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PEDIATRIC AND CONGENITAL HEART DISEASE

Original Studies

Hybrid Approach for Pulmonary Atresia With Intact Ventricular Septum: Early Single Center Results and Comparison to the Standard Surgical Approach

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Objectives: To examine acute and mid-term patient outcomes following the hybrid approach to pulmonary atresia with intact ventricular septum (PA-IVS) compared with the standard surgical approach. Background: A subset of PA-IVS patients with the prospect of biventricular circulation typically undergo surgical or transcatheter right ventricular (RV) outflow tract opening. A recently described hybrid procedure, involving perventricular pulmonary valve perforation, was shown to be safe and effective in single-center series. Methods: A single-center retrospective review of all patient with PA-IVS who underwent either surgical or hybrid RV decompression between January 2002 and December 2011 was completed and acute and mid-term patient outcomes were compared between the surgical and hybrid cohorts. Additionally, a systematic literature review was completed to compare a transcatheter cohort to the hybrid cohort. Results: Seven patients with PA-IVS underwent a hybrid procedure; the procedure was technically successful in all attempts, and none required CPB. No patients required surgical reintervention prior to hospital discharge, and none died during the study period. Surgical RV decompression was performed in 17 patients with a median CPB time of 80 min. Patient outcomes were nearly identical between cohorts. By systematic review, the transcatheter approach has a procedural success of 75–95% but up to 75% of patients require operation in the neonatal period. Conclusions: The hybrid approach is a safe and feasible alternative to the standard surgical and transcatheter approaches to PA-IVS. Acute and mid-term patient outcomes are comparable with those treated with a standard surgical approach and neonatal CPB is completely avoided.

Key words: congenital heart defect; patient outcome assessment; pediatric interventions; perventricular procedure; hybrid cardiac surgery

INTRODUCTION

Pulmonary atresia with intact ventricular septum (PA-IVS) is a rare form of complex congenital heart disease with significant morphologic heterogeneity. Because of this heterogeneity, repair or palliation strategies vary widely, ranging from single ventricle

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palliation to complete biventricular repair. Overall, regardless of anatomical subtype, survival is poor, reported to be as low as 50% at 5 years [1–5]. For patients with anatomy favorable for a biventricular repair (i.e., adequate tricuspid valve, adequate right ventricle, and no evidence of right ventricular dependent coronary circulation), the initial procedural focus is on creation of a patent right ventricular outflow tract (RVOT) to decompress the right ventricle and to allow for anterograde pulmonary blood flow. This procedure may be performed surgically or percutaneously and, in select patients, might result in growth of the right ventricle [6,7] with the ability to proceed to a biventricular circulation [1,2]. Both techniques, however, have limitations and risks. The surgical approach requires a sternotomy and cardiopulmonary bypass (CPB) and has 1- and 5-year survival rates of 70–75% and 60–67%, respectively [1–3]. With risk-stratification based on several morphologic criteria, however, the mid-term survival rate was as high as 98% in one series [5]. The percutaneous transcatheter approach, which involves pulmonary valve perforation (via directed stiff guidewire, laser-assisted, or radiofrequency-assisted perforation) and balloon valvuloplasty, avoids sternotomy and CPB but has a variable rate of procedural failure (5–25%), a significant risk of cardiac perforation (5–50%), a procedural mortality of up to 17%, and hospital mortality of up to 50% [6–14]. In addition, patients treated with the percutaneous approach have a significant risk (up to 76%) of requiring surgical intervention in the neonatal period either to augment pulmonary blood flow or to repair a complication associated with the initial transcatheter procedure [4,6,7,9–13].

Recently, a hybrid approach combining surgical access with a transcatheter intervention to open the RVOT was described [15]. Potential advantages of the hybrid approach include avoidance of neonatal CPB, mitigation of the technical failure rate of the percutaneous approach, due to direct access to the RVOT, and a lower complication rate (i.e., no risk of RVOT perforation and associated sequelae) [16–19]. While the hybrid balloon pulmonary valvuloplasty procedure has been detailed in limited case reports and a single-center series, it has yet to be compared rigorously with a contemporaneous cohort treated with the standard surgical approach. We sought to compare acute and mid-term outcomes following the hybrid approach to the standard surgical approach in initial treatment of pulmonary atresia with intact ventricular septum.

METHODS

After obtaining institutional review board approval, we performed a single-center review of all patients with PA-IVS who underwent an RV decompression procedure between January 2002 and December 2011. Patients were identified using a combination of our internal surgical database (LUMEDX Corporation, Oakland, CA) and by performing a keyword search in our electronic medical record system (CareWeb, non-commercial, live since 1998) for the terms "pulmonary atresia" and "intact ventricular septum." Medical record review was completed to ensure only patients who underwent RV decompression as the initial surgical repair were included in the analysis. At our institution, the hybrid approach to PA-IVS was instituted in October 2010; previously, the surgical approach was the treatment of choice and subsequently, only 2 patients were managed with the surgical approach. Patients who underwent a hybrid procedure for PA-IVS were identified by search of the institutional hybrid procedure database. Data were collected on all patients to assess baseline demographic information, pre-operative procedural risk factors and echocardiographic assessment of cardiac structure and function, as well as post-procedural patient outcomes during the initial hospitalization and for 2 years following the procedure. Whenever possible, all echocardiographic assessments, measurements and grading were performed by the core Pediatric Cardiology Echocardiography Laboratory at our institution.

