Results of Primary Repair Versus Shunt Palliation in Ductal Dependent Infants With Pulmonary Atresia and Ventricular Septal Defect

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Background. **The 2 management strategies of neonates born with ductal-dependent pulmonary atresia and ventricular septal defect (PAVSD) include single stage primary biventricular repair (BVR) or staged palliation with modified Blalock-Taussig shunt (BTS) followed by second stage repair. Each approach is associated with specific benefits and drawbacks. We report outcomes of those 2 different strategies.**

Methods. **Between 2002 and 2012, 86 neonates with ductal-dependent PAVSD underwent surgery using primary repair (BVR group: n = 28, 33%) or shunt palliation (BTS group: n = 58, 67%). Early and late results were compared between the 2 groups.**

Results. **Median age was 6 days (interquartile range [IQR] 3–17) and median weight was 2.8 kg (IQR 2.5–3.3) with 27 patients (31%) 2.5 kg or less. Associated risk factors such as prematurity 36 weeks or less and genetic or extra-cardiac malformations were present in 30% and 40% of patients, respectively.**

Hospital mortality occurred in 5 (5.8%) patients (1 [3.6%] for BVR versus 4 [6.9%] for BTS, $p = 1.00$). Overall 8-year survival was 76.5% (85.5% for BVR versus 72.2% for BTS, $p = 0.189$). On multivariable analysis, risk factors for mortality were genetic or extra-cardiac malformations (hazard ratio [HR], 2.8 (95% confidence interval [CI] 1.7% to 16.0%), $p = 0.036$) and postoperative extracorporeal membrane oxygenation (ECMO) (HR, 4.0 [95% CI, 1.1% to 14.4), $p = 0.039$). Freedom from right ventricular outflow tract reoperation after achievement of repair was 63.2% at 8 years (52.4% for BVR versus 70.2% for BTS, $p = 0.170$). On multivariable analysis, risk factors for reoperation were the use of conduit (HR, 8.7 [95% CI, 1.1% to 65.8%], $p = 0.037$) and prematurity (HR, 2.8 [95% CI, 1.1% to 7.2%], $p = 0.028$).

Conclusions. **Primary BVR of neonates with ductal-dependent PAVSD is associated with a trend for improved survival due to hospital and interstage mortality with the staged approach. Genetic or extra-cardiac malformations are common and are associated with worse survival.**

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Pulmonary atresia and ventricular septal defect (PAVSD) is a congenital cardiac anomaly characterized by the absence of continuity between the right ventricle and pulmonary arteries, together with the presence of a malalignment ventricular septal defect due to the anterior deviation of the infundibular septum [1]. While the intracardiac anatomy is generally constant, PAVSD is an extremely heterogeneous malformation due to great differences in the development of the pulmonary circulation [1–3]. The source of pulmonary blood flow in PAVSD varies and ranges from a simple form associated with well developed intra-pericardial pulmonary arteries, to the other extreme arrangement in which there is absence of the intra-pericardial pulmonary arteries with pulmonary arterial supply derived exclusively from multiple aortopulmonary collateral arteries (MAPCAs) [1–3].

Timing and mode of management of PAVSD varies based on the complexity of the pulmonary circulation. Surgical management of neonates born with the simple form of PAVSD is naturally less complicated than that of those born with MAPCAs [2–4]. Nonetheless, patients born with the simple form of PAVSD have ductal-dependent pulmonary blood flow and require early neonatal palliation or repair. The 2 surgical treatment strategies that are applied in ductal-dependent PAVSD patients include either a single stage strategy of primary neonatal biventricular repair (BVR) or a staged strategy of initial palliation with a modified Blalock-Taussig shunt (BTS) followed by a second stage repair. Each of those two strategies is associated with specific advantages and

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drawbacks [2–8]. We aim in the current series to report current era results of surgical treatment of neonates born with ductal-dependent PAVSD at our institution; to examine risk factors affecting early and late outcomes and to compare early mortality, late survival, and right ventricular outflow tract (RVOT) reoperation risk between the 2 management strategies.

Patients and Methods

Inclusion Criteria

Between 2002 and 2012, 86 neonates with ductal-dependent PAVSD underwent surgery at Children's Healthcare of Atlanta, Emory University. Patients with PAVSD and MAPCAs were not included. Patients were identified using our institutional surgical database. Demographic, morphologic, clinical, operative, and hospital details were abstracted from the medical records for analysis. Approval of this study was obtained from our hospital's Institutional Review Board and requirement for individual consent was waived for this observational study.

