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CVN Interview

Percutaneous Pulmonary Valve Implantation in the Young

2-Year Follow-Up

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Objectives The aim of this study was to investigate physiological and clinical consequences of percutaneous pulmonary valve implantation (PPVI) in patients with chronic right ventricular outflow tract (RVOT) obstruction and volume overload.

Background The PPVI is a nonsurgical technique to address RVOT conduit dysfunction.

Methods Twenty-eight adolescents (median age 14.9 years; age range 10.9 to 19 years) underwent PPVI due to RVOT stenosis and/or pulmonary regurgitation (PR). Before and after PPVI echocardiographic and magnetic resonance imaging, cardiopulmonary exercise tests were obtained.

Results The RVOT gradient ($p < 0.001$) and right ventricular (RV) systolic pressure decreased ($p < 0.001$), acutely. Magnetic resonance imaging (median 6 months) documented reduction in RV end-diastolic (149 ± 49 ml/m^2 vs. 114 ± 35 ml/m^2, $p < 0.005$) volume, increases in left ventricular (LV) end-diastolic ($p < 0.007$) volume and cardiac output (RV: $p < 0.04$ and LV: $p < 0.02$), and reduced PR fraction ($24 \pm 10\%$ to $7 \pm 7\%$, $p < 0.0001$). Symptoms, aerobic exercise performance (maximal oxygen consumption: $p < 0.0001$) and ventilatory response to carbon dioxide production ($p < 0.003$) improved. After 24 months, echocardiography demonstrated the RV/systemic-pressure ratio, and RVOT peak pressure gradient reductions persisted, and PR was absent in 93% ($n = 12$ of 13) of the cohort. Freedom from surgery was 91%, 83%, and 83%, and freedom from transcatheter reintervention was 91%, 80%, and 80%, at 12, 24, and 36 months, respectively. There were no acute device-related complications, with stent fractures noted in 10.8%.

Conclusions Percutaneous pulmonary valve implantation is feasible and safe in the young with dysfunctional RVOT conduits. An improvement in symptoms, hemodynamic status, and objective findings of exercise performance occurs. Early follow-up demonstrates persistent improvement in ventricular parameters, PR, and objective exercise capacity. (J Am Coll Cardiol Intv 2010;3:439–48)

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Reconstruction of the right ventricular outflow tract (RVOT) with a conduit or bioprosthetic valve is often required in strategies applied to children with complex heart disorders (1–3). As such, the longevity of the RVOT reconstruction is limited (4–6), with pulmonary regurgitation (PR) identified as a risk factor for long-term morbidity and mortality (7–9) and the primary indication for reoperation (9,10). Although surgical outflow tract revision is associated with a low morbidity and mortality (7,11), such replacements have a limited life span and require additional open heart procedures. The potential for an effective percutaneous implantation of a pulmonary valve to address obstructive and/or regurgitant lesions would have a significant impact on developing treatment algorithms.

In this regard, percutaneous pulmonary valve implantation (PPVI) was introduced by Bonhoeffer et al. (12) as a nonsurgical treatment of RVOT dysfunction, with the largest reported experience in 155 patients implanted at a median age of 21 years (13). Implantation was technically successful with a low complication rate and marked improvement in right ventricular (RV) hemodynamic status (13). In this study, described are the acute results and clinical outcomes of PPVI in a unique childhood population with dilated RVs and early-term follow-up.

Abbreviations and Acronyms

EF = ejection fraction

LV = left ventricle/ventricular

LVEDV = left ventricular end-diastolic volume

MRI = magnetic resonance imaging

PPVI = percutaneous pulmonary valve implantation

PR = pulmonary regurgitation

RV = right ventricle/ventricular

RVEDV = right ventricular end-diastolic volume

RVOT = right ventricular outflow tract

VE/VCO_2 = ventilatory response to carbon dioxide production

Methods

Patients. Between October 2005 and December 2008, 28 adolescents underwent PPVI at the Hospital for Sick Children, Toronto, Canada. Written consent was obtained from older children and/or the parents as appropriate. Ethics committee approval was obtained for this review, and consent was waived as to the retrospective nature of the study. Inclusion and exclusion criteria are outlined in Table 1.

Assessment of RV function, outflow gradient, and PR. The RV functional status and degree of dilation were assessed in all, with a Philips IE-33 (Andover, Massachusetts) 2-dimensional transthoracic echocardiographic system. The RVOT gradient was calculated from velocity flow, and the degree of PR was determined qualitatively by color-flow Doppler. The PR was categorized as none = 0; trivial = 1 (width of the regurgitant color jet <1/3 the diameter of the pulmonary valve annulus); mild = 2 (width of the regurgitant color jet >1/3 but <1/2 the diameter of the pulmonary valve annulus); moderate = 3 (width of the regurgitant color jet >1/2 but < the diameter of the pulmonary valve annulus); and severe = 4 (width of the regurgitant color jet equal to the diameter of the pulmonary valve annulus with flow reversal in the branch pulmonary arteries). Grade 3 regurgitation or greater was considered significant. An estimate of RV pressure was determined from the tricuspid regurgitant jet velocity plus 5 mm Hg and compared to a simultaneously obtained arm cuff blood pressure. Right ventricular end-diastolic dimensions were obtained from the long-axis parasternal view from the M-mode images. Tricuspid valve annulus diameter was measured in apical 4-chamber view and a *z*-score assigned from our institutional normative data.