Normally distributed variables were compared using Students *t*-test. Chi square was used to compare categorical variables, and nonparametric, ordinal variables were compared using Wilcoxon Rank Sum. A P value of < 0.05 was considered statistically significant.

A systematic review of the literature was performed to examine patient outcomes after the percutaneous transcatheter treatment of PA-IVS. Using key word searches for the following terms and combination of terms: "pulmonary atresia," "intact ventricular septum," "perforation," "transcatheter," and "percutaneous," we searched the English language literature with PubMed and OVID databases for all studies published between 1997 and 2012. Inclusion criteria for the literature search were single center studies, multi-center studies, and published systematic reviews or meta-analyses which focused on patient outcomes. Exclusion criteria were case reports or duplications of previously published data. All references were evaluated from the manuscripts to confirm inclusion of all pertinent studies. Specific data collected during the systematic review included rates of procedural success/failure, procedural complications including RVOT perforations and mortality, need for subsequent cardiac operation(s), and rate of achieving an eventual biventricular circulation. Descriptive comparison between the percutaneous transcatheter and hybrid cohorts was performed.

Hybrid Procedural Description

A midline sternotomy is performed and the pericardium suspended. Circumferential control of the ductus arteriosus is obtained. Using transesophageal echocardiographic (TEE) guidance exclusively, a location on the right ventricular free wall which will allow a straight path to the pulmonary valve is identified, and a pledgeted pursestring suture is placed. A 22-gauge needle is then inserted through the pursestring and directed across the atretic pulmonary valve into the main pulmonary artery under TEE guidance. A guidewire is then advanced through the needle, into the main pulmonary artery, across the ductus arteriosus and down the descending aorta. The needle is removed over the wire, and a 4 French sheath cut to a length of 2 cm is advanced over the wire into the RVOT. Serial balloon pulmonary valvuloplasty is performed over the wire. The largest balloon diameter is selected to be approximately 110–120% of the pulmonary annulus, as measured by echocardiogram. After the final balloon dilation, the ductus arteriosus snare is engaged and the sheath is attached to a pressure transducer to measure right ventricle pressure. If the patient develops systemic desaturation, the ductal snare is released and an off-CPB modified Blalock-Taussig (BT) shunt is added. The ductus arteriosus is then ligated. If the patient remains hemodynamically stable with adequate oxygen saturations and subsystemic RV pressure with the ductus snared, then the ductus is ligated without addition of a BT shunt.

RESULTS

Baseline Characteristics

Twenty-four patients underwent an RV decompression procedure during the study period. The surgical cohort consisted of 17 patients who underwent transannular patch placement ($n = 12$) or pulmonary valvotomy ($n = 5$). All surgical patients received a BT shunt. The hybrid cohort consisted of 7 patients who underwent perventricular transcatheter balloon pulmonary valvuloplasty, of which 5 (71%) underwent concomitant placement of a BT shunt.

The baseline clinical characteristics and preoperative risk factors for the cohorts are shown in Table I. There were no differences between the cohorts in gender, age, weight, gestational age, genetic or noncardiac anomalies, preoperative echocardiographic assessment of right heart size or function, or the presence of RV sinusoids as assessed by echocardiogram. Although uncommon in the cohort overall, preoperative use of extracorporeal membrane oxygenation (ECMO) support and the presence of extracardiac organ system dysfunction were only present in the hybrid group.

Hospital Outcomes

There were no significant differences between cohorts in the maximum vasoactive-inotropic score (VIS), duration of mechanical ventilation, length of intensive care unit stays, or overall length of hospital stay (Table II). The overall complication rate was similar for both cohorts. There was no in-hospital mortality in the study population during the initial hospital stay. One patient in the surgical cohort required reoperation prior to hospital discharge for placement of a right ventricle to pulmonary artery conduit due to persistent cyanosis. No patient in the hybrid cohort required a repeat surgical intervention during the initial hospital stay, although 1 patient in this cohort underwent percutaneous pulmonary valvuloplasty. No patient in the hybrid cohort required CPB at the initial palliative procedure or at any other time prior to hospital discharge. Median CPB time in the surgical cohort was 80 min (IQR 69–108 min).

At hospital discharge, median oxygen saturations were not different between cohorts.

Post-Discharge Outcomes

During the 2-year follow-up period, there were 2 deaths in the surgical cohort (11.8%) and none in the hybrid cohort (Table III). One patient died suddenly at home 14 days after hospital discharge, and one patient died peri-operatively following a Nissen fundoplication, 15 months after the initial surgical palliation.

