Percutaneous Pulmonary Valve Implantation

Impact of Evolving Technology and Learning Curve on Clinical Outcome

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Background—Percutaneous pulmonary valve implantation was introduced in the year 2000 as a nonsurgical treatment for patients with right ventricular outflow tract dysfunction.

Methods and Results—Between September 2000 and February 2007, 155 patients with stenosis and/or regurgitation underwent percutaneous pulmonary valve implantation. This led to significant reduction in right ventricular systolic pressure (from 63±18 to 45±13 mm Hg, $P<0.001$) and right ventricular outflow tract gradient (from 37±20 to 17±10 mm Hg, $P<0.001$). Follow-up ranged from 0 to 83.7 months (median 28.4 months). Freedom from reoperation was 93% (±2%), 86% (±3%), 84% (±4%), and 70% (±13%) at 10, 30, 50, and 70 months, respectively. Freedom from transcatheter reintervention was 95% (±2%), 87% (±3%), 73% (±6%), and 73% (±6%) at 10, 30, 50, and 70 months, respectively. Survival at 83 months was 96.9%. On time-dependent analysis, the first series of 50 patients (log-rank test $P<0.001$) and patients with a residual gradient >25 mm Hg (log-rank test $P=0.01$) were associated with a higher risk of reoperations.

Conclusions—Percutaneous pulmonary valve implantation resulted in the ability to avoid surgical right ventricular outflow tract revision in the majority of cases. This procedure might reduce the number of operations needed over the total lifetime of patients with right ventricle–to–pulmonary artery conduits. **(*Circulation*. 2008;117:1964-1972.)**

Key Words: pulmonary valve ■ heart defects, congenital ■ catheterization ■ stenosis ■ regurgitation

Dysfunction of the right ventricular outflow tract (RVOT) with pulmonary stenosis and/or regurgitation is a common and challenging condition in children and adults with congenital heart defects. Surgical RVOT revision can be performed with a very low mortality,[1,2] but valved conduits have a limited lifespan, often <10 years.[3–7] As a result, the majority of patients with right ventricle (RV)–to–pulmonary artery (PA) conduits undergo multiple open heart operations. To prolong conduit lifespan, bare-metal stenting in the setting of the RVOT obstruction has been performed.[8–10] This leads to a reduction in RV pressures and sometimes symptomatic improvement but causes free pulmonary regurgitation (PR) with detrimental effects on RV function and risk of arrhythmia.[11–13] Transcatheter valve insertion in the pulmonary position has been shown to be a safe and feasible treatment for both pulmonary stenosis and PR.[14,15] We now describe early and late results of percutaneous pulmonary valve implantation (PPVI) and the impact of evolving technology and a learning curve on clinical outcome in our total experience of 155 consecutive patients.

Clinical Perspective p 1972

Methods

Patients

Between September 2000 and February 2007, 155 patients underwent PPVI (Figures 1 and 2). Patients had to fulfill clinical and morphological criteria to be considered suitable candidates. Inclusion criteria, summarized in Table 1, were based on surgical indications for RVOT revision.[16] Exclusion criteria were pregnancy, occluded central veins, active infection, and weight <20 kg. Valve implantation was performed to reduce RVOT dysfunction and thereby delay surgery and prolong conduit lifespan. Criteria for surgical or transcatheter reintervention were based on the initial inclusion criteria.