Table 1. Patient Selection Criteria

Inclusion
Clinical criteria
RV systolic pressure >2/3 systemic with clinical symptoms or
RV systolic pressure >3/4 of systemic with no clinical symptoms and/or
Moderate to severe PI and 1 of the following
Symptoms
Severe RV dysfunction
Severe RV dilation
Decreased exercise capacity (peak VO_2max <65% predicted for normal)
Arrhythmias
Morphological criteria
RVOT dimensions <22 × 22 mm
RVOT dimensions >14 × 14 mm (by sizing balloon)
Weight >20 kg
Exclusion
Age <5 yrs or weight <20 kg
Pregnancy
Occluded central veins
Active infection
Coronary anatomy at risk of compression at the time of implant

PI = pulmonary insufficiency; RV = right ventricle; RVOT = right ventricular outflow tract; VO_2max = oxygen consumption at peak exercise.

The outflow tracts were classified as primarily stenotic (peak gradient ≥40 mm Hg); regurgitant (peak gradient <40 mm Hg and regurgitation grade ≥3); or mixed (stenosis with peak gradient ≥40 mm Hg and regurgitation grade ≥3) (Fig. 1), from the echocardiographic studies.

Metabolic exercise testing. Exercise testing was performed on a programmable ergometer (Ergometrics-800S, Ergoline, Bitz, Germany) with a ramp protocol, with respiratory data collected and analyzed breath-to-breath and averaged over 20 s with a metabolic cart (Max-1, Physio-Dyne Instrument Corporation, Quogue, New York).

Magnetic resonance imaging (MRI). Cardiac MRI was performed with a 1.5-T magnet (Siemens Avanto, Erlangen, Germany, or CV/i, GE Healthcare, Milwaukee, Wisconsin). Patients were excluded from imaging if they had

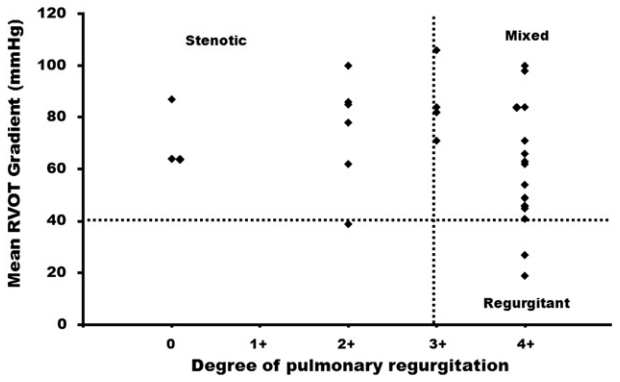

Figure 1. Type of Lesion

A mean right ventricular outflow tract (RVOT) gradient of ≥40 mm Hg was used as a cutoff for pulmonary stenosis—grade 3 or more for pulmonary insufficiency.

previous implants that would interfere with image acquisition (i.e., Harrington rods, pulmonary artery stents).

Ventricular volumes and function assessment. Electrocardiogram-gated steady state free precession cine magnetic resonance images of the heart were acquired in the short-axis, vertical long-axis, 4-chamber, and RVOT planes covering both ventricles in entirety. Assessment of left ventricular (LV) and RV volumes was performed manually at end-diastole and systole (Mass Analysis and CV Flow, Medis Medical Imaging Systems, Leiden, the Netherlands). Cardiac output was obtained by multiplying the heart rate and effective forward flow through ascending aorta for LV output and main pulmonary artery for RV output. In the presence of PR, RV stroke volume was calculated as a difference between RV forward blood flow volume and PR volume.

Flow assessment. Phase-contrast velocity mapping of the flows was performed parallel to the RVOTs and LV outflow tracts with PR fraction calculated as percent backward flow over forward flow.

Cardiac catheterization protocol. All procedures were performed under general anesthesia. Coronary angiography was obtained in all, and simultaneous balloon inflation in the RVOT was performed in those thought potentially at risk for coronary compression during valve implantation. The conduct of the catheterization procedure was similar to that outlined previously (13,14).

Statistical analysis. Data are described as mean ± SD and median with minimum and maximum values as appropriate. A normalized *z*-score was calculated for dimensional variables on the basis of body surface area. Freedom from reintervention and surgery was depicted with Kaplan-Meier nonparametric estimates. Paired *t* tests were performed to compare echocardiographic and angiographic measurements, exercise test results, and MRI investigations before and after PPVI. Changes over time in echocardiographic parameters were assessed in linear regression models and adjusted for repeated measures though an autoregressive covariance structure with the echocardiographic parameter as the dependent variable and the time since implantation as the independent variable. For the ventilatory response to carbon dioxide production (VE/VCO_2) parameter, the PPVI cohort were matched to normal adolescents with structurally normal hearts, undergoing evaluation for a family history of a cardiac disorder, palpitations, chest pain, or syncope. For each implant, 2 sex- and age-matched control subjects were selected. The VE/VCO_2 parameters between groups (control subjects and patients) were compared with linear regression models adjusted for matching through a compound symmetry covariance structure. A p value of <0.05 was considered statistically significant. Statistical analysis was performed with SAS Statistical Software version 9.1 (SAS Institute, Cary, North Carolina).

