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Physiological and Clinical Consequences of Relief of Right Ventricular Outflow Tract Obstruction Late After Repair of Congenital Heart Defects

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Background—Right ventricular outflow tract obstruction (RVOTO) is a common problem after repair of congenital heart disease. Percutaneous pulmonary valve implantation (PPVI) can treat this condition without consequent pulmonary regurgitation or cardiopulmonary bypass. Our aim was to investigate the clinical and physiological response to relieving RVOTO.

Methods and Results—We studied 18 patients who underwent PPVI for RVOTO (72% male, median age 20 years) from a total of 93 who had this procedure for various indications. All had a right ventricular outflow tract (RVOT) gradient >50 mm Hg on echocardiography without important pulmonary regurgitation (less than mild or regurgitant fraction <10% on magnetic resonance imaging [MRI]). Cardiopulmonary exercise testing, tissue Doppler echocardiography, and MRI were performed before and within 50 days of PPVI. PPVI reduced RVOT gradient (51.4 to 21.7 mm Hg, $P<0.001$) and right ventricular systolic pressure (72.8 to 47.3 mm Hg, $P<0.001$) at catheterization. Symptoms and aerobic (25.7 to 28.9 mL · kg^{-1} · min^{-1}, $P=0.002$) and anaerobic (14.4 to 16.2 mL · kg^{-1} · min^{-1}, $P=0.002$) exercise capacity improved. Myocardial systolic velocity improved acutely (tricuspid 4.8 to 5.3 cm/s, $P=0.05$; mitral 4.7 to 5.5 cm/s, $P=0.01$), whereas isovolumic acceleration was unchanged. The tricuspid annular velocity was not maintained on intermediate follow-up. Right ventricular end-diastolic volume (99.9 to 89.7 mL/m^2, $P<0.001$) fell, whereas effective stroke volume (43.7 to 48.3 mL/m^2, $P=0.06$) and ejection fraction (48.0% to 56.8%, $P=0.01$) increased. Left ventricular end-diastolic volume (72.5 to 77.4 mL/m^2, $P=0.145$), stroke volume (45.3 to 50.6 mL/m^2, $P=0.02$), and ejection fraction (62.6% to 65.8%, $P=0.03$) increased.

Conclusions—PPVI relieves RVOTO, which leads to an early improvement in biventricular performance. Furthermore, it reduces symptoms and improves exercise tolerance. These findings have important implications for the management of this increasingly common condition. **(*Circulation*. 2006;113:2037-2044.)**

Key Words: congenital heart defects ■ catheterization ■ echocardiography ■ magnetic resonance imaging ■ valves

Right ventricular outflow tract obstruction (RVOTO) is a common problem in patients with repaired congenital heart disease, particularly in the setting of homograft valve degeneration or after the arterial switch operation.[1–3] Despite widespread belief that pulmonary stenosis is well tolerated,[4] it has been demonstrated that relief of acquired RVOTO with a bare stent reduces right ventricular systolic pressure, improves symptoms, and may defer reoperation, albeit with the consequence of pulmonary regurgitation.[5–7] This, however, is of concern, because recent evidence has shown detrimental effects on right ventricular function, exercise capacity, and arrhythmia potential with long-standing pulmonary regurgitation.[8–10]

Clinical Perspective p 2044

Percutaneous pulmonary valve implantation (PPVI) provides a potentially superior catheter-based treatment option to bare stenting (Figures 1 and 2), because relief of stenosis is not replaced with regurgitation when the valve is trapped.[11] Moreover, it provides a unique model to study the impact of chronic RVOTO on ventricular function and its potential for recovery, without the confounding effects of cardiac surgery and pulmonary incompetence. The purpose of the present study was to investigate, for the first time, the early clinical and physiological response to relief of chronic RVOTO late after repair of a range of complex congenital cardiac malformations.

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Figure 1. The percutaneous pulmonary valve (NuMed, Hopkinton, NY).

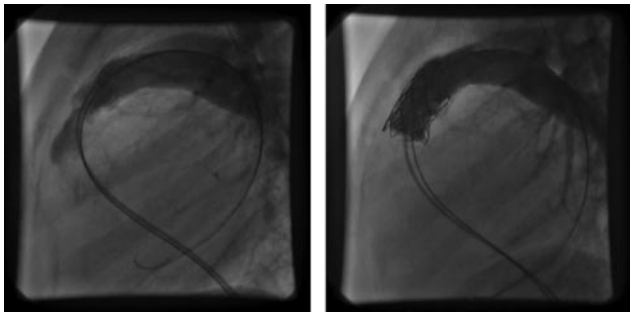

Figure 2. Lateral angiogram before (A) and after (B) PPVI in a stenosed RVOT.