The number of patients who underwent elective BT shunt occlusion or ASD closure procedures, either surgically or percutaneously, was not different between the cohorts. Excluding these procedures, 6 patients (35%) in the surgical cohort required an additional surgical procedure, including augmentation of the RVOT ($n = 3$), RPA augmentation ($n = 1$), and hemiFontan procedure (superior cavopulmonary anastomosis) for single ventricle palliation ($n = 1$); the sixth patient underwent surgery prior to hospital discharge as described above. Four patients in the surgical cohort (24%) underwent interventional catheterization procedures for pulmonary balloon valvuloplasty ($n = 2$), branch pulmonary artery angioplasty ($n = 1$), and branch pulmonary artery stent placement ($n = 1$). In comparison, 1 patient (14%) in the hybrid cohort underwent cardiac surgery for patch augmentation of the RVOT and bidirectional Glenn anastomosis ($1\frac{1}{2}$ ventricle repair) and 2 patients (29%) underwent percutaneous pulmonary balloon valvuloplasty (includes the 1 patient who underwent pulmonary balloon valvuloplasty prior to initial hospital discharge). Of note, the two patients who underwent pulmonary balloon valvuloplasty after the hybrid procedure were the same two patients who did not have a BT shunt placed

TABLE I. Demographic and Clinical Characteristics

Characteristics	Approach			
	All	Surgical ($n = 17$)	Hybrid ($n = 7$)	P-value[a]
Male sex	12 (50.0)	10 (58.8)	2 (28.6)	0.37
Age at surgery, days	6 (0–14)	5 (0–14)	7 (5–12)	0.06
Weight at surgery, kg	3.0 (1.4–4.3)	3.0 (1.5–4.3)	3.1 (1.4–4.0)	0.92
Body surface area at surgery, m[b]	0.21 (0.13–0.25)	0.20 (0.14–0.25)	0.21 (0.13–0.23)	0.95
Non-cardiac abnormality	1 (4.2)	1 (5.9)	0 (0.0)	1.00
Genetic syndrome	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Gestational age, weeks	39 (30–41)	39 (32–41)	39 (30–41)	1.00
Pre-Operative				
ECMO	1 (4.2)	0 (0.0)	1 (14.3)	0.29
Mechanical ventilation	15 (62.5)	10 (58.8)	5 (71.4)	0.67
Organ system dysfunction	2 (8.3)	0 (0.0)	2 (28.6)	0.08
Pre-Operative Echocardiographic Measurements				
Tricuspid valve size, mm	10.0 (6.5–15.1)	10.0 (6.9–15.1)	8.5 (6.5–13.3)	0.41
Tricuspid valve z-score	−0.48 (−3.1–4)	−0.36 (−2.5–4)	−1.3 (−3.1–3.2)	0.47
Tricuspid regurgitation				
None/Trivial	1 (4.2)	0 (0.0)	1 (14.3)	
Mild	2 (8.3)	2 (11.8)	0 (0.0)	
Mild to Moderate	5 (20.8)	4 (23.5)	1 (14.3)	1.00[b]
Moderate	11 (45.8)	7 (41.2)	4 (57.1)	
Moderate to Severe	5 (20.8)	4 (23.5)	1 (14.3)	
RV size				
Normal	5 (20.8)	3 (17.6)	2 (28.6)	
Mildly hypoplastic	9 (37.5)	7 (41.2)	2 (28.6)	
Moderately hypoplastic	6 (25.0)	3 (17.6)	3 (42.9)	0.64[c]
Severely hypoplastic	1 (4.2)	1 (5.9)	0 (0.0)	
Unknown	3 (12.5)	3 (17.6)	0 (0.0)	
RV systolic function				
Normal	1 (4.2)	0 (0.0)	1 (14.3)	
Mildly depressed	0 (0.0)	0 (0.0)	0 (0.0)	0.29[d]
Moderately depressed	10 (41.7)	9 (52.9)	1 (14.3)	
Severely depressed	13 (54.2)	8 (47.1)	5 (71.4)	
Pulmonary valve annulus size, mm	6 (2.9–8.2)	6.2 (2.9–8.2)	6 (4–7)	0.55
Pulmonary valve annulus z-score	−1.5 (−3.7– −0.1)	−1.45 (−3.7– −0.1)	−1.8 (−3.4– −0.5)	0.89
Sinusoids present (non-RV dependent)	11 (45.8)	8 (47.1)	3 (42.9)	1.00

Abbreviations: ECMO, extracorporeal membrane oxygenation; RV, right ventricular; N/A, not applicable.

* Data are presented as N (%) for categorical variables and Median (min-Max) for continuous variables.

[a]*P*-value from Fisher's exact test for categorical variables and Wilcoxon Rank Sum test for continuous variables on comparison of each characteristic between two approaches (surgical vs. hybrid).

[b]Comparison was made between None/trivial/Mild/Mild-to-Moderate vs. Moderate/Moderate-to-Severe and *p*-value was from Fisher's exact test.

[c]Comparison was made between Normal/mildly hypoplastic vs. moderately/severely hypoplastic and *p*-value was from Fisher's exact test.

[d]Comparison was made between Normal/mildly depressed vs. moderately/severely depressed and *p*-value was from Fisher's exact test.

at the time of the initial procedure. The valvuloplasty was performed at a median of 41 days (range, 37–45 days) after the initial procedure.

At 1- and 2-year follow-up visits, median oxygen saturation was 89.5% and 92% for the surgical cohort and 93% and 95% for the hybrid cohort, respectively. Echocardiographic assessment of right heart size and function was nearly identical between the two cohorts at 1- and 2-year follow-up, as demonstrated in Table IV.