Results

Patient characteristics. Between October 2005 and December 2008, a PPVI was attempted in 28 adolescents (16 male subjects; median age 14.9 years, age range 10.9 to 19 years; weight 57.7 kg, range 40 to 90.6 kg) (Table 2). Most (n = 16; 57%) had a variant of Fallot's tetralogy with pulmonary atresia. Eleven of the group (39%) had Hancock RV to pulmonary artery valved conduits (Medtronic, Minneapolis, Minnesota) or Hancock valves (n = 6; 21%) placed at surgery, whereas 7 (25%) had pulmonary (n = 5) or aortic (n = 2) homografts. Two had Symbion (Symbion, Salt Lake City, Utah) valves, 1 of which was stented, and the other was balloon-dilated at an earlier procedure, and an additional 2 had their RVOTs stented after a Réparation à l'Etage Ventriculair procedure (15). Three (30%) of the 10 Hancock conduits, 2 (33%) of the 6 Hancock valves, and 2 (28%) of the 7 homografts were also stented at an earlier procedure to address stenosis. Sixty-four percent of the group had ≥2 surgical procedures, and 61% had ≥2 interventional procedures before the PPVI. Age at primary repair was 1.7 ± 1.9 years, with 10 (36%) having initial palliation in the form of a Blalock-Taussig shunt. The time from last intervention to PPVI was 5.2 ± 2.8 years (range 88 days to 9 years). Seventeen (61%) had a mixed lesion, 9 (32%) exclusively stenosis, and 2 (7%) isolated pulmonary insufficiency (Fig. 1).

Immediate results. The Melody (Medtronic) valve was successfully implanted in all, with a femoral venous approach in 23 and a transjugular approach in 5. The median procedure time was 150 min (range 65 to 309 min), and fluoroscopy time was 34 min (range 5 to 107 min). Additional procedures performed included: pre-PPVI RVOT stenting in 7 (25%), right pulmonary artery stent dilation in 2 (7%), and

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Table 2. Group Characteristics

Children	28
Male/female	16/12
Primary diagnosis	
PA/VSD	9 (32)
TOF	7 (25)
PAT	5 (18)
DORV, TGA/PS	2 (7)
AI	2 (7)
ccTGA/PS	2 (7)
AoA/VSD	1 (4)
Primary repair	
RV–PA conduit	17 (61)
TAP	6 (21)
Ross	1 (4)
Ross-Konno	1 (4)
Yasui	1 (4)
REV	2 (6)
Age at primary repair (yrs)	1.7 ± 1.9
Previous palliation:	
Left or right BT shunt	10 (36)
Previous surgeries	2.25 ± 0.5
Previous interventions	1.5 ± 0.4
Time from last intervention to PPVI (yrs)	5.2 ± 2.8
Age at implantation (yrs)	14.9 ± 2.6
Weight (kg)	57.7 ± 12.7
RVOT morphology	
Hancock valve	6 (21)
Hancock conduit	10 (36)
Homograft	7 (25)
Other	5 (18)
Procedure time (min)	150 (65–309)
Fluoroscopy time (min)	34 (5–107)
Additional procedures at time of PPVI	RVOT stent (7) RPA stent dilation (2)

Data presented as n, n (%), mean ± SD, or n (range).

AI = aortic insufficiency; AoA = aortic atresia; BT = Blalock-Taussig; ccTGA = congenitally corrected transposition of great arteries; DORV = double outlet right ventricle; IVC = inferior vena cava; PA/VSD = pulmonary atresia/ventricular septal defect; PAT = persistent arterial trunk; PPVI = percutaneous pulmonary valve implantation; PR = pulmonary regurgitation; PS = pulmonary stenosis; REV = Réparation à l'Etage Ventriculair; RPA = right pulmonary artery; RVOT = right ventricular outflow tract; RV–PA = right ventricle to pulmonary artery; TAP = transannular patch; TOF = tetralogy of Fallot.

an inferior caval vein stent dilation in 1 child (3%). After implantation, the valve appeared abutted to the sternum in 43% (12 of 28) and away from the sternum in 39% (11 of 28) of the cohort. In 5 (18%), the valve was away from the sternum but in a horizontal position. Acute complications included 1 balloon rupture during conduit pre-dilation without vessel injury and 1 conduit disruption after balloon dilation. In the latter, bleeding was contained without effecting hemodynamic status, the tear sealed by the valve implant. There was 1 local vascular complication (arterial aneurysm), which resolved with ultrasound guided compression.

Overall results. At catheterization, the RVOT gradient, RV systolic pressure, and systolic-pressure/systemic-pressure ratio fell significantly, whereas aortic systolic pressure increased (Table 3, Fig. 2). The entire cohort demonstrated, angiographically, a significant reduction in PR associated with an increase in pulmonary artery diastolic pressure.

Acute results by dominant lesion. There were no significant differences between the stenotic and mixed lesion groups in the degree of RV-to-pulmonary artery gradient and RV systolic pressure reduction. Improvement in PR was similar in both lesion types. The sample size was too small (n = 2) to make statistically significant conclusions in the purely regurgitant group.