Methods

Study Population

Between September 2000 and July 2005, we performed PPVI in 93 patients. All patients had a conventional surgical indication for revision of their right ventricular outflow tracts (RVOTs) to treat either a regurgitant, stenosed, or mixed lesion.[12] Suitability for PPVI required outflow tract anatomy with a potential device implantation site that had a diameter of ≤22 mm. The patients referred for this procedure represented the more severe end of the spectrum, with a median of 3 prior operations (range 1 to 5). From this population, we selected patients with isolated RVOTO (peak RVOT gradient >50 mm Hg on echocardiography). Patients who had evidence of a pulmonary regurgitant fraction >10% on MRI (n=51) or, if MRI was not performed, more than mild pulmonary regurgitation on transthoracic echocardiography (n=15) were excluded. Of a total of 27 eligible patients, 9 had a contraindication to or could not undergo MRI and were not included and therefore did not undergo formal assessment according to the research protocol. The remaining 18 patients are the subjects of the present study. None had branch pulmonary artery stenosis or significant intracardiac shunting. Assessment of New York Heart Association functional class, cardiopulmonary exercise testing, tissue Doppler echocardiography, and MRI were performed before and early after PPVI. Separate investigators performed the clinical assessment (SK), metabolic exercise testing (GD), tissue Doppler echocardiography (LC), and MRI (AT); all were blinded to the results of the other tests, with postprocessing performed in a random fashion with no prior knowledge of whether the examination was preintervention or postintervention. The local research ethics committees approved the study, and all subjects (and/or a parent/guardian) gave informed written consent.

TABLE 1. Patient Characteristics

Patient No.	Sex	Age, y	Diagnosis	Age at Repair, y	Outflow Tract	Previous Operations, n	NYHA Class
1	M	15	TOF	1	21-mm homograft	4	2
2*	M	16	TGA, PS, VSD	1	18-mm homograft	2	2
3*	M	38	AVD (Ross)	36	23-mm homograft	3	2
4*	M	19	PA/VSD	4	18-mm homograft	3	2
5*	F	26	TOF	4	22-mm homograft	4	3
6	M	9	Truncus	0	23-mm homograft	2	2
7*	M	10	Truncus	1	19-mm homograft	2	2
8*	M	20	TGA, PS, VSD	10	20-mm homograft	2	1
9	M	20	PA/VSD	0	25-mm homograft	2	2
10*	F	25	AVD (Ross)	6	Homograft (unknown)	3	2
11*	M	28	TOF	4	23-mm homograft	2	2
12	F	51	TOF	1	25-mm homograft	3	2
13*	M	9	TGA	0	Native	1	2
14	M	16	TOF	2	19-mm Homograft	2	2
15	F	35	PA/VSD	21	Homograft (unknown)	3	2
16	M	16	TOF	0	24-mm homograft	5	3
17	M	25	PA/VSD	0	22-mm homograft	3	2
18*	M	20	AVD (Ross)	12	Homograft (unknown)	3	3

NYHA indicates New York Heart Association; M, male; F, female; TOF, tetralogy of Fallot; TGA, VSD, PS, transposition of the great arteries with ventricular septal defect and pulmonary stenosis; AVD (Ross), aortic valve disease treated with the Ross operation; PA/VSD, pulmonary atresia and ventricular septal defect; and TGA, simple transposition of the great arteries.

*These patients returned to our centers for echocardiographic follow-up.

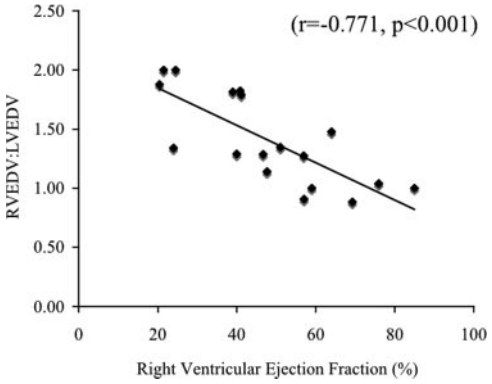

Figure 3. Relationship between RVEDV:LVEDV ratio and right ventricular ejection fraction at baseline assessed by MRI.

Invasive Pressure Monitoring

PPVI was performed under general anesthesia as described previously.[11] One patient had an additional bare stent placed in the main pulmonary artery. Right ventricular systolic and end-diastolic pressure and pulmonary artery systolic and diastolic pressure (beyond the obstruction) were measured before and after PPVI.