The rates of eventual biventricular circulation were 82% and 86% for the surgical and hybrid cohorts, respectively, with only one patient requiring single ventricle palliation (surgical cohort). The remaining 3 patients (surgical cohort $n = 2$, and hybrid cohort $n = 1$) underwent a $1\frac{1}{2}$ ventricle palliation (RV-PA connection plus cavopulmonary anastomosis).

Systematic Review of Percutaneous Transcatheter Approach

There were 8 manuscripts published between 1998 and 2012 describing percutaneous transcatheter procedures for the initial palliation of PA-IVS performed

TABLE II. Hospital Outcomes and Complications

Outcomes/Complications	All	Approach: Surgical ($n = 17$)	Approach: Hybrid ($n = 7$)	P-value[a]
Maximum vasoactive-inotropic score[b]	17 (5–34)	18 (5–34)	8 (5–28)	0.25
Length of intubation, days	5 (2–20)	4 (2–12)	8 (3–20)	0.08
ICU length of stay, days	6 (4–58)	6 (4–25)	11 (4–58)	0.21
Hospital length of stay, days	17.5 (8–129)	18 (8–38)	17 (8–129)	0.83
Post-operative ECMO	1 (4.2)	0 (0.0)	1 (14.3)	0.29
Re-operation prior to hospital discharge	1 (4.2)	1 (5.9)	0 (0.0)	1.00
Interventional cardiac catheterization prior to hospital discharge	1 (4.2)	0 (0.0)	1 (14.3)	0.29
PA repair prior to hospital discharge	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Oxygen saturation levels at hospital discharge (%)	85 (75–97)	84.5 (75–97)	86 (81–97)	0.29
Any complications	14 (58.3)	10 (58.8)	4 (57.1)	1.00
Arrhythmia	4 (16.7)	3 (17.6)	1 (14.3)	1.00
Cardiac arrest	2 (8.3)	2 (11.8)	0 (0.0)	1.00
Renal insufficiency or failure	3 (12.5)	1 (5.9)	2 (28.6)	0.19
Neurologic injury or seizure	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Infections	5 (20.8)	3 (17.6)	2 (28.6)	0.61
NEC	5 (20.8)	4 (23.5)	1 (14.3)	1.00
Death	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Other	1 (4.2)	1 (5.9)	0 (0.0)	1.00
Discharge echocardiogram data[c]				
RVOT gradient	$n =$ 19	$n = 14$	$n = 5$	
"None" (n)	10 (52.6)	8 (57.1)	2 (40.0)	0.63
PIPG (mmHg)	22 (10–60)	21 (10–32)	30 (22–60)	0.14
RV pressure	$n =$ 18	$n = 12$	$n = 6$	
TR velocity (mmHg + right atrial pressure)	35 (27–70)	35 (27–54)	38 (28–70)	0.93
Age at time of echocardiogram (days)	$n =$ 21	$n = 15$	$n = 6$	
	21 (10–139)	20 (10–94)	24 (12–139)	0.68

Abbreviations: ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation; NEC, necrotizing enterocolitis; PA, pulmonary artery; N/A, not applicable; RVOT, right ventricular outflow tract; PIPG, peak instantaneous pressure gradient; RV, right ventricle; TR, tricuspid regurgitation.

* Data are presented as N (%) for categorical variables and Median (min-Max) for continuous variables.

[a]P-value from Fisher's exact test for categorical variables and Wilcoxon Rank Sum test for continuous variables on comparison of each outcome between two approaches (surgical vs. hybrid).

[b]Highest hourly vasoactive-inotropic score in the first 48 hours after the initial procedure.

[c]Based on echocardiogram performed in closest proximity but prior to discharge from the hospital

between 1990 and 2010. All were single-center studies, except the article by Bensen et al., which included data published in 15 studies between 1993 and 2002. Thus the total number of studies included in the systemic review was 22. In this cohort of 267 patients, the procedural success was 75–95%. Procedural complication rates were 15–75%, with RVOT perforation occurring in 5–50% of procedures. Procedural mortality was 5.6% with an overall mortality rate (during study follow-up periods) of 0–50%, and 33–75% of patients required a surgical procedure in the neonatal period with indications of augmenting pulmonary blood flow (71%), transcatheter procedural failure (18%) and cardiac perforation repair (8%). Patients went on to biventricular circulation in 80% of cases.

DISCUSSION

In patients with PA-IVS and anatomy favorable for a future biventricular repair, the hybrid approach to initial palliation offers a safe and feasible alternative to surgical and percutaneous techniques for RV decompression. In our single-center experience with the hybrid approach to RV decompression, we achieved a 100% procedural success rate with no peri-procedural mortality. Moreover, no hybrid-treated patient required CPB in the neonatal period and both acute and mid-term outcomes did not differ significantly from those treated with the standard surgical approach.

Comparison With the Surgical Approach

Compared to standard surgical approaches for the initial treatment of PA-IVS, the hybrid approach achieved nearly identical rates of procedural success and peri-procedural complications, in cohorts with no baseline differences. Likewise, the acute and mid-term patient outcomes are similar between cohorts.