Echocardiographic observations. Echocardiography performed within the first 24 h after valve implantation, compared with studies obtained immediately before catheterization (Table 4), noted that the RV pressure significantly decreased, the RVOT gradient fell, and RV/aortic pressure ratio decreased. Nineteen (68%) of 28 had moderate-to-severe PR (≥grade 3) before implant, and 1 month later, 19 (80%) had no detectable PR ($p < 0.001$) (Fig. 3).

MRI. Cardiac MRI was performed in 14 of the cohort (50%) at a median 183 days (range 1 to 449 days) after implantation (Table 5, Fig. 4). In 5, MRI was not possible due to an artifact from the previously stented RVOT. Six of the cohort did not have a cardiac MRI before the procedure, and 3 moved, and follow-up MRI was not available. Eleven had cardiac MRI performed before and after PPVI, whereas 3 were awaiting follow-up studies at the time of this report. In 1, PR fraction was not calculated.

There was a significant decrease in right ventricular end-diastolic volume (RVEDV) and RV end-systolic volume with an improvement in RV cardiac output and effective stroke volume, indicating an improvement in RV systolic function; however, there was no significant change in RV ejection fraction (EF). Sixty-four percent of the cohort (7 of 11) had a PR fraction >20% (moderate or severe PR) before implant and a significant reduction in the

Table 3. Catheterization Data (n = 28)

	Before PPVI	After PPVI	p Value
RV-PA gradient (mm Hg)	36 ± 15	12 ± 7	<0.001
RVSp (mm Hg)	61 ± 16	41 ± 11	<0.001
RVDp (mm Hg)	11 ± 5	10 ± 4	0.04
MPAPs (mm Hg)	26 ± 8	30 ± 9	0.02
MPAPd (mm Hg)	11 ± 4	15 ± 5	0.003
AoPs (mm Hg)	86 ± 10	94 ± 11	0.001
AoPd (mm Hg)	56 ± 7	61 ± 8	0.001
RV/Ao ()	70 ± 16	44 ± 11	<0.001

AoPs = aortic pressure systolic; AoPd = aortic pressure diastolic; AoPm = aortic pressure mean; MPAPd = main pulmonary artery pressure (diastolic); MPAPm = main pulmonary artery pressure (mean); MPAPs = main pulmonary artery pressure (systolic); RVSp = right ventricular systolic pressure; RVDp = right ventricular diastolic pressure; RV/Ao = right ventricular to aortic pressure ratio; other abbreviations as in Table 2.

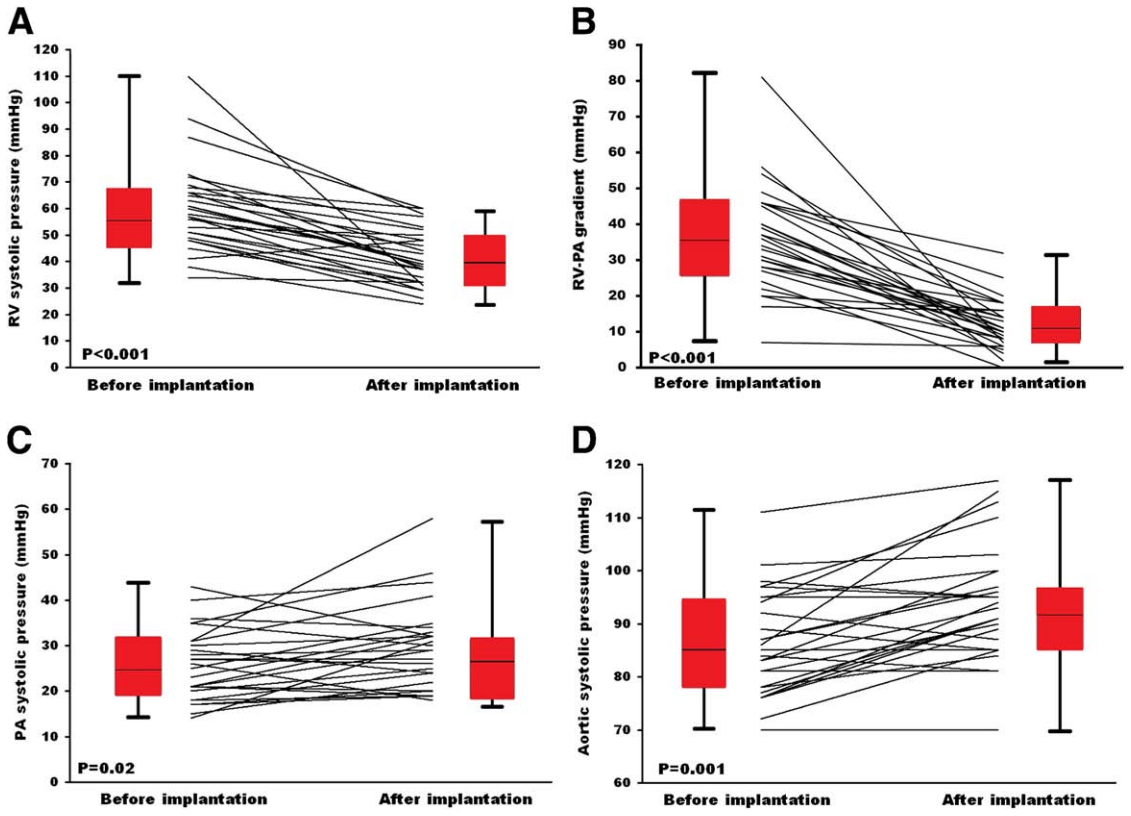

Figure 2. Catheterization Hemodynamic Data Before and After PPVI

Plots (**bold lines** = mean; **red boxes** = ±SD; upper and lower limits). **(A)** Right ventricle (RV) systolic pressure; **(B)** RV to pulmonary artery (PA) gradient; **(C)** PA systolic pressure; and **(D)** aorta systolic pressure before and after percutaneous pulmonary valve implantation (PPVI).