Cardiopulmonary Exercise Testing

Cardiopulmonary exercise testing was performed on a bicycle ergometer (Sensormedics Ergoline 800, Blitz, Germany) with respiratory gas exchange analysis before PPVI and at a median of 20 days (range 3 to 42 days) after PPVI. Work rate was increased with a ramp protocol. A 12-lead ECG was monitored continuously and blood pressure recorded every 2 minutes during exercise. Breath-by-breath respiratory gas exchange measurements were recorded throughout the test and averaged over a peak width of 20 seconds at the end of exercise to determine maximum values. Anaerobic threshold was determined by the modified V-slope method.[13]

Conventional and Tissue Doppler Echocardiography

Transthoracic imaging of the heart was performed with a Vivid 7 (GE Vingmed, Milwaukee, Wis) with a transducer frequency of 3.5 MHz before PPVI and at a median of 1 day (range 1 to 4 days) after PPVI. A subset of the studied population (n=10) who were able to return to our institutions for follow-up underwent further detailed imaging at 1 and 3 months. These patients are indicated in Table 1. Right ventricular systolic pressure was calculated from the continuous-wave Doppler profile of the tricuspid regurgitation jet,[14] and peak RVOT gradient was calculated in the same way from the signal across the RVOT. Right ventricular wall thickness was measured in the parasternal long-axis view to assess the presence of hypertrophy.[15] The right ventricular free wall and left ventricular lateral wall were imaged from the apical position during quiet breathing. Color-coded myocardial velocities of the tricuspid and mitral annulus were acquired with a mean frame rate of 166 ± 27 s^{-1}. A cineloop of 3 consecutive cardiac cycles was digitally stored for offline analysis with Echopac software (GE Vingmed, Milwaukee, Wis). Isovolumic acceleration, a relatively load independent parameter,[16,17] and peak myocardial velocity during systole (Sa), which has been demonstrated to correlate with ejection fraction,[18,19] were measured at the lateral tricuspid and mitral annuluses to assess global systolic function. Myocardial velocities during early diastole (Ea) and late diastole (Aa) were also measured. Tracking of the region of interest to myocardial motion was performed. Measurements were performed on 3 consecutive cardiac cycles, and the average of these values was calculated.

Magnetic Resonance Imaging

MRI was performed at 1.5 T (Symphony Maestro Series; Siemens Medical Systems, Erlangen, Germany) before PPVI and at a median of 6 days (range 1 to 50 days) after PPVI. Retrospective gated steady-state free-precession cine magnetic resonance images of the heart were acquired in the vertical long-axis, 4-chamber view, short-axis views that included the extent of both ventricles (9 to 12 slices), and 2 long-axis planes of the RVOT and left ventricular outflow tract for positioning of through-plane flow quantification.[20] Images were acquired during a single breath-hold. The cine SSFP sequence parameters were as follows: repetition time 2.8 ms, echo time 1.4 ms, flip angle 51°, slice thickness 8 mm, matrix 192×256, field of view 300 to 380 mm, and temporal resolution 25 to 40 phases.

Assessment of right ventricular and left ventricular volumes was performed by manually defining the endocardial outline at end diastole and end systole in each of the short-axis cine images (Argus; Siemens Medical Systems, Erlangen, Germany). The end-diastolic volume and end-systolic volume were calculated with Simpson's rule for each ventricle, and from these volumes, the stroke volume and ejection fraction were derived.

Pulmonary artery flow data were acquired with a flow-sensitive gradient echo sequence (repetition time 8 ms, echo time 3.8 ms, flip angle 30°, slice thickness 6 mm, matrix 256×256) during free breathing. A phase-correction filter was used to correct for phase errors introduced by eddy currents and Maxwell terms. Image planes were located at the midpoint of the pulmonary trunk/conduit before PPVI and just above the stent after PPVI, to avoid stent artifact. Through-plane flow data (40 phases per cardiac cycle) was acquired with retrospective cardiac gating. The velocity-encoded peak velocity was varied according to the degree of pulmonary trunk/homograft stenosis. Pulmonary flow was calculated from the phase-contrast images with a semiautomatic vessel edge-detection algorithm with

TABLE 2. Characteristics of Excluded Patients

Patient No.	Sex	Age, y	Diagnosis	Age at Repair, y	Outflow Tract	Previous Operations, n	NYHA Class
1	M	13	PA/VSD	4	Carpentier-Edwards	3	2
2	M	10	PA/VSD	6	Hancock	4	1
3	M	11	APV	1	Carpentier-Edwards	3	1
4	M	38	AVD (Ross)	36	Homograft	2	2
5	M	18	AVD (Ross)	17	Homograft	2	3
6	F	13	PA/VSD	0	Hancock	3	3
7	M	11	Aortic atresia	0	Homograft	1	2
8	F	14	TGA, VSD, PS	3	Homograft	2	2
9	M	25	PA/VSD	0	Homograft	3	2

M indicates male; F, female; PA/VSD, pulmonary atresia and ventricular septal defect; APV, absent pulmonary valve syndrome; AVD (Ross), aortic valve disease treated with the Ross operation; and TGA, VSD, PS, transposition of the great arteries with ventricular septal defect and pulmonary stenosis.