PPVI was performed by a single operator at Hôpital Necker Enfants Malades (Paris, France), Great Ormond Street Hospital for Children, The Heart Hospital, and The Harley Street Clinic (London,

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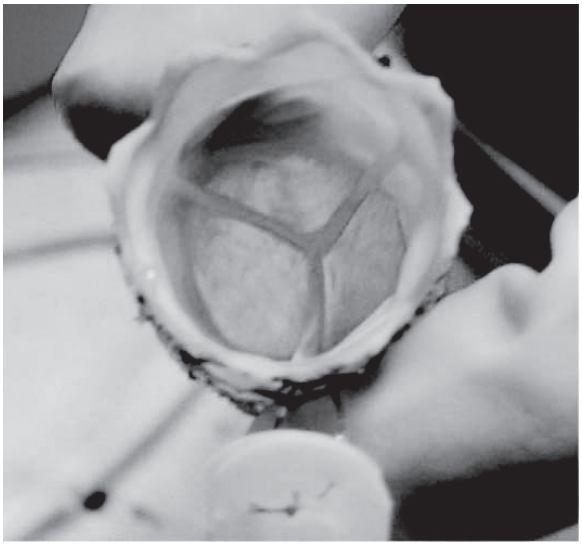

Figure 1. The percutaneous pulmonary valve (Melody, Medtronic, Minneapolis, Minn).

United Kingdom). Written informed consent was obtained from patients and parents as appropriate. The ethics committees at these institutions approved the study protocol. The study was approved by CCPPRB (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale; Paris, France) and MHRA (Medical Health Regulatory Authority; London, United Kingdom) and performed under humanitarian exemption in a case-by-case controlled fashion.

Protocol

Patients were assigned to New York Heart Association functional classes I through IV. Objective exercise capacity was measured by cardiopulmonary exercise testing unless contraindicated. Transthoracic echocardiography was performed in all patients. The RV systolic pressure was estimated from the tricuspid regurgitant jet and the RVOT gradient calculated from the velocity across the RVOT.[17] PR was defined qualitatively by color flow Doppler,[18] whereas RV dysfunction and dilatation were assessed by 2-dimensional echocardiography.

Morphological suitability for PPVI was either assessed by magnetic resonance imaging or, in those who had contraindications for magnetic resonance imaging, by biplane angiography.[15,19] With increasing experience, balloon sizing of the RVOT was added to the assessment protocol in patients with borderline anatomy. The utility of this technique has been demonstrated in the setting of other transcatheter interventions such as atrial septal defect closure[20] and PA stenting.[21] After coronary obstruction due to PPVI in 1 patient, angiography in the ascending aorta was performed in all patients. Simultaneous balloon inflation in the RVOT and coronary angiography were performed in patients at risk for coronary obstruction.[8,22,23]

Table 1. Inclusion/Exclusion Criteria

Clinical criteria
RV systolic pressures >2/3 of systemic plus symptoms, or
RV systolic pressures >3/4 of systemic in absence of symptoms, and/or Moderate/severe PR and 1 of following criteria:
Symptoms
Severe RV dysfunction
Severe RV dilatation
Impaired exercise capacity (peak oxygen consumption <65% of predicted)
Morphological criteria
RVOT dimensions <22×22 mm
RVOT dimensions >14×14 mm

Valve implantation was performed under general anesthesia. Pressure measurements and angiography were performed before and after PPVI. The technique has been reported previously.[15] Echocardiographic follow-up was performed at 1, 6, 12, 36, and 70 months, respectively. Echocardiograms were performed (P.L., L.C., S.K., and J.N.); follow-up echocardiograms performed at patients' local institutions were reviewed by the investigators.

Predictors for Reoperation and Transcatheter Reintervention

We assessed the impact of learning curve by dividing the patient population into a cohort that consisted of the first 50 patients who underwent PPVI and a second cohort representing the following 105 patients. After the 50th patient, the device design was frozen, and the authors believed that the learning curve had been completed in terms of technical experience and patient selection. To predict outcome related to hemodynamic results, we assessed the impact of a residual gradient on rate of reoperation and transcatheter reintervention. This was defined by a pullback gradient across the valved stent of >25 mm Hg, measured immediately after device deployment.