PR fraction after implant. Five remained with detectable PR, of which 80% (4 of 5) had RVOT reconstruction with Hancock valve or conduit. Analysis of LV systolic indexes documented a significant increase in left ventricular end-diastolic volume (LVEDV), LV stroke volume, and LV cardiac output but no change in LVEF. The ratio of RVEDV/LVEDV improved.

Exercise capacity. Twenty-four of the group (86%) underwent cardiopulmonary exercise testing before implantation, and 19 underwent cardiopulmonary exercise testing after (median 6 months; range 1 to 26 months) implantation (Table 6). There was a significant improvement in oxygen consumption at peak exercise and workload, with no significant change in anaerobic threshold. The VE/VCO_2 improved; however, a normal level (31 ± 5) was not achieved, where there remained a significant difference between matched control subjects and the cohort after the implant.

Clinical follow-up. Follow-up ranged from 0 to 37 months (median 27.6 months). There was no mortality, and freedom from reoperation was 91%, 83%, and 83% at 12, 24, and 36 months, respectively (Fig. 5). In 1 child, the implant was positioned within a bare-metal stent, placed to reinforce the conduit that abutted the sternum. Compression, stent fracture (both bare-metal and Melody valve), and recurrent

Table 4. Follow-Up Echocardiographic Assessment

	Before PPVI	After PPVI	1 Month	3 Months	6 Months	12 Months	24 Months	36 Months	p Value
RV–PA gradient (mm Hg)	67 ± 23	41 ± 16	36 ± 11	34 ± 11	32 ± 12	32 ± 11	36 ± 16	31 ± 5	<0.001
RVSp (mm Hg)	78 ± 22	58 ± 17	56 ± 8	58 ± 19	54 ± 14	53 ± 12	56 ± 13	54 ± 11	<0.001
RV/Ao ratio (%)	75 ± 16	54 ± 13	52 ± 7	53 ± 17	50 ± 13	48 ± 9	50 ± 9	44 ± 7	<0.001
Patients (n)	28	24	24	21	21	16	13	3	

Abbreviations as in Table 3.

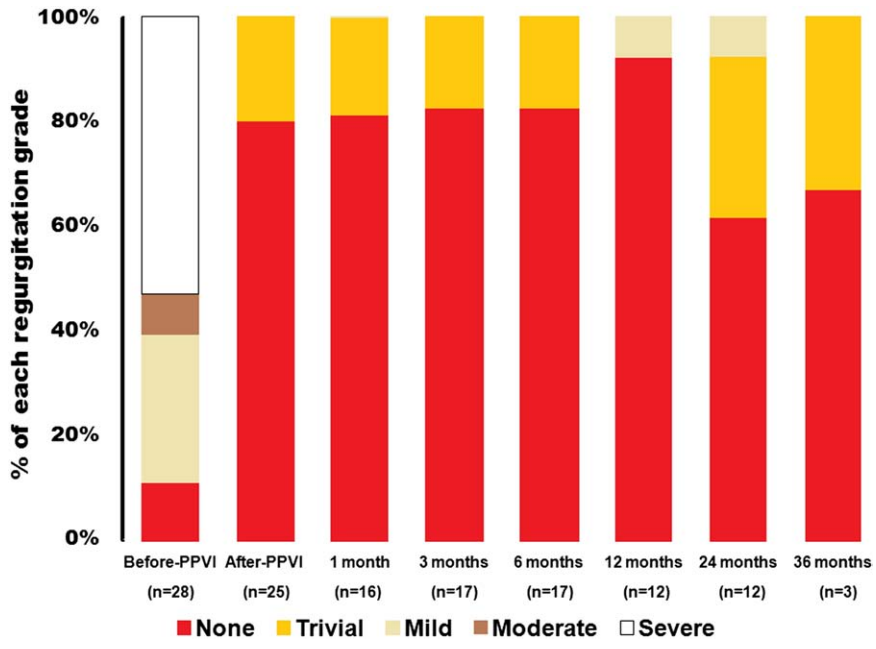

Figure 3. Pulmonary Valve Competence at Follow-Up by Echocardiography

PPVI = percutaneous pulmonary valve implantation.

stenosis were noted 3 months after the procedure. A small component of the bare-metal stent embolized to the left pulmonary artery without obstruction, whereas the Melody valve remained competent; the child subsequently underwent elective surgical repair. A second child, after repair of a persistent arterial trunk had valve implantation due to conduit stenosis and RV hypertension. The child subsequently underwent stenting of the branch pulmonary arteries; however, they remained obstructive, and additional balloon dilation did not improve the hemodynamic status (RV hypertension). As a result, the child underwent conduit replacement with bilateral pulmonary arterioplasties. There were no additional device-related complications noted in follow-up.