TABLE 3. Pressures at Catheterization

Parameter	Pre-PPVI	Post-PPVI	*P*
Right ventricular systolic pressure, mm Hg	72.8±18.2	47.3±9.6	<0.001
Right ventricular end diastolic pressure, mm Hg	11.3±4.4	9.6±4.3	0.04
Pulmonary artery systolic pressure, mm Hg	21.4±6.2	25.7±8.5	0.04
Pulmonary artery diastolic pressure, mm Hg	10.8±3.6	11.9±8.6	0.16
RV to PA pullback gradient, mm Hg	51.4±21.1	21.7±8.9	<0.001

RV indicates right ventricle; PA, pulmonary artery.

operator correction. Regurgitant fraction was calculated as the percent backward flow over forward flow. All volume and flow measurements were indexed for body surface area and expressed in mL/m^2.

Statistical Analysis

All parametric data are expressed as mean±SD, and comparisons before and after PPVI were made with a paired Student *t* test. Nonparametric data were summarized with the median and compared before and after PPVI with the Mann-Whitney *U* test. Correlation between parametric variables was assessed with Pearson's test. Statistical significance was inferred when $P<0.05$. All statistical testing and data analysis were performed with SPSS version 11 (SPSS Inc, Chicago, Ill).

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Baseline Characteristics

Study Population

We studied 18 patients (72% male; median age 20 years [range 9 to 51 years]; 56% with tetralogy of Fallot or subtype; Table 1) with late RVOTO. The mean right ventricular wall thickness was 6.3±1.0 mm, which indicates the presence of right ventricular hypertrophy according to published normal values[15] (normal value ≤5 mm). The ratio of right ventricular end-diastolic volume (RVEDV) to left ventricular end-diastolic volume (LVEDV) assessed by MRI was increased at 1.41±0.39, which indicates the presence of relative right ventricular dilatation[21] (normal value=1.15). A strong negative correlation was seen between right ventricular ejection fraction and the RVEDV:LVEDV ratio ($r=-0.771$, $P<0.001$; Figure 3). Isovolumic acceleration at the tricuspid annulus was 0.94±0.32 m/s^2 and was reduced compared with published data in normal individuals with a comparable age distribution (normal value=1.8 m/s^2).[16,22]

Excluded Patients

Nine patients were not included in the present study protocol because they were unable to undergo magnetic resonance scanning (5 patients formed part of the initial feasibility series[23] that did not undergo MRI, 2 had arrhythmia that precluded useful imaging, and 2 patients would have required general anesthesia, which was not part of our imaging protocol). The characteristics of these 9 patients are shown in Table 2.

Invasive Pressure Monitoring

PPVI was performed successfully in all subjects (procedure time 77.6±38.3 minutes, fluoroscopy time 12.9±8.2 minutes). After valve implantation, right ventricular systolic pressure (from 72.8±18.2 to 47.3±9.6 mm Hg, $P<0.001$) and right ventricular end-diastolic pressure (from 11.3±4.4 to 9.6±4.3 mm Hg, $P=0.04$) fell. Pulmonary artery systolic pressure increased (from 21.4±6.2 to 25.7±8.5 mm Hg,

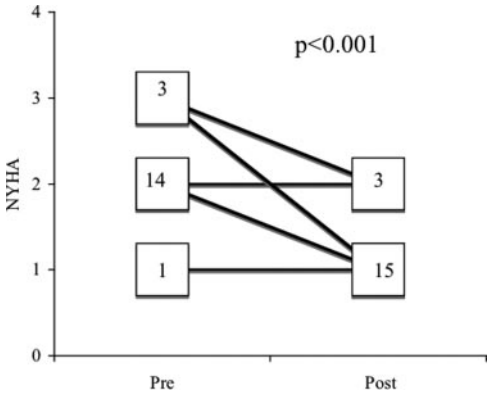

Figure 4. Change in New York Heart Association (NYHA) functional class before and 1 month after relief of RVOT obstruction with PPVI.