Avoidance of CPB in the neonatal period is a major advantage of the hybrid approach in this patient

TABLE III. Post-Discharge Outcomes

Outcomes	All	Approach: Surgical ($n = 17$)	Approach: Hybrid ($n = 7$)	P-value[a]
Re-operation within 2 years of procedure	10 (41.7)	8 (47.1)	2 (28.6)	0.65
Excluding BT shunt occlusion and ASD closure	7 (29.2)	6 (35.3)	1 (14.2)	0.65
Interventional cardiac catheterization within 2 years of procedure	10 (41.7)	6 (35.3)	4 (57.1)	0.39
Excluding BT shunt occlusion and ASD closure	6 (25.0)	4 (23.5)	2 (28.6)	1.00
PA repair within 2 years of procedure	5 (20.8)	5 (29.4)	0 (0.0)	0.27
Oxygen saturation levels				
at 1 year post-operation ($n = 20$)	91.5 (81–100)	89.5 (81–100)	93 (85–97)	0.97
at 2 year post-operation ($n = 15$)	93 (83–100)	92 (83–100)	95 (85–98)	0.23
Current physiology				
1V	1 (4.2)	1 (5.9)	0 (0.0)	
1.5V	3 (12.5)	2 (11.8)	1 (14.3)	1.00[b]
2V	20 (83.3)	14 (82.3)	6 (85.7)	
Current patient status (Dead)	2 (8.3)	2 (11.8)	0 (0.0)	1.00

Abbreviations: BT, Blalock-Taussig; PA, pulmonary artery; V, ventricle.

* Data are presented as N (%) for categorical variables and Median (min-Max) for continuous variables.

[a]*P*-value from Fisher's exact test for categorical variables and Wilcoxon Rank Sum test for continuous variables on comparison of each outcome/complication between two approaches (surgical vs. hybrid).

[b]Comparison was made between 1V or 1.5V vs. 2V and *p*-value was from Fisher's exact test.

population. Neonatal CPB has both acute consequences related to systemic inflammatory response as well as longer term impact on end-organ development and neurocognitive and psychomotor function [20–30]. Unfortunately, the acute impact of CPB is difficult to assess. In this study, maximal vaso-active inotropic score, which has been used to predict early post-operative outcome in neonates after cardiac surgery, was not statistically different between cohorts [31–33]. Similarly, the long-term impact of CPB will likely require long-term follow-up with performance of neurocognitive testing. Thus, the most important advantage of the hybrid approach may require many years to be realized.

Comparison With the Percutaneous Approach

The major differences between the percutaneous and hybrid approaches to PA-IVS are the lower rates of procedural success, higher rates of procedural complications, and higher mortality for the percutaneous cohort. The risk of RVOT perforation is eliminated by the surgical and hybrid approaches. Most importantly, there is a high rate of neonatal surgery required in the percutaneous cohort. These operations are usually performed secondary to inadequate pulmonary blood flow following the initial percutaneous transcatheter procedure, but are also sometimes required because of procedural failure and RVOT perforations. While the percutaneous transcatheter approach theoretically avoids CPB, it is clear that this approach does not avoid CPB in up to 33–75% of patients.

FUTURE APPROACHES AND STUDIES

In our study, off-CPB BT shunts were placed at the time of the initial procedure for patients who underwent the hybrid approach and experienced a precipitous decrease in oxygen saturations with occlusion of the ductus arteriosus. There are two alternatives to this approach. First, ductal patency could be maintained with a continued prostaglandin infusion. Even with adequate balloon valvuloplasty, the primary limitations to anterograde pulmonary blood flow are poor RV compliance and sub-valvar infundibular obstruction due to RV hypertrophy. In many patients, these improve with time and watchful waiting may obviate the need for placement of an additional source of pulmonary blood flow (e.g. a BT shunt). This approach, however, requires prolonged hospitalization for prostaglandin infusion, exposes patients to the risks of chronic prostaglandin administration, and places a subset of patients at risk during a second cardiothoracic surgical procedure [34–36]. A second alternative is to stent the ductus arteriosus in lieu of placing a BT shunt. Ductal stenting is now commonly performed as a palliative procedure in several forms of congenital heart disease and has been described for patients with PA-IVS [8,37–42]. The procedural success rate, peri-operative complication profile, and long-term impact on future operations and pulmonary artery anatomy, however, are not yet available. Thus, while maintaining ductal patency with prostaglandin infusion or stent implantation are viable alternatives to placement of a BT shunt, the relative risks and benefits require further study to determine the optimal approach.