Statistical Analysis

Baseline variables were calculated as mean±SD or n (%). Survival curves were obtained by Kaplan–Meier plots. Reoperation and transcatheter reintervention-free survival was calculated from date of valve implantation to latest follow-up or date of surgery/catheterization and was expressed as percentage ±SEM. Patients who underwent second PPVI were not excluded from analysis of freedom from reoperation. Kaplan–Meier survival curves were used to assess the impact of the learning curve and the initial hemodynamics on reoperation-free and transcatheter reintervention-free survival. Log-rank testing was performed to compare groups. A paired *t* test was

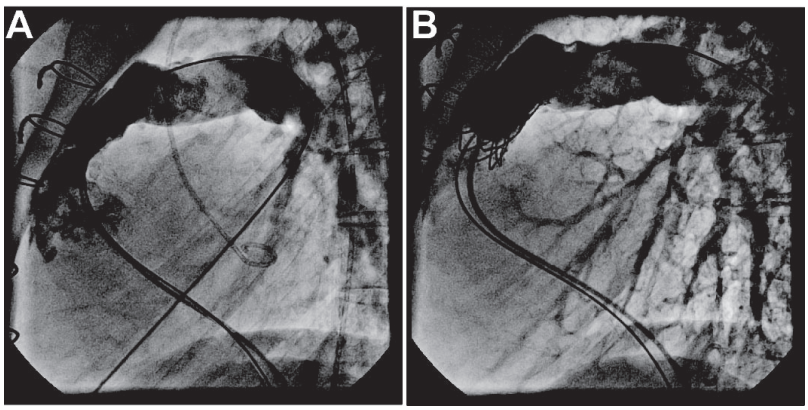

Figure 2. Lateral angiogram before (A) and after (B) PPVI in a patient with homograft obstruction and regurgitation.

Table 2. Patient Characteristics

Parameter	Total Population (n=155)	Predominantly Stenosis* (n=63)	Predominantly Regurgitation† (n=47)	Combined Lesions‡ (n=45)
Age at implantation, median (range), y	21.2 (7–71)	19.6 (9–54)	22.6 (7–58)	21.9 (9–71)
Diagnosis				
Tetralogy of Fallot variant, n (%)	94 (60.6)	36 (57.1)	33 (70.2)	25 (55.6)
Pulmonary stenosis	35	10	13	12
Pulmonary atresia	51	21	19	11
APV	8	5	1	2
Double-outlet RV, n (%)	9 (5.8)	3 (4.8)	5 (10.6)	1 (2.2)
TGA, VSD, PS, n (%)	14 (9.0)	8 (12.7)	0 (0)	6 (13.3)
Ross procedure, n (%)	12 (7.7)	7 (11.1)	1 (2.1)	4 (8.9)
Truncus arteriosus, n (%)	17 (11.0)	5 (7.9)	5 (10.6)	7 (15.6)
Other, n (%)	9 (5.8)	4 (6.3)	3 (6.3)	2 (4.4)
RVOT characteristics, n (%)				
Homograft	126 (81.3)	51 (80.9)	37 (78.7)	38 (84.4)
Hancock	11 (7.1)	7 (11.1)	1 (2.1)	3 (6.7)
Other conduit type	7 (4.5)	3 (4.7)	3 (6.4)	1 (2.2)
Patch-extended RVOT	2 (1.3)	1 (1.6)	1 (2.1)	0
Native outflow tract	5 (3.2)	1 (1.6)	2 (4.2)	2 (4.4)
Other	4 (2.6)	0 (0)	3 (6.4)	1 (2.2)
Open heart surgeries, mean	1.8±0.9	1.9±0.9	1.5±0.8	1.9±0.9
Operations in total, mean	2.5±1.1	2.6±1.1	2.4±1.0	2.5±12
Transcatheter interventions	0.4±0.8	0.4±0.7	0.3±0.6	0.6±1.0
NYHA class, n (%)				
1	17 (11.0)	7 (11.1)	3 (6.4)	7 (15.6)
2	82 (52.9)	38 (60.3)	23 (48.9)	21 (46.7)
3	45 (29.0)	16 (25.4)	17 (36.2)	12 (26.7)
4	11 (7.1)	2 (3.2)	4 (8.5)	5 (11.1)
CPEX (n=130)				
Peak $\dot{V}o_2$, $kg \cdot mL^{-1} \cdot min^{-1}$	23.2±7.3	24.2±7.1	21.8±7.1	23.6±7.6
% of predicted $\dot{V}o_2$	60.7±15.9	62.0±15.7	58.9±15.3	61.2±17.1
Echocardiography				
RV SP, mm Hg	66.6±21.6	81.4±17.9	47.3±15.9	66.6±15.9
Peak RVOT gradient, mm Hg	57.0±23.9	75.9±17.5	32.7±10.8	65.2±14.5
RV to sys pressure ratio	0.68±0.2	0.82±0.14	0.51±0.14	0.65±0.14