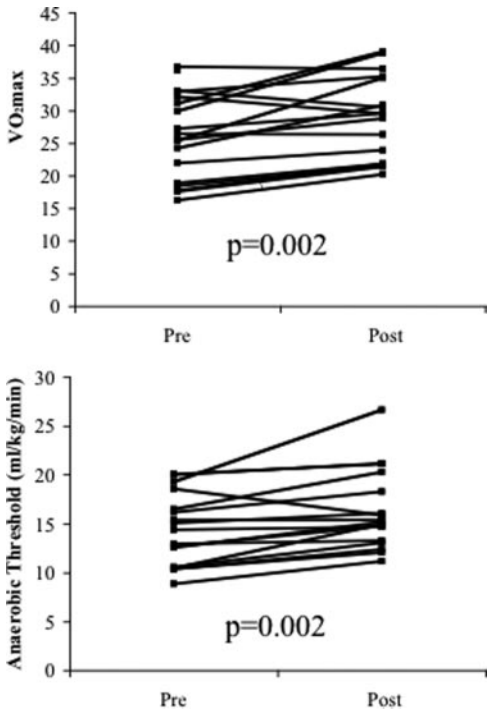

Figure 5. $\dot{V}O_2$max (A) and anaerobic threshold (B) before and after PPVI.

TABLE 4. Cardiopulmonary Exercise Testing

Parameter	Pre-PPVI	Post-PPVI	*P*
Peak $\dot{V}o_2$, mL · kg^{-1} · min^{-1}	25.7±6.4	28.9±6.4	0.002
Anaerobic threshold, mL · kg^{-1} · min^{-1}	14.4±3.6	16.2±3.9	0.002
Workload, W	131.5±42.8	145.9±45.4	0.015
Peak heart rate, bpm	159.5±25.0	165.9±16.7	0.170
Peak systolic blood pressure, mm Hg	143.6±21.7	152.4±21.9	0.05
Respiratory exchange ratio	1.15±0.14	1.16±0.16	0.622

$P<0.001$) and RVOT gradient fell (from 51.4±21.1 to 21.7±8.9 mm Hg, $P<0.001$). Pressures are summarized in Table 3. The 9 patients excluded from this analysis demonstrated similar pressure changes after PPVI (right ventricular systolic pressure decreased from 71.4±13.2 to 49.8±16.2 mm Hg, $P=0.003$; right ventricular end-diastolic pressure decreased from 13.1±5.2 to 11.9±3.1 mm Hg, $P=0.329$; pulmonary artery systolic pressure increased from 20.4±8.8 to 26.1±5.4 mm Hg, $P=0.025$; and pulmonary artery diastolic pressure increased from 8.4±2.6 to 13.2±8.9 mm Hg, $P=0.002$).

New York Heart Association Class

New York Heart Association class fell from a median of 2 to 1 ($P<0.001$) 1 month after PPVI (Figure 4).

Cardiopulmonary Exercise Testing

Seventeen of 18 patients completed maximal exercise tests (1 patient had a viral infection after PPVI and was excluded from the analysis). After PPVI, there was a marked improvement in peak $\dot{V}o_2$ (from 25.7±6.4 to 28.9±6.4 mL · kg^{-1} · min^{-1}, $P=0.002$; Figure 5) and in anaerobic threshold (from 14.4±3.6 to 16.2±3.9 mL · kg^{-1} · min^{-1}, $P=0.002$; Figure 5). The workload achieved also increased significantly (from 131.5±42.8 to 145.9±45.4 W, $P=0.015$). Exercise parameters are summarized in Table 4.

Conventional and Tissue Doppler Echocardiography

There was a significant fall in right ventricular systolic pressure (from 84.9±17.5 to 50.7±14.4 mm Hg, $P<0.001$) and in RVOT gradient (from 85.2±19.0 to 41.1±12.3 mm Hg, $P<0.001$) after PPVI. In the subset of patients who were studied at 1 and 3 months, these findings were sustained (Figure 6). The discrepancy between echocardiographic and catheter measurements of RVOT pressure gradients are likely to reflect both the conscious state of the patient and the technical differences between the 2 techniques.[24] Peak systolic velocity improved acutely at both the tricuspid annulus (from 4.8±1.1 to 5.3±1.1 cm/s, $P=0.05$) and the mitral annulus (from 4.7±1.5 to 5.5±1.8 cm/s, $P=0.01$). Isovolumic acceleration did not change significantly at the tricuspid annulus (from 0.94±0.32 to 1.0±0.48 m/s^2, $P=0.482$) or the mitral annulus (from 0.94±0.41 to 0.98±0.35 m/s^2, $P=0.673$). Diastolic velocities showed no change, with the exception of peak late diastolic velocity (Aa) at the tricuspid annulus, which fell (from −4.6±−1.9 to −4.0±−1.5 cm/s, $P=0.03$). In the subset of patients who were studied at 1 and 3 months after PPVI, the increase in systolic velocity at the mitral annulus tended to remain elevated, whereas

