td></td>
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<td></td>
<td>0.19 (0.1, 0.29)</td>
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<tr>
<td></td>
<td>bhm proportion (CI)</td>
<td>0.26 (0.14,0.40)</td>
<td>0.22 (0.1,0.35)</td>
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<td></td>
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<td></td>
<td>0.09 (0.02,0.18)</td>
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<td></td>
<td></td>
<td></td>
<td>0.20 (0.09,0.31)</td>
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<tr>
<td></td>
<td>difference in trimmed means with Stent (baseline) [CI]</td>
<td>-0.04 [-0.21,0.14]</td>
<td><strong>-0.17 [-0.33,-0.01]</strong></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>-0.06 [-0.24,0.12]</strong></td>
<td></td>
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<tr>
<td></td>
<td><strong>Genetic syndrome</strong></td>
<td><strong>0.25 (0.15, 0.4)</strong></td>
<td><strong>0.20 (0.11, 0.30)</strong></td>
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<td></td>
<td></td>
<td></td>
<td><strong>0.16 (0.07, 0.25)</strong></td>
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<td></td>
<td></td>
<td></td>
<td><strong>0.17 (0.08, 0.27)</strong></td>
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<tr>
<td></td>
<td>bhm proportion (CI)</td>
<td>0.31 (0.17,0.45)</td>
<td>0.2 (0.1, 0.33)</td>
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<td></td>
<td></td>
<td>0.14 (0.05,0.25)</td>
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<td></td>
<td>0.16 (0.07,0.27)</td>
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<td></td>
<td>difference in trimmed means with Stent (baseline) [CI]</td>
<td>-0.11 [-0.28,0.07]</td>
<td><strong>-0.17 [-0.34,0.01]</strong></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>-0.15 [-0.32,0.03]</strong></td>
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<tr>
<td>MAPCAs</td>
<td>bhm proportion(CI)</td>
<td>boot proportion (CI)</td>
<td>difference in trimmed means with Stent(baseline) [CI]</td>
<td></td>
<td></td>
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<td>-------------------------------</td>
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<td>----------------------</td>
<td>-----------------------------------------------------</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>0.29 (0.16, 0.43)</td>
<td>0.06 (0, 0.13)</td>
<td>-0.11 [-0.29,0.07]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.06 (0.06, 0.14)</td>
<td>0.02 (0,0.07)</td>
<td><strong>-0.17 [-0.34,-0.01]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.03 (0, 0.08)</td>
<td>0.04 (0,0.11)</td>
<td>-0.15 [-0.32,0.03]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.04 (0,0.11)</td>
<td></td>
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</tbody>
</table>

Abbreviations: bhm, Bayesian hierarchical model with CI, 95% highest posterior density credible intervals; boot trim mean, bootstrap trimmed mean (trimmed by 0.2 from each end) with 95% confidence intervals boot proportion; bootstrap proportion with 95% confidence intervals ; AVSD, atrioventricular septal defect; CI, 95% highest posterior density credible interval; DORV, double outlet right ventricle; GI, gastrointestinal; MAPCAs, multiple aortopulmonary collateral arteries; NEC, necrotizing enterocolitis; PGE, prostaglandin; pre-op, pre-operative.
Statistical Supplement Table 5.

Pulmonary artery dimensions. Bayesian hierarchical model (median and 95% credible interval) and bootstrap estimates