TABLE IV. Echocardiographic Characteristics at 1- and 2-Year Follow-Up[a]

	Surgical Approach		Hybrid Approach		*P*-value[b]	
	1-year $n=14$	2-year $n=10$	1-year $n=6$	2-year $n=6$	1-year	2-year
Tricuspid regurgitation						
Less than moderate	11 (78.6)	7 (70.0)	5 (83.3)	4 (66.7)	1.00[c]	1.00[c]
Moderate or severe	3 (21.4)	3 (30.0)	1 (16.7)	2 (33.3)		
Tricuspid stenosis						
None or trivial	13 (92.9)	10 (100.0)	6 (100.0)	6 (100.0)	1.00	N/A
Moderate	1 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)		
RV size						
Normal to mildly hypoplastic	9 (64.3)	10 (100.0)	6 (100.0)	6 (100.0)	0.51[d]	N/A[d]
Moderate or severely hypoplastic	3 (21.4)	0 (0.0)	0 (0.0)	0 (0.0)		
RV systolic function						
Less than moderately depressed	12 (85.7)	10 (100.0)	6 (100.0)	6 (100.0)	1.00[e]	N/A[e]
Moderate or severely depressed	1 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)		
Pulmonary stenosis						
None/trivial	12 (85.7)	9 (90.0)	6 (100.0)	6 (100.0)		
Mild	1 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)	1.00	1.00
Moderate	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)		
Pulmonary insufficiency						
Moderate or less	1 (7.1)	0 (0.0)	1 (16.7)	2 (33.3)	1.00[f]	0.13[f]
Severe	12 (85.7)	10 (100.0)	5 (83.3)	4 (66.7)		
ASD direction of shunting						
R→L	5 (35.7)	3 (30.0)	3 (50.0)	3 (50.0)		
Bidirectional with R→L	4 (28.6)	4 (40.0)	0 (0.0)	1 (16.7)	N/A	N/A
Bidirectional	2 (14.3)	1 (10.0)	3 (50.0)	2 (33.3)		
No shunt or no ASD	1 (7.1)	2 (20.0)	0 (0.0)	0 (0.0)		

RV, right ventricular; ASD, atrial septal defect; R-to-L, right to left; N/A, not applicable.
Data are presented as *N* (%).
[a]Whenever possible, echocardiographic assessment and subjective grading was performed by the core Pediatric Cardiology Echocardiography Laboratory at our institution. For 4 patients, 3 in the surgical cohort and 1 in the hybrid cohort, review of the echocardiographic images was not available and data presented are based on review of echocardiography reports.
[b]*P*-value from Fisher's exact test for categorical variables and Wilcoxon Rank Sum test for continuous variables on comparison of each characteristic between two approaches (surgical vs. hybrid).
[c]Comparison was made between None/trivial/Mild/Mild-to-Moderate vs. Moderate/Moderate-to-Severe and *P*-value was from Fisher's exact test.
[d]Comparison was made between Normal/mildly hypoplastic vs. moderately/severely hypoplastic and *P*-value was from Fisher's exact test.
[e]Comparison was made between Normal/mildly depressed vs. moderately/severely depressed and *P*-value was from Fisher's exact test.
[f]Comparison was made between Mild to Moderate/Moderate vs. Severe and *P*-value was from Fisher's exact test and *P*-value was from Fisher's exact test.

As mentioned above, long-term follow-up of these patient cohorts might help delineate the impact of cardiopulmonary bypass on neurodevelopmental outcomes. Since the acute- and mid-term outcomes of the hybrid and surgical approaches to PA-IVS are similar, this patient population might be ideal to evaluate the long term neurodevelopmental outcomes of CPB. This would be best approached in a multi-institutional trial, given the rarity of PA-IVS, especially the morphologic variant amenable to RV decompression and possible biventricular repair.

LIMITATIONS

The major limitations of our study are the small sample size, the retrospective approach, and the lack of a concomitant local percutaneous transcatheter-treated cohort with which to compare the surgical and hybrid groups. At our institution, the transcatheter approach for patients with PA-IVS is seldom performed. While we have attempted to compare descriptively the hybrid approach to the percutaneous transcatheter approach, the systematic literature review includes procedures performed as early as 1990. The recent increased use of radiofrequency-guided pulmonary valve perforation in PA-IVS may result in increased procedural safety. Even the most contemporary studies, however, have relatively high procedural complication rates and, most importantly, a large number of patients requiring subsequent neonatal operations following the initial transcatheter approach to therapy.

CONCLUSIONS

This is the first study to compare the hybrid approach for RV decompression in PA-IVS to the

standard surgical and percutaneous approaches. The hybrid approach is a safe and feasible alternative with a high rate of technical success and low rate of procedural complications. Overall, the acute- and mid-term patient outcomes are comparable to those treated with a standard surgical approach. In addition, use of the hybrid procedure avoids neonatal exposure to CPB, which may have long-term detrimental effects, particularly in neonates.