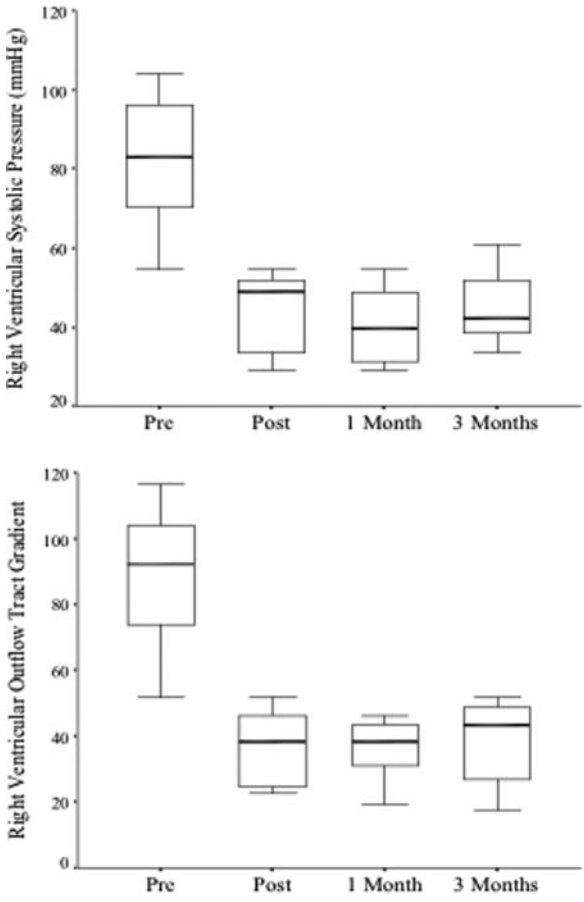

Figure 6. Right ventricular systolic pressure and RVOT gradient, measured echocardiographically, at 1 and 3 months in a subset of patients (n=10) after PPVI.

at the tricuspid annulus, it appeared transient. Diastolic parameters did not change. There was a negative correlation between baseline isovolumic acceleration at the tricuspid annulus and improvement in exercise capacity ($r=-0.57$, $P=0.02$; Figure 7). There was no significant change in heart rate before PPVI or during follow-up. Echocardiography parameters are summarized in Table 5 and Table 6.

Magnetic Resonance Imaging

Patient selection ensured that the pulmonary regurgitant fraction before PPVI was small, and this did not increase after

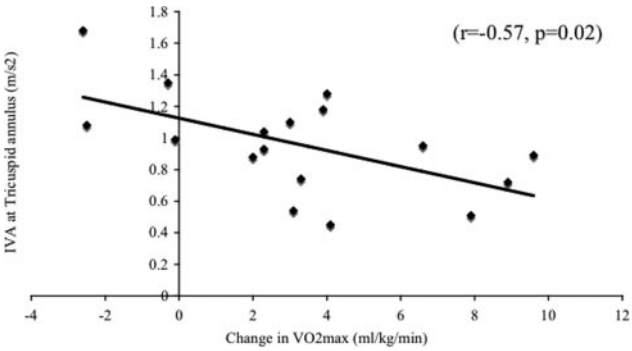

Figure 7. Relationship between isovolumic acceleration (IVA) at the tricuspid annulus and improvement in exercise capacity.

TABLE 5. Echocardiography Before and Immediately After PPVI

Parameter (n=18)	Pre-PPVI	Post-PPVI	*P*
Heart rate, bpm	68.3±12.8	69.1±10.6	0.806
RVSP, mm Hg	84.9±17.5	50.7±14.4	<0.001
Peak RVOT gradient, mm Hg	85.2±19.0	41.1±12.3	<0.001
Tricuspid Sa, cm/s	4.8±1.1	5.3±1.1	0.05
Tricuspid Ea, cm/s	−6.9±−1.8	−6.5±−1.6	0.180
Tricuspid Aa, cm/s	−4.6±−1.9	−4.0±−1.5	0.03
Tricuspid IVA, m/s^2	0.94±0.32	1.0±0.48	0.482
Mitral Sa, cm/s	4.7±1.5	5.5±1.8	0.01
Mitral Ea, cm/s	9.4±−3.6	−9.3±−5.3	0.865
Mitral Aa, cm/s	−3.7±−1.6	−3.7±−1.3	0.867
Mitral IVA, m/s^2	0.94±0.41	0.98±0.35	0.673

RVSP indicates right ventricular systolic pressure; Sa, peak systolic velocity; Ea, peak early diastolic velocity; Aa, peak late diastolic velocity; and IVA, isovolumic acceleration.