APV indicates absent pulmonary valve syndrome; TGA, transposition of the great arteries; VSD, ventricular septal defect; PS, pulmonary stenosis; CPEX, cardiopulmonary exercise test; peak $\dot{V}o_2$, peak oxygen consumption; RV SP, RV systolic pressure; RV to sys pressure ratio, RV to systemic systolic pressure ratio.

*RVOT gradient >50 mm Hg on echocardiography and less than moderate PR on echocardiography.

†At least moderate PR on echocardiography and RVOT gradient <50 mm Hg on echocardiography.

‡Patients who did not fit either the "predominantly stenosis" or "predominantly regurgitant" categories.

used to evaluate differences in invasively measured pressures before and after PPVI. Echocardiographic data were evaluated for changes from 1 month postprocedure to 6, 12 and 36 months using a linear model with an unstructured covariance structure and time as a repeated variable. A P value of <0.05 was considered statistically significant. Statistical analysis was performed on SPSS 11.0 for Mac (SPSS Inc., Chicago, Ill, USA).

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

Results

Study Population and Characteristics

Out of 163 patients enrolled, 8 patients did not meet the morphological criteria and therefore did not undergo PPVI. The reasons were unfavorable RVOT dimensions as assessed by balloon sizing in 6 patients. Another reason for abandonment of PPVI was proven risk of left coronary artery

Table 3. Pressures at Catheterization

	Total Population (n=151)			Predominantly Stenosis (n=61)			Predominantly Regurgitant (n=46)			Combined Lesions (n=44)		
Parameter	Pre	Post	*P*	Pre	Post	*P*	Pre	Post	*P*	Pre	Post	*P*
RV systolic pressure, mm Hg	63±18	45±13	<0.001	72±16	46±13	<0.001	48±13	43±12	0.002	62±15	46±12	<0.001
RV end-diastolic pressure, mm Hg	12±4	10±5	<0.001	12±4	9±4	<0.001	11±5	10±5	0.016	11±4	11±5	0.507
PA systolic pressure, mm Hg	27±11	29±12	0.056	25±11	26±9	0.373	31±10	31±9	0.917	25±9	29±13	0.027
PA diastolic pressure, mm Hg	10±4	14±9	<0.001	10±4	12±4	0.003	11±5	15±6	<0.001	9±4	13±6	<0.001
RV-to-PA gradient, mm Hg	37±20	17±10	<0.001	48±18	19±12	<0.001	20±13	13±9	<0.001	37±18	17±8	<0.001
Aortic systolic pressure, mm Hg	94±15	101±16	<0.001	92±15	98±14	0.004	94±14	102±16	0.002	94±17	105±17	0.001
Aortic diastolic pressure, mm Hg	54±10	58±10	<0.001	54±9	57±10	0.021	55±9	58±8	0.01	53±11	59±11	0.004
RV-to-systemic pressure, %	69±19	45±14	<0.001	81±16	47±12	<0.001	52±15	42±11	<0.001	67±11	44±15	<0.001

Pre indicates before PPVI; Post, after PPVI; and PA, pulmonary artery.