Table 5. MRI Volumetric Data (n = 14)

	Before PPVI	After PPVI	p Value
RVEDV (ml/m^2)	149 ± 49	114 ± 35	0.005
RVESV (ml/m^2)	85 ± 48	63 ± 29	0.005
RV effSV (ml/m^2)	44 ± 12	48 ± 8	0.04
RVEF (%)	42 ± 15	46 ± 13	0.43
RV CO (l/min)	2.7 ± 0.5	3.4 ± 0.8	0.04
LVEDV (ml/m^2)	90 ± 19	97 ± 20	0.007
LVESV	37 ± 10	39 ± 11	0.6
LV effSV (ml/m^2)	50 ± 13	57 ± 14	0.02
LVEF (%)	56 ± 9	60 ± 7	0.24
LV CO	2.7 ± 0.6	3.2 ± 0.6	0.02
RV/LVEDV	1.75 ± 0.5	1.24 ± 0.27	0.001
PR (%)	24 ± 10	7 ± 7	<0.0001

effSV = effective forward flow stroke volume; LV CO = left ventricular cardiac output; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricle ejection fraction; LVESV = left ventricular end-systolic volume; LVSV = left ventricular stroke volume; MRI = magnetic resonance image; RVEDV = right ventricular end-diastolic volume; RV CO = right ventricular cardiac output; RVEF = right ventricle ejection fraction; RVESV = right ventricular end-systolic volume; RVSV = right ventricular stroke volume; other abbreviations as in Table 2.

Freedom from transcatheter reintervention was 91%, 80%, and 80%, at 12, 24, and 36 months, respectively (Fig. 5). Balloon dilation of the implant (n = 5) was performed an average of 14.5 ± 9 months (range 3.9 to 23.7 months) after the index procedure. Indications for intervention included RV-to-pulmonary artery gradient of >60 mm Hg and/or an elevated RV systolic pressure/aortic ratio (>0.7) by echocardiography. The etiology of the recurrent obstruction was most often due to initial underdeployment. At catheterization the RV-to-pulmonary artery gradient was 40 ± 21 mm Hg, and RV systolic pressure/aortic ratio was 72 ± 21%. After balloon dilation, the gradient fell to 28 ± 21 mm Hg ($p < 0.001$), and RV systolic/aortic pressure ratio was 62 ± 24% ($p < 0.01$). The incidence of stent fracture was 10.7% (n = 3), from a review of digital radiographic images an average of 7.5 months (range: 1 day to 2.8 years) after implantation. None of the 5 catheter-reintervened patients had stent fractures.

Echocardiographic follow-up. Median follow-up was 27.6 months, with serial studies available for review: 21 (75%) studied at 6 months after the index procedure, 16 (57%)