Follow-Up

Time-related outcomes were determined from recent office visits documented in the electronic charts of Children's Healthcare of Atlanta system or from direct correspondence with pediatric cardiologists outside the system. Follow-up was 91% complete. Mean follow-up duration was 5.4 ± 3.9 years and was 5.8 ± 3.7 years for neonates who underwent single stage repair versus 5.1 ± 3.9 years for those who underwent initial palliation ($p = 0.47$).

Statistical Analysis

Data are presented as means with standard deviations, medians with interquartile ranges (IQR) or frequencies as appropriate. Normality of continuous outcomes intensive care unit length of stay, duration of mechanical ventilation, and postoperative length of stay was assessed using histograms and density plots and the Anderson-Darling test for normality. Patient demographics and surgical characteristics were compared among treatment groups using χ^2 tests, Wilcoxon rank sum tests, and 2-sample Kolmogorov-Smirnov tests. Time-dependent outcomes (death and RVOT reoperation) after initial surgery were parametrically modeled. Parametric probability estimates for time-dependent outcomes uses models based on multiple, overlapping phases of risk (available for use with the SAS system [SAS Institute Inc, Cary, NC] at http://www.clevelandclinic.org/heartcenter/hazard. The hazard procedure uses maximum likelihood estimates to resolve risk distribution of time to event in up to 3 phases of risk (early, constant, and late). For the outcomes death an early phase risk model provided the best first to the data. For the outcome reoperation after initial surgery, a late phase risk model provided the best fit to the data. Risk factors mortality and reoperation were examined using parametric survival models. Initial models examined 1 risk factor at a time. Variables potentially influencing the likelihood of outcomes were sought from demographic, anatomic, transplant, and surgical variables. Multivariable models were created using forward entry of variables significant in the univariate models. Effects of covariates on the probability of outcomes are given as hazard ratio (HR) with 95% confidence intervals. All statistical analyses were performed using SAS v9.3.

Results

Patients' Characteristics, Morphologic and Operative Details

During the study period, 86 neonates with ductal-dependent PAVSD underwent their first surgery at our institution. There were 52 males (61%). Median age at time of surgery was 6 days (IQR 3–17) and median weight was 2.8 kg (IQR 2.5–3.3) with 27 patients (31%) 2.5 kg or less. Gestational age was known in 83 patients and 25 (30%) were born prematurely 36 weeks or less gestation. Thirty-four patients (40%) had genetic syndromes or major extra-cardiac malformations that included DiGeorge syndrome (n = 8), Down syndrome (n = 3), CHARGE (coloboma, heart defect, atresia choanae, retarded growth and development, genital abnormality, and ear abnormality) syndrome (n = 3), Dandy-Walker syndrome (n = 2), Holt-Oram syndrome (n = 2), pentalogy of Cantrell (n = 1), other chromosomal anomalies (n = 6), VACTERL [vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula, renal anomalies, and limb abnormalities] association (n = 5), renal agenesis (n = 2), duodenal atresia (n = 1), and cystic hygroma (n = 1).

Twenty-eight patients (33%) underwent primary neonatal biventricular repair (BVR group) while 58 (67%) underwent initial palliation with a shunt (BTS group). The characteristics of patients in the 2 treatment groups are listed in Table 1. There was no difference in age, weight, sex, incidence of prematurity, or low weight 2.5 or less kg, although there was a trend for higher incidence of genetic and extra-cardiac malformations in the BVR group. A comparison of the size of the branch pulmonary arteries and the presence of detectable segment of the main pulmonary artery on preoperative echocardiograms was performed. The right pulmonary artery diameter was 4.4 ± 1.1 mm in the BVR group versus 3.9 ± 1.1 mm in the BTS group, $p = 0.73$ while the left pulmonary artery diameter was 3.6 ± 0.7 mm in the BVR group versus 3.4 ± 0.8 mm in the BTS group, $p = 0.64$. A main pulmonary artery segment was detected in 70% of patients in the BVR group versus 43% of patients in the BTS group, $p = 0.063$. At time of surgery, 30 patients (35%) underwent concomitant patch augmentation of the pulmonary arteries. Additional surgery included division of a vascular ring (n = 2) and tricuspid valve repair (n = 1). In the BVR group, the continuity between the right ventricle and pulmonary artery was established with a right ventricle to pulmonary artery (RV-PA) conduit in 14 patients (50%) and with a trans-annular patch (TAP) in 14 patients (50%). In comparison, among the 46 patients who underwent second stage biventricular repair after initial palliation in