Long-Term Outcomes of Total Anomalous Pulmonary Venous Drainage Repair in Neonates and Infants

Matthew S. Yong, MBBS, Nima Yaftian, MD, Sophie Griffiths, MD, Johann Brink, MD, Terry Robertson, MBBS, Luigi D'Orsogna, MBBS, Robert G. Weintraub, MBBS, Yves d'Udekem, MD, PhD, Christian P. Brizard, MD, and Igor E. Konstantinov, MD, PhD

Departments of Cardiac Surgery and Cardiology, Royal Children's Hospital, Melbourne, Victoria; Department of Pediatrics, University of Melbourne, Melbourne, Victoria; Murdoch Children's Research Institute, Melbourne, Victoria; Department of Cardiology, Women's and Children's Hospital, Adelaide, South Australia; and Department of Cardiology, Princess Margaret Hospital, Perth, Western Australia, Australia

Background. **Outcomes of operations for total anomalous pulmonary venous drainage (TAPVD) have improved. However, operations in the neonatal period and the development of postoperative pulmonary venous obstruction are associated with a high mortality rate.**

Methods. **A retrospective review was conducted for all neonates and infants (n = 214) who underwent operations for isolated TAPVD (1973 to 2014).**

Results. **Median age was 18 days (1 day to 1 year). There were 17 (7.9%) early deaths. Risk factors for early death were prolonged cardiopulmonary bypass time ($p = 0.005$) and neonatal age at the operation ($p = 0.048$). Early mortality was 2.5% for infants (n = 81) and 11% for neonates (n = 133; $p = 0.021$) during the entire study period. Hospital deaths for neonates remained unchanged during the four eras of 1973 to 1988, 1989 to 1998, 1999 to 2008, and 2009 to 2014. Survival at 10 and 20 years was 88% ± 2.2% (95% confidence interval, 82% to 91%). Reoperation for postoperative pulmonary venous obstruction was required in 22 patients (10%). Risk factors for reoperation were prolonged cardiopulmonary bypass time ($p = 0.015$), lower operative weight ($p = 0.003$), and an episode of postoperative pulmonary hypertensive crisis ($p = 0.005$). Freedom from reoperation at 20 years was 86% ± 3.2% (95% confidence interval, 78% to 91%). All survivors were asymptomatic at a mean of 13 ± 9 years (range, 1 month to 42 years) after the operation.**

Conclusions. **Although isolated TAPVD repair in infants can be performed without death, the operation is associated with a high mortality rate in neonates that remained unchanged during the long study period. Survival beyond 1 year after the operation is associated with excellent long-term outcomes.**

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Total anomalous pulmonary venous drainage (TAPVD) comprises 1.5% of all congenital heart defects [1]. The management of this condition has improved in recent decades, and operative death for isolated TAPVD repair is low [2]. However, two key issues remain in the management of TAPVD. Firstly, the mortality rate continues to be higher in neonates [3]. These patients often present in extremis and represent the most severe end of the disease spectrum. Secondly, postoperative pulmonary venous obstruction (PVO) develops in approximately 10% to 20% and is associated with an extremely poor prognosis [4]. Understanding and improving management of patients within these two areas is of current interest. Hence, we retrospectively reviewed all patients who underwent repair of isolated TAPVD at a single institution to determine outcomes and risk factors.

Patients and Methods

Patients

The Royal Children's Hospital Institutional Research Ethics Board approved the study. All patients who underwent operations for TAPVD at the Royal Children's Hospital within the first year of life from 1973 to 2014 were identified. The analysis excluded international patients. TAPVD patients with cardiac anomalies other than an atrial septal defect, patent ductus arteriosus, or ventricular septal defect were considered "complex" and were excluded. Data were obtained by review of medical records from the initial admission until the last follow-up. The patients were

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Address correspondence to Dr Konstantinov, University of Melbourne, Royal Children's Hospital, Flemington Rd, Parkville, VIC 3029, Australia; email: igor.konstantinov@rch.org.au.

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monitored with echocardiogram at intervals of 3 to 6 months during the first 2 years after the operation, followed by an annual assessment. Telephone interviews were conducted to obtain up-to-date follow-up for each patient.