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stent (baseline)</th>
<th>Stent (pre-op)</th>
<th>early-PA</th>
<th>early-PS</th>
<th>Surg&gt;3mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=42</td>
<td>n=37</td>
<td>n=49</td>
<td>n=44</td>
<td>n=45</td>
</tr>
<tr>
<td>PV Z-score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bhm median (CI)</td>
<td>-7.0 (-7.7, -6.3)</td>
<td>-7.6 (-10.4, -4.9)</td>
<td>-4.7 (-5.4, -4.0)</td>
<td>-2.4 (-3.1, -1.8)</td>
<td></td>
</tr>
<tr>
<td>boot trim mean (CI)</td>
<td>-6.8 (-7.5, -6.1)</td>
<td>-6.3 (-9.0, -3.8)</td>
<td>-4.7 (-5.6, -3.9)</td>
<td>-2.8 (-3.6, -1.9)</td>
<td></td>
</tr>
<tr>
<td>difference in trimmed means with Stent(baseline) [CI]</td>
<td>-0.9 [-3.7, 2.1]</td>
<td>2.2 [1.1, 3.3]</td>
<td>4.2 [3.2, 5.3]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PV (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>bhm median (CI)</td>
<td>3.7 (3.4, 4.0)</td>
<td>3.5 (2.4, 4.6)</td>
<td>5.1 (4.7, 5.5)</td>
<td>7.5 (6.9, 8.1)</td>
<td></td>
</tr>
<tr>
<td>boot trim mean (CI)</td>
<td>3.6 (3.4, 3.9)</td>
<td>4.0 (3.0, 5.3)</td>
<td>5.0 (4.5, 5.5)</td>
<td>7.1 (6.6, 7.8)</td>
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<tr>
<td>difference in trimmed means with Stent(baseline) [CI]</td>
<td>2.3 [1.0, 3.5]</td>
<td>-0.4 [-1.5, 0.9]</td>
<td>3.5 [2.7, 4.8]</td>
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<td>LPA Z-score</td>
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<td>bhm median (CI)</td>
<td>-3.8 (-4.4, -3.1)</td>
<td>-1.7 (-2.6, -0.9)</td>
<td>-1.7 (-2.2, -1.1)</td>
<td>-2.4 (-3.0, -1.8)</td>
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<td>boot trim mean (CI)</td>
<td>-3.6 (-4.3, -3.0)</td>
<td>-1.6 (-2.5, -0.8)</td>
<td>-1.7 (-2.2, -1.2)</td>
<td>-2.2 (-2.7, -1.8)</td>
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<td>difference in trimmed means with Stent(baseline) [CI]</td>
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<td>2.0 [1.2, 2.8]</td>
<td>1.3 [0.5, 2.1]</td>
<td>3.0 [2.1, 4.0]</td>
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<td>bhm median (CI)</td>
<td>3.0 (2.7, 3.3)</td>
<td>4.9 (4.3, 5.4)</td>
<td>3.9 (3.6, 4.2)</td>
<td>3.8 (3.5, 4.0)</td>
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<td>Boot Trim Mean (CI)</td>
<td>Difference in Trimmed Means with Stent (Baseline) (CI)</td>
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<td><strong>RPA Z-score</strong></td>
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<td>-4.0 (-4.7, -3.3)</td>
<td>-1.5 (-2.2, -0.8)</td>
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<tr>
<td>boot trim mean (CI)</td>
<td>-3.8 (-4.6, -3.0)</td>
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<td><strong>RPA (mm)</strong></td>
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<td>bhm median (CI)</td>
<td>3.0 (2.8, 3.3)</td>
<td>4.3 (4.0, 4.5)</td>
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<tr>
<td>boot trim mean (CI)</td>
<td>3.0 (2.7, 3.3)</td>
<td>4.2 (3.9, 4.6)</td>
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<td><strong>Nakata Index (mm²/m²)</strong></td>
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<td>bhm median (CI)</td>
<td>76.5 (65.6, 87.4)</td>
<td>146.1 (131.4, 159.6)</td>
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<td>boot trim mean (CI)</td>
<td>74.8 (63.5, 84.7)</td>
<td>136.7 (122.9, 156.4)</td>
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<td>Abbreviations: bhm, Bayesian hierarchical model with CI, 95% highest posterior density credible intervals; boot trim mean, bootstrap trimmed mean (trimmed by 0.2 from each end) with 95% confidence intervals; LPA, left pulmonary artery; PV, pulmonary valve; RPA, right pulmonary artery.</td>
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Supplement Table 6. Peri-operative data (trimmed mean, bootstrap 95% confidence intervals)