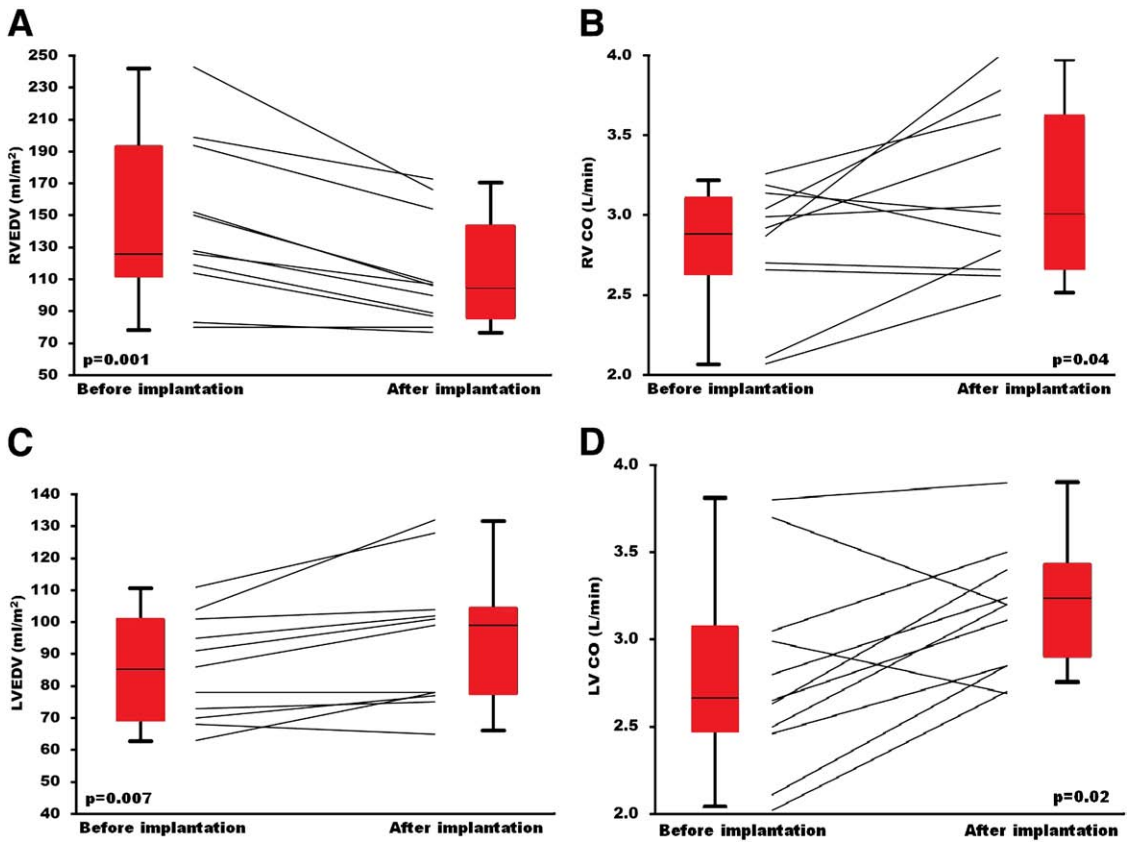

Figure 4. MRI Ventricular Volume Parameters Before and After Pulmonary Valve Implantation

Plots (**bold lines** = mean; **red boxes** = ±SD; upper and lower limits). **(A)** Right ventricular end-diastolic volume (RVEDV); **(B)** right ventricular (RV) cardiac output (CO); **(C)** left ventricular end-diastolic volume (LVEDV); and **(D)** left ventricular (LV) CO. MRI = magnetic resonance image.

studied at 24 months, and 3 (11%) studied at 36 months after the procedure. Reductions in RV-to-pulmonary artery gradient, RV systolic pressure, and RV/systemic pressure ratio (Table 4) were preserved throughout the follow-up. At 24 months, only 1 child had moderate PI (grade 3), whereas 62% had no PR, and 31% had trivial PR (Fig. 3). The RV end-diastolic dimensions (expressed as *z*-scores) were improved on the 6-month follow-up study (before PPVI: 2.8 [range 0.0 to 5.9] to 1.3 [range −2.5 to 5.3], $p < 0.001$) reflecting RV reverse remodeling.

Table 6. Cardiopulmonary Exercise Test

	Before PPVI (n = 24)	After PPVI (n = 14)	p Value
Peak VO_2 (ml/kg/min)	24 ± 5	28 ± 4	<0.0001
VO_2 AT (ml/kg/min)	18 ± 3	20 ± 3	<0.07
% predicted VO_2	55 ± 12	63 ± 11	<0.0002
VE/VCO_2	39 ± 5	36 ± 5	<0.003
Workload (W)	86 ± 15	99 ± 25	<0.003
Peak HR (beats/min)	167 ± 24	171 ± 21	<0.40
RR	51 ± 11	55 ± 8	<0.13
RER	1.13 ± 0.09	1.19 ± 0.09	<0.20

HR = heart rate; RER = respiratory exchange ratio; RR = respiratory rate; VE/VCO_2 = ventilatory response to carbon dioxide production; VO_2 = oxygen consumption; VO_2 AT = oxygen consumption at anaerobic threshold.

Discussion

We report our experience with 28 adolescents who underwent percutaneous pulmonary valve implantation. This is the largest and longest single-centre experience described in North America to date and constitutes the youngest group reported. Unique to this report is the outcomes in a pediatric population with very dilated RVs (RVEDV >140 ml/m^2). We have shown that PPVI is an effective and safe treatment for RVOT dysfunction, which can be achieved with minimal complications and no mortality. Additionally in this study, most patients (57%, 16 of 28) had the Melody valve implanted within a bioprosthetic valve, in contrast to the previous reports (13). In this regard, the incidence of stent fracture (10%) as compared with the previously reported

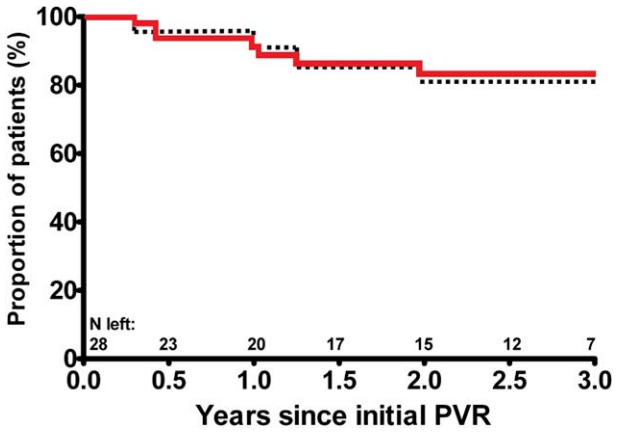

Figure 5. Freedom From Reoperation or Reintervention

Freedom from reoperation **(solid red line)** or reintervention **(dashed black line)**. PVR = pulmonary valve replacement.

20% (16–18) might be explained by better stability within the valve-in-valve implant.

There was a significant decrease, acutely, in RV hypertension, relief of outflow obstruction, and near-elimination of regurgitation, in both stenotic and mixed lesion groups. The longevity of the hemodynamic improvements is critical to determine whether this therapy will have an impact on clinical course. In this regard, follow-up echocardiographic data demonstrated sustained reduction in RV-to-pulmonary artery gradients and RV pressures in those with pressure-overloaded and/or volume-loaded ventricles. Furthermore, we observed a sustained decrease in RVED dimensions throughout the follow-up.