Definitions

Neonates were defined as children who underwent repair within the first month of life, and infants were defined as those who underwent repair after the first month of life but within the first year of life. Pulmonary arterial pressure monitoring was performed in all patients postoperatively by a catheter placed into the pulmonary artery through the right ventricular wall intraoperatively. Pulmonary hypertensive crisis was defined as at least one event in which pulmonary arterial systolic pressure equaled or exceeded systemic levels, followed by a rapid fall in systemic arterial pressure. Urgency of the operation was retrospectively determined and categorized as follows: an emergent operation was defined as a life-saving operation in a hemodynamically unstable patient within the first 24 hours of diagnosis, an urgent operation was defined as an operation performed 24 to 48 hours from the diagnosis, and all other patients were classified as nonurgent. Prematurity was defined as birth at less than 37 weeks of gestation.

Hospital death was defined as death occurring within 30 days of the operation or before hospital discharge. All other deaths were considered late.

Preoperative PVO was defined by evidence of anatomical obstruction on preoperative imaging with symptoms of cardiac failure. Postoperative PVO was defined as obstruction of the pulmonary veins as identified by echocardiogram, computed tomography angiogram, or magnetic resonance imaging developing at any time after the operation. Reoperation was performed in symptomatic (dyspnea, fatigue) patients with documented PVO. PVO was further subdivided into postoperative PVO that developed at the site of the anastomosis (anastomotic stenosis) or distant from the site of anastomosis. Patients were considered lost to follow-up if no information was available after their hospital discharge.

Data Analysis

Data were analyzed with Stata 12 software (StataCorp, College Station, TX). Continuous data are expressed as mean ± SD or as median with the interquartile range (IQR), as appropriate. Inferential comparisons were made using the Pearson χ^2 test, Mann-Whitney test, and the two-sample mean comparison t test, where appropriate.

Kaplan-Meier actuarial survival curves were used to analyze and plot time-related end points. The log-rank test was used to determine the significance between survival curves. Risk factors for binary outcomes (hospital death) were identified by logistic regression analysis. Cox proportional hazards analysis was used to identify hazards for time-related outcomes. Variables included in the univariate analysis were sex, age, neonatal age at the operation, preoperative PVO, supracardiac type, cardiac type, infracardiac type, mixed type, prematurity, syndrome diagnosis, preoperative intubation, operative weight, vertical vein ligation, sutureless repair technique, cardiopulmonary bypass (CPB) time, cross-clamp time, postoperative pulmonary hypertensive episode, and surgical era. A p value of 0.05 was used for variable inclusion and exclusion on multivariable analysis. Backward stepwise methods were used such that variables were removed until all p values in the multivariable model were significant. All tests were two-tailed, and p values of less than 0.05 were considered significant.

Results

Detailed preoperative patient characteristics are listed in Table 1. Operations were performed with standard CPB, and circulatory arrest was used if required. The operation was nonurgent in 84 of the 214 (39%), urgent in 89 (42%), and emergent in 41 (19%). The mean CPB time was 80 ± 41 minutes (range, 31 to 359 minutes), and the mean cross-clamp time was 44 ± 23 minutes (range, 14 to 214 minutes). Circulatory arrest was used in 110 patients (51%), with a mean time of 31 ± 12 minutes (range, 1 to 69

Table 1. Patient Preoperative Characteristics

Variable[a]	Value (N = 214)
Demographics	
Sex	
Male	137 (64%)
Female	77 (36%)
Age at operation, d	18 (3–65)
Weight at operation, kg	3.8 ± 1.1 (1.6–8.5)
<2.0 kg	3 (1.4)
2.0–2.5 kg	20 (9)
>2.5 kg	191 (89)
Height at operation, cm	53.3 ± 5.5 (42–74)
Body surface area, m^2	0.22 ± 0.043 (0.13–0.4)
Diagnosis	
Prematurity	19 (8.9)
Anatomical type	
Supracardiac	91 (43)
Cardiac	45 (21)
Infracardiac	60 (28)
Mixed	18 (8.4)
Preoperative obstruction	112 (52)
Atrial septal defect	214 (100)
Patent ductus arteriosus	109 (51)
Ventricular septal defect	13 (6.1)
Syndromal diagnosis	17 (757)
Interventions	
Preoperative intubation	121 (57)
Balloon atrial septostomy	10 (4.7)
Preoperative ECMO	4 (1.9)
Previous operation	4 (1.9)
Patent ductus arteriosus ligation	1 (0.47)
Noncardiac	3 (1.4)

[a] Continuous data are reported as mean ± SD (range) or median (interquartile range) and categoric data as number (%).

ECMO = extracorporeal membrane oxygenation.