TABLE 7. Magnetic Resonance Imaging

Parameter	Pre-PPVI	Post-PPVI	*P*
PRF, %	3.6±3.9	1.4±2.5	0.06
RVEDV, mL/m^2	99.9±29.3	89.7±23.4	0.001
RVESV, mL/m^2	54.2±29.0	40.6±20.9	0.001
RVSV, mL/m^2	45.7±15.9	49.1±11.5	0.327
Eff RVSV, mL/m^2	43.7±13.8	48.3±11.0	0.06
RVEF, %	48.0±18.8	56.8±15.2	0.01
LVEDV, mL/m^2	72.5±15.8	77.4±14.1	0.145
LVESV, mL/m^2	27.1±8.9	26.6±10.2	0.799
LVSV, mL/m^2	45.3±12.2	50.6±11.2	0.02
LVEF, %	62.6±10.3	65.8±10.0	0.03
RVEDV/LVEDV	1.4±0.4	1.2±0.2	0.001

PRF indicates pulmonary regurgitant fraction; RVEDV/LVEDV, right/left ventricular end-diastolic volume; RVESV/LVESV, right/left ventricular end-systolic volume; RVSV/LVSV, right/left ventricular stroke volume; Eff RVSV, effective right ventricular stroke volume; and RVEF/LVEF, right/left ventricular ejection fraction.

valve implantation (from 3.6±3.9% to 1.4±2.5%, $P=0.06$). However, after PPVI, there was a significant reduction in right ventricular end-systolic volume (from 54.2±29.0 to 40.6±20.9 mL/m^2, $P=0.001$) and in RVEDV (from 99.9±29.3 to 89.7±23.4 mL/m^2, $P<0.001$). Effective right ventricular stroke volume increased, although the change did not quite reach statistical significance (from 43.7±13.8 to 48.3±11.0, mL/m^2, $P=0.06$). Right ventricular ejection fraction improved substantially (from 48.0±18.8% to 56.8±15.2%, $P=0.01$). LVEDV tended to increase (from 72.5±15.8 to 77.4±14.1 mL/m^2, $P=0.145$), and there was a significant improvement in left ventricular stroke volume (from 45.3±12.2 to 50.6±11.2 mL/m^2, $P=0.02$) and in left ventricular ejection fraction (from 62.6±10.3% to 65.8±10.0%, $P=0.03$). There was no significant change in heart rate, which indicates that cardiac output increased after PPVI. Magnetic resonance parameters are summarized in Table 7.

Discussion

The present study shows that relief of late RVOTO with PPVI in patients with complex congenital heart defects leads to an early improvement in symptoms, exercise tolerance, and ventricular function. The spectrum of abnormalities and their pattern of change suggest that the right ventricle, before PPVI, is in a decompensated state as a result of the increased afterload. When the abnormal loading conditions are relieved, improvement in biventricular performance occurs as the pressure-volume relationship of the right ventricle shifts back to the compensatory limb of the Frank-Starling curve. This clinical and functional benefit argues in favor of early treatment with PPVI, while right ventricular dysfunction is reversible.

Studies in patients with congenital pulmonary valvar stenosis who are treated with balloon pulmonary valvuloplasty have suggested that RVOTO is well-tolerated.[25–27] These findings, however, do not apply to acquired RVOTO in patients with complex congenital lesions, for whom this approach is not effective.[28,29] Furthermore, the impact of acquired RVOTO relief has been hard to study because of the confounding effect of cardiopulmonary bypass with surgery[30] or the inevitable pulmonary regurgitation that complicates the alternative treatment of bare-stent implantation.[5–7] PPVI permits, for the first time, investigation of the direct effects of relief of chronic right ventricular pressure overload on cardiac function in this increasingly common clinical situation.

The change in right ventricular performance after PPVI facilitates interpretation of the structure and function seen before intervention. We found the expected increase in right ventricular end-systolic volume, RVEDV, wall thickness, and end diastolic pressure, which are adaptive measures to maintain right ventricular stroke volume in the presence of increased afterload, whereas the reduced isovolumic acceleration reflected intrinsic myocardial impairment. However,

TABLE 6. Systolic Tissue Doppler Parameters at 1 and 3 Months in a Subset of Patients (n=10)

Parameter	Pre-PPVI	Post-PPVI	1-Month Follow-Up	3-Month Follow-Up
Heart rate, bpm	67.1±13.7	65.3±9.5	70.1±13.1	69.3±14.1
Tricuspid Sa, cm/s	4.8±0.5	5.4±1.0	4.8±0.5	5.2±1.2
Tricuspid IVA, m/s^2	0.89±0.21	0.97±0.52	0.81±0.26	0.94±0.37
Mitral Sa, cm/s	5.1±1.6	5.9±2.1	5.9±2.2	5.7±1.7
Mitral IVA, m/s^2	0.91±0.42	0.96±0.38	0.86±0.33	0.91±0.28