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REFERENCES

1. Ashburn DA, Blackstone EH, Wells WJ, Jonas RA, Pigula FA, Manning PB, Lofland GK, Williams WG, McCrindle BW. Determinants of mortality and type of repair in neonates with pulmonary atresia and intact ventricular septum. J Thorac Cardiovasc Surg 2004;127:1000–1007; discussion 1007–1008.
2. Daubeney PE, Wang D, Delany DJ, Keeton BR, Anderson RH, Slavik Z, Flather M, Webber SA. Pulmonary atresia with intact ventricular septum: Predictors of early and medium-term outcome in a population-based study. J Thorac Cardiovasc Surg 2005;130:1071.
3. Dyamenahalli U, McCrindle BW, McDonald C, Trivedi KR, Smallhorn JF, Benson LN, Coles J, Williams WG, Freedom RM. Pulmonary atresia with intact ventricular septum: Management of, and outcomes for, a cohort of 210 consecutive patients. Cardiol Young 2004;14:299–308.
4. Hirata Y, Chen JM, Quaegebeur JM, Hellenbrand WE, Mosca RS. Pulmonary atresia with intact ventricular septum: Limitations of catheter-based intervention. Ann Thorac Surg 2007;84:574–579; discussion 579–580.
5. Jahangiri M, Zurakowski D, Bichell D, Mayer JE, del Nido PJ, Jonas RA. Improved results with selective management in pulmonary atresia with intact ventricular septum. J Thorac Cardiovasc Surg 1999;118:1046–1055.
6. Alcibar-Villa J, Rubio A, Pena N, Galdeano JM, Luis M, Arriola J, Inguanzo R, Perez-Asenjo J, Aramendi JI, Barrenechea JI. [Pulmonary atresia with intact ventricular septum. Perforation and pulmonary valvuloplasty using a modified mechanical technique. Medium-term follow-up]. Rev Esp Cardiol 2007;60:833–840.
7. Ovaert C, Qureshi SA, Rosenthal E, Baker EJ, Tynan M. Growth of the right ventricle after successful transcatheter pulmonary valvotomy in neonates and infants with pulmonary atresia and intact ventricular septum. J Thorac Cardiovasc Surg 1998;115:1055–1062.
8. Chubb H, Pesonen E, Sivasubramanian S, Tibby SM, Simpson JM, Rosenthal E, Qureshi SA. Long-term outcome following catheter valvotomy for pulmonary atresia with intact ventricular septum. J Am Coll Cardiol 2012;59:1468–1476.
9. Qureshi SA. Collaborative approach in the management of pulmonary atresia with intact ventricular septum. J Interv Cardiol 2001;14:377–384.
10. Agnoletti G, Piechaud JF, Bonhoeffer P, Aggoun Y, Abdel-Massih T, Boudjemline Y, Le Bihan C, Bonnet D, Sidi D. Perforation of the atretic pulmonary valve. Long-term follow-up. J Am Coll Cardiol 2003;41:1399–1403.
11. Hasan BS, Bautista-Hernandez V, McElhinney DB, Salvin J, Laussen PC, Prakash A, Geggel RL, Pigula FA. Outcomes of transcatheter approach for initial treatment of pulmonary atresia with intact ventricular septum. Catheter Cardiovasc Interv 2013;81:1111–1118.
12. Liava'a M, Brooks P, Konstantinov I, Brizard C, d'Udekem Y. Changing trends in the management of pulmonary atresia with intact ventricular septum: The Melbourne experience. Eur J Cardiothorac Surg 2011;40:1406–1411.
13. McLean KM, Pearl JM. Pulmonary atresia with intact ventricular septum: Initial management. Ann Thorac Surg 2006;82:2214–2219; discussion 2219–2220.
14. Benson LN, Nykanen D, Collison A. Radiofrequency perforation in the treatment of congenital heart disease. Catheter Cardiovasc Interv 2002;56:72–82.
15. Zhang H, Li SJ, Li YQ, Wang H, Hu SS. Hybrid procedure for the neonatal management of pulmonary atresia with intact ventricular septum. J Thorac Cardiovasc Surg 2007;133:1654–1656.
16. Burke RP, Hannan RL, Zabinsky JA, Tirotta CF, Zahn EM. Hybrid ventricular decompression in pulmonary atresia with intact septum. Ann Thorac Surg 2009;88:688–689.
17. Li S, Chen W, Zhang Y, Zhang H, Hua Z, Wang D, Hu S. Hybrid therapy for pulmonary atresia with intact ventricular septum. Ann Thorac Surg 2011;91:1467–1471.
18. Li SJ, Zhang H, Sheng XD, Yan J, Deng XC, Chen WD, Hu SS. Intraoperative hybrid cardiac surgery for neonates and young children with congenital heart disease: 5 years of experience. Ann Thorac Cardiovasc Surg 2010;16:406–409.
19. Lin MC, Wei HJ, Fu YC, Jan SL. A novel hybrid therapy for pulmonary atresia with intact ventricular septum. Int J Cardiol 2010;144:438–439.
20. Kozik DJ, Tweddell JS. Characterizing the inflammatory response to cardiopulmonary bypass in children. Ann Thorac Surg 2006;81:S2347–S2354.
21. Tirilomis T, Tempes T, Waldmann-Beushausen R, Ballat C, Bensch M, Schoendube FA. Histological changes in neonatal kidneys after cardiopulmonary bypass and deep hypothermic circulatory arrest. Thorac Cardiovasc Surg 2009;57:7–9.
22. Tirilomis T, Zwiehoff JM, Waldmann-Beushausen R, Schneider S, Schoendube FA. The effect of cardiopulmonary bypass and hypothermic circulatory arrest on hepatic histology in newborn animals: An experimental study. Artif Organs 2013;37:E35–E39.
23. Tabbutt S, Gaynor JW, Newburger JW. Neurodevelopmental outcomes after congenital heart surgery and strategies for improvement. Curr Opin Cardiol 2012;27:82–91.
24. Marino BS, Lipkin PH, Newburger JW, Peacock G, Gerdes M, Gaynor JW, Mussatto KA, Uzark K, Goldberg CS, Johnson WH, Jr., Li J, Smith SE, Bellinger DC, Mahle WT. Neurodevelopmental outcomes in children with congenital heart disease: Evaluation and management: A scientific statement from the American Heart Association. Circulation 2012;126:1143–1172.
25. Hovels-Gurich HH, Bauer SB, Schnitker R, Willmes-von Hinckeldey K, Messmer BJ, Seghaye MC, Huber W. Long-term outcome of speech and language in children after corrective surgery for cyanotic or acyanotic cardiac defects in infancy. Eur J Paediatr Neurol 2008;12:378–386.
26. Hovels-Gurich HH, Konrad K, Skorzenski D, Herpertz-Dahlmann B, Messmer BJ, Seghaye MC. Attentional