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<tr>
<th>Variable</th>
<th>Stent (n=37)</th>
<th>early-PA (n=49)</th>
<th>early-PS (n=44)</th>
<th>Surg&gt;3mo (n=45)</th>
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<tr>
<td><strong>CPB time (min)</strong></td>
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<td>trimmed mean (CI)</td>
<td>137.5 (119.9, 160.6)</td>
<td>115.8 (110.6, 121.4)</td>
<td>109.9 (99.9, 122.3)</td>
<td>103.6 (93.6, 114.0)</td>
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<td>comparison with Stent group, difference in trimmed means [CI]</td>
<td>-21.7 [-44.6,-3.5]</td>
<td>-27.6 [-52.2,-5.9]</td>
<td>-34.0 [-58.3,-13.2]</td>
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<td><strong>Cross clamp time (min)</strong></td>
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<td>trimmed mean (CI)</td>
<td>87.7 (76.3, 101.0)</td>
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<td>-8.1 [-23.1,5.0]</td>
<td>-4.4 [-19.8, 9.81]</td>
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<td><strong>PV preserved</strong></td>
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<td>proportion (CI)</td>
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<td>0</td>
<td>0.41 (0.27, 0.55)</td>
<td>0.69 (0.56, 0.82)</td>
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<td>comparison with Stent group, difference in proportions [CI]</td>
<td>0 [0, 0]</td>
<td>0.41 [0.27, 0.57]</td>
<td>0.69 [0.56,0.82]</td>
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<td><strong>Transannular patch</strong></td>
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<td>proportion (CI)</td>
<td>0.78 (0.65, 0.92)</td>
<td>0.43 (0.29, 0.57)</td>
<td>0.59 (0.45, 0.73)</td>
<td>0.31 (0.18, 0.44)</td>
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<td>comparison with Stent group, difference in proportions [CI]</td>
<td>-0.36 [-0.54,0.16]</td>
<td>-0.19 [-0.39,0.01]</td>
<td>-0.47 [-0.66,-0.28]</td>
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<td><strong>Conduit</strong></td>
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<td>proportion (CI)</td>
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<td>0.04 [-0.15,0.23]</td>
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<td>-0.02 [-0.21,0.16]</td>
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<td>proportion (CI)</td>
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<td>0.45 (0.31, 0.59)</td>
<td>0.41 (0.27, 0.55)</td>
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<td>RV/Ao pressure</td>
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<td>0.47 (0.42, 0.53)</td>
<td>0.11 (0.03, 0.22)</td>
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<td>0.51 (0.47, 0.56)</td>
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<td>difference in proportions (CI)</td>
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<td>Trimmed mean (CI)</td>
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<td>Stent Group, Difference in Proportions [CI]</td>
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<td><strong>LOS cumulative (days)</strong> trimmed mean (CI)</td>
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<td>0.24 (0.11, 0.38)</td>
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<td>16.1 (13.4, 20.8)</td>
<td>-0.02 [-0.2, 0.16]</td>
<td>0.27 (0.14, 0.41)</td>
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<td>7.2 (6.3, 8.4)</td>
<td>-0.27 [0.14, 0.41]</td>
<td>0.03 [0.16, 0.22]</td>
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<td><strong>LOS pre-op (days)</strong> trimmed mean (CI)</td>
<td>14.3 (8.3, 23.8)</td>
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<td>2.1 [-0.2, 12.2]</td>
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<td>12.1 (10.1, 15.8)</td>
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<td>2.9 (1.8, 4.5)</td>
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<td>2.1 [-0.2, 12.2]</td>
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<td>-0.02 [-0.2, 0.16]</td>
<td>2.1 [-0.2, 12.2]</td>
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<td><strong>LOS ICU cumulative (days)</strong> trimmed mean (CI)</td>
<td>11.4 (7.7, 19.3)</td>
<td>-0.03 [-0.16, 0.1]</td>
<td>5.2 (3.6, 7.6)</td>
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<td>12.4 (10.1, 15.9)</td>
<td>-0.7 [-10.2, 12.2]</td>
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<td>6.9 (5.3, 8.9)</td>
<td>-0.02 [-0.2, 0.16]</td>
<td>6.1 (4.9, 7.5)</td>
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<td>2.2 (1.9, 2.7)</td>
<td>-0.02 [-0.2, 0.16]</td>
<td>2.2 (1.9, 2.7)</td>
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<td><strong>LOS ICU post-op (days)</strong> trimmed mean (CI)</td>
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<td>-0.03 [-0.16, 0.1]</td>
<td>2.3 [-0.3, 4.7]</td>
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<td>7.5 (6.4, 9.2)</td>
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<td>-0.02 [-0.2, 0.16]</td>
<td>2.2 (1.9, 2.7)</td>
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</table>

The mean is trimmed by a fraction of 0.2 from each end. Abbreviations: Ao, aorta; CI, 95% confidence intervals for the trimmed mean (bootstrap percentile); CPB, cardiopulmonary bypass; ECMO, extracorporeal oxygenation; ICU, intensive care unit; LOS, length of stay; MAPCA, multiple aortopulmonary collateral arteries; min, minutes; RV, right ventricle; VSD, ventricular septal defect.
References for Statistical Supplement


6. https://cran.r-project.org/web/packages/coda/index.html

7. https://cran.r-project.org/web/packages/rjags/index.html

8. https://cran.r-project.org/web/packages/runjags/index.html


Supplement Video Legend

Angiogram demonstrating a tiny amount of antegrade flow across pulmonary valve diagnosed with TOF-PA by echocardiography (A). RVOT-stenting has been performed on the same infant (B).