The RVEDV and right ventricular end-systolic volume improved significantly; however, they did not normalize to the same degree as found in the patients after surgical RVOT reconstruction (19). As such, surgical populations tend to address predominantly volume-overloaded ventricles due to PR, whereas our cohort had a predominantly mixed lesion (both pulmonary stenosis and PR). Furthermore, the MRI follow-up in our study, performed at 6 months after PPVI, assessed the ventricle at a time when complete remodeling might not be fully manifest. In contrast to other PPVI studies (14), this young population demonstrated a significant reduction (24% change) in RV volumes, in very large chambers (on average 50 ml/m^2 larger then reported in prior PPVI studies), underscoring that significant reverse remodeling can be obtained if performed early in the clinical course (19). Additionally noted was an improvement in RV cardiac output without a change in RVEF. This is consistent with earlier studies in PPVI populations where improvement in RVEF was seen only in the patients with primary RV obstruction and minimal PR (13,20,21) but not in the PR group or combined cohort of mixed lesions (stenosis and regurgitation). Similar surgical series have also noted that valve implantation causes little improvement in RVEF (22–26). The effects of severe PR on RV function in patients with RVOT obstruction (by cardiac MRI) also result in an elevated RVEDV and reduced RVEF (27), with RVEF lower in patients with both RV pressure and volume overload when compared with pressure-overloaded RV alone (27). These observations reflect interplay among chronic volume overload, myocardial stretch, decreased contractile reserve, and fibrosis.

The RVEF on cardiac MRI study in our population revealed no significant change in EF with an increase in RV stroke volume, which reflected a reduction in PR. The effective stroke volume (stroke volume minus pulmonary regurgitant volume) improvement reflected the improvement in RV cardiac output and therefore overall RV performance, not requiring an increase in EF in this young population with predominantly regurgitant or mixed lesions.

After valve implantation and relief of RVOT obstruction, there was a concomitant improvement in LV performance: LVEDV, LV stroke volume, and LV cardiac output significantly increased. These improvements in function correlated with improvements in maximal exercise capacity, as previously noted in other PPVI series (13,21), with exception of patients with volume-overloaded ventricles (21). In contrast, surgical series show minimal improvements (24,28) or no improvement (19) in exercise capacity. We postulate that the improvement in maximal oxygen consumption in our population is a consequence of increased LV size due to decreased RV volumes and improvement in LV cardiac output after relief of RV regurgitation. This could be manifest due to the shorter exposure of the ventricle to altered loading conditions. Furthermore, this observation suggests that earlier intervention on patients with conduit dysfunction can normalize ventricular function and exercise capacity.

The improvement in VE/VCO_2 reflects improved pulmonary perfusion due to an increase in RV forward flow. As a predictor of mortality and morbidity in patients with congenital heart disease (29,30), these findings are most encouraging. Although we observed an improvement in VE/VCO_2, when compared with age- and sex-matched control subjects, the improvement after 6 months was not into the normal range. The question of whether further improvement in VE/VCO_2 is possible will require longer-term study.

It has been suggested in previous reports that the increase in LVEDV and reduction in RVEDV, as noted in this study after implantation, leads to clinical improvement related to improved diastolic chamber interactions (31), an increase in LV preload, increased stroke volume, and subsequently cardiac output. Furthermore, abnormalities of LV diastolic function have been reported as important determinants of exercise intolerance (32). Intervention in

this age group demonstrated an improvement of LV indexes and exercise tolerance, reflected by improvements in the RVEDV/LVEDV ratio after implantation (1.75 to 1.25, normal 1.15), reflecting a shift toward normalization in ventricular interaction.

Study limitations. Although we have reported immediate benefits of PPVI with early-term follow-up, longer-term studies will be needed to determine longevity of the percutaneous valve compared with surgical interventions. In our cohort, there was no mortality, and the rate of re-intervention and reoperation was minimal despite the impact of a learning curve. The subjects suffered from complex lesions with multiple previous operations on the RVOT, heterogeneous in terms of diagnosis and RVOT morphologies. Most were younger than 20 years of age (median age 14.9 years) and had very dilated RVs, making the cohort homogenous with regard to age. A comparison with groups of children with less-dilated RVs would be needed to evaluate the potential for RV reverse remodeling and sustainability of symptomatic relief. Cardiopulmonary exercise testing could not be obtained in the entire cohort. Cardiac MRI was not performed in all before PPVI. In those patients with previous RVOT stent, MRI was not optimal due to image distortion. Echocardiographic indexes of diastolic function were not obtained, making more detailed assessment unavailable.

Conclusions

In summary, these data describe a unique population of adolescents with significantly enlarged RV chambers, poor exercise performance, and dysfunctional conduits who underwent PPVI. The RV chamber dimensions decreased, exercise performance improved, and LV chamber dimensions and cardiac output improved. This unique series of observations supports earlier studies, which suggest that regurgitation and/or outflow tract obstruction should be addressed early, with excellent immediate and early-term clinical and hemodynamic outcomes.

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Key Words: pulmonary insufficiency ■ pulmonary stenosis ■ pulmonary valve implant ■ right ventricular outflow tract obstruction ■ tetralogy of Fallot.