dysfunction in children after corrective cardiac surgery in infancy. Ann Thorac Surg 2007;83:1425–1430.
27. Hovels-Gurich HH, Konrad K, Skorzenski D, Minkenberg R, Herpertz-Dahlmann B, Messmer BJ, Seghaye MC. Long-term behavior and quality of life after corrective cardiac surgery in infancy for tetralogy of Fallot or ventricular septal defect. Pediatr Cardiol 2007;28:346–354.
28. Hovels-Gurich HH, Konrad K, Skorzenski D, Nacken C, Minkenberg R, Messmer BJ, Seghaye MC. Long-term neurodevelopmental outcome and exercise capacity after corrective surgery for tetralogy of Fallot or ventricular septal defect in infancy. Ann Thorac Surg 2006;81:958–966.
29. Rappaport LA, Wypij D, Bellinger DC, Helmers SL, Holmes GL, Barnes PD, Wernovsky G, Kuban KC, Jonas RA, Newburger JW. Relation of seizures after cardiac surgery in early infancy to neurodevelopmental outcome. Boston Circulatory Arrest Study Group. Circulation 1998;97:773–779.
30. Augoustides JG. The inflammatory response to cardiac surgery with cardiopulmonary bypass: Should steroid prophylaxis be routine? J Cardiothorac Vasc Anesth 2012;26:952–958.
31. Butts RJ, Scheurer MA, Atz AM, Zyblewski SC, Hulsey TC, Bradley SM, Graham EM. Comparison of maximum vasoactive inotropic score and low cardiac output syndrome as markers of early postoperative outcomes after neonatal cardiac surgery. Pediatr Cardiol 2012;33:633–638.
32. Davidson J, Tong S, Hancock H, Hauck A, da Cruz E, Kaufman J. Prospective validation of the vasoactive-inotropic score and correlation to short-term outcomes in neonates and infants after cardiothoracic surgery. Intensive Care Med 2012;38:1184–1190.
33. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, Charpie JR, Hirsch JC. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. Pediatr Crit Care Med 2010;11:234–238.
34. Kaufman MB, El-Chaar GM. Bone and tissue changes following prostaglandin therapy in neonates. Ann Pharmacother 1996;30: 269–74, 277.
35. Peled N, Dagan O, Babyn P, Silver MM, Barker G, Hellmann J, Scolnik D, Koren G. Gastric-outlet obstruction induced by prostaglandin therapy in neonates. N Engl J Med 1992;327:505–510.
36. Woo K, Emery J, Peabody J. Cortical hyperostosis: A complication of prolonged prostaglandin infusion in infants awaiting cardiac transplantation. Pediatrics 1994;93:417–420.
37. Bacha EA, Daves S, Hardin J, Abdulla RI, Anderson J, Kahana M, Koenig P, Mora BN, Gulecyuz M, Starr JP, Alboliras E, Sandhu S, Hijazi ZM. Single-ventricle palliation for high-risk neonates: The emergence of an alternative hybrid stage I strategy. J Thorac Cardiovasc Surg 2006;131:163–171 e2.
38. Chen Q, Parry AJ. The current role of hybrid procedures in the stage 1 palliation of patients with hypoplastic left heart syndrome. Eur J Cardiothorac Surg 2009;36:77–83.
39. Galantowicz M, Cheatham JP. Lessons learned from the development of a new hybrid strategy for the management of hypoplastic left heart syndrome. Pediatr Cardiol 2005;26:190–199.
40. Galantowicz M, Cheatham JP, Phillips A, Cua CL, Hoffman TM, Hill SL, Rodeman R. Hybrid approach for hypoplastic left heart syndrome: Intermediate results after the learning curve. Ann Thorac Surg 2008;85:2063–2070; discussion 2070–2071.
41. Gutgesell HP, Lim DS. Hybrid palliation in hypoplastic left heart syndrome. Curr Opin Cardiol 2007;22:55–59.
42. Matter M, Almarsafawey H, Hafez M, Attia G, Abuelkheir MM. Patent ductus arteriosus stenting in complex congenital heart disease: Early and Midterm Results for a Single-Center Experience at Children Hospital, Mansoura, Egypt. Pediatr Cardiol 2013;34:1100–1106.