Sa indicates peak systolic velocity; IVA, isovolumic acceleration.

after PPVI, the increase in right ventricular stroke volume and ejection fraction that accompanied the reduction in right ventricular end-systolic volume, RVEDV, and end-diastolic pressure indicates that the observed adaptive mechanisms were only partially successful. Our interpretation is that relief of RVOTO, in this population, caused a shift back to the compensatory limb of the Frank-Starling curve by a ventricle that was "overstretched" and decompensated before intervention. The alternative explanation of an increase in stroke volume due to improved contractility is not supported by either the lack of change in isovolumic acceleration or the observed reduction in end-diastolic pressure. The improvement in systolic velocity at the tricuspid annulus is difficult to interpret in view of its response to both contractility and loading conditions, especially given the finding that this improvement was transient. Heart rate remained unchanged before and after PPVI and thus is unlikely to have played a role in the observed improvement.

The benefits of relief of RVOTO were also seen in the left ventricle: there was an increase in LVEDV, left ventricular stroke volume, and left ventricular ejection fraction, which disputes previous reports that right ventricular pressure overload does not affect left ventricular ejection fraction.[31] There are several potential explanations for this. One factor is likely to be an increase in left ventricular preload that results in increased diastolic myocardial stretch and thus stroke volume. This mechanism is supported by the increase in systolic velocity observed at the mitral annulus by tissue Doppler evaluation that was maintained at 3 months. Another potential contributor to improved left ventricular performance is restoration of more normal septal behavior as a result of unloading the right ventricle.[32] The strong correlation between right ventricular ejection fraction and relative ventricular size, before PPVI, underscores the importance of ventricular interaction in the determination of right ventricular performance. Finally, a third mechanism, an increase in intrinsic contractility, remains possible but is not supported by our isovolumic acceleration measurements, which did not change. A more detailed study of ventricular interaction is required to better understand this complex physiology. Importantly, the changes in right and left ventricular function were accompanied by improvement in both subjective and objective measures of symptoms and exercise performance.

The findings in the present study population are not necessarily applicable to other patients with RVOTO. It is possible that RVOTO may lead to irrecoverable myocardial dysfunction if baseline function is poor or exposure to obstruction is more prolonged. The association between hypertrophy and nonviable myocardium has been seen in other examples of a pressure-overloaded right ventricle,[33] and progression to irreversible cardiac failure in this situation is the probable consequence. Nevertheless, in the present study population, we observed the best improvement in the subjects with the most impaired initial right ventricular function. The observed improvement, however, resulted from improved loading conditions and not recovery of intrinsic myocardial contractile function.

PPVI did not completely relieve RVOTO in this group, and the long-term fate of the valved stent is still unknown. Furthermore, our finding of improved biventricular performance will need to be demonstrated in the longer term before PPVI can be recommended as the definitive treatment for pure RVOTO. This and the potential for right ventricular remodeling remain important areas for future study. A direct comparison with bare stenting or surgical treatment of RVOT obstruction may also offer further information about the relative benefit of this procedure. However, this exciting new technique permits, for the first time, relief of RVOTO without new pulmonary regurgitation or myocardial damage from cardiopulmonary bypass. The rapid clinical and functional benefits from relief of RVOTO support the current trend for early intervention with the aim of preserving cardiac function and avoiding the risk of irreversible myocardial damage associated with chronic right ventricular pressure overload.

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CLINICAL PERSPECTIVE

Right ventricular outflow tract obstruction (RVOTO) is a common residual problem for those who have had repair of congenital heart defects in childhood. It typically occurs in degenerated homografts or conduits that have been placed as part of the primary repair or for subsequent relief of pulmonary regurgitation. It is thought that ventricular function is well-tolerated in this situation, despite evidence that relief of obstruction with a bare stent can improve symptoms and hemodynamics. Percutaneous pulmonary valve implantation (PPVI) is a novel procedure that relieves RVOTO without the inevitable pulmonary regurgitation that follows placement of a bare stent. It therefore provides a unique model with which to study the true response of the heart after relief of RVOTO and thus to understand better the effect of these adverse loading conditions on baseline cardiac performance. We studied 18 patients with isolated RVOTO, before and after PPVI, with detailed imaging and objective assessment of exercise capacity. The results of our study indicate that at baseline, in our population, biventricular performance was compromised by the effect of the abnormal loading conditions on the impaired right ventricle. However, reversibility was seen when RVOTO was relieved by PPVI, and cardiac output increased. Importantly, this was associated with an improvement in subjective and objective exercise capacity. Although the longevity of PPVI remains unknown at this stage, our results support a growing inclination for earlier intervention in this patient group before right ventricular dysfunction becomes irreversible.