Four patients were excluded from analysis because no postprocedural pressure measurements were performed because of procedural complication. Grouping of patients was performed according to criteria outlined in the legend of Table 2.

compression demonstrated by balloon inflation within the RV-to-PA conduit (n=1).[22]

The median age of the present patient population was 21.2 years (range 7 to 71 years); 57 patients were <16 years old (37%), and 42% were female (Table 2). Most patients (61%) had tetralogy of Fallot or a variant morphology; 92% had an RV-to-PA conduit placed at previous surgery, 81% of which were homografts. Before the procedure, an RV-to–systemic pressure ratio of >2/3 was present in 58% of patients; echocardiography showed moderate or severe PR in 64%. The vast majority of patients complained of symptoms (138 of 155 patients), and 61% had impaired exercise capacity (defined as a peak oxygen consumption <65% of predicted). In total, 17 asymptomatic patients underwent PPVI. Indications for intervention in the absence of symptoms were RV-to–systemic pressure ratio >3/4 (0.89±0.13) in 9, peak oxygen consumption <65% of predicted (54.7±1.0%) in 4, and severe RV dilatation in 4 (*z* score for RV end-diastolic diameter assessed on echocardiography 5.9±2.3).

All but 8 patients in the present series were suitable for surgical RV-to-PA conduit replacement. In these 8, contraindications for surgery were pulmonary hypertension (n=4), severe chest deformity (n=2), and cardiogenic shock when referred for PPVI (n=2).

Procedural Results

Procedures were performed via a femoral venous approach in all but 7 cases. In these 7 patients, transjugular access was necessary owing to femoral venous occlusion or azygous vein continuity. After successful valve implantation, RV systolic pressure (63±18 to 45±13 mm Hg, $P<0.001$) and RVOT gradient (37±20 to 17±10 mm Hg, $P<0.001$) fell significantly (Table 3). In addition, postprocedural angiography showed relief of PR, which was reflected in an increase in diastolic PA pressure (from 10±4 to 14±9 mm Hg, $P<0.001$). No patient had more than mild PR on angiography after valve implantation.

Seven major procedural complications were seen: device instability, including dislodgement of the device (n=2); homograft rupture (n=3); compression of the left main coronary artery after device deployment (n=1); and obstruction of the origin of the right PA (n=1).[1] Other complications included guidewire injury of a distal PA with minor bronchial bleeding (n=2); partial homograft rupture that led to confined extravasation of contrast medium (n=1); and damage to the tricuspid valve caused by the balloon of the delivery system, which led to moderate tricuspid regurgitation (n=2). Five patients who had major complications required surgical RVOT revision; none of these procedures led to mortality. However, prolonged resuscitation after homograft rupture in 1 patient led to neurological sequelae followed by good recovery. One patient required surgery for hemostasis after homograft rupture, but the valved stent was conserved.

Follow-Up

Follow-up ranged from 0 to 83.7 months (median 28.4 months). Follow-up was 100% complete for death, reoperation, and transcatheter reintervention. Freedom from reoperation was 93±2%, 86±3%, 84±4%, and 70±13% at 10, 30, 50, and 70 months, respectively. Patients who underwent reoperation are summarized in Table 4.

Reinterventions in the form of balloon dilation of the device (n=3) and second valve implantation with a "stent-in-stent" technique (n=19) were performed in 22 patients. Freedom from transcatheter reintervention was 95±2%, 87±3%, 73±6%, and 73±6% at 10, 30, 50, and 70 months, respectively. Indication for reintervention was predominantly obstruction related to the "hammock" effect in 7 patients and stent fractures in 9 cases. The incidence of stent fractures in the total population in the present study was 21%. The nature of and reasons for the hammock effect and stent fractures have been described previously.[15,24] Other reasons for second valve implantation were restenosis of unknown origin (n=4) and a residual RVOT gradient after the first procedure (n=2). Second PPVI led to a significant decrease in RVOT gradient (from 47.6±18.2 to 19.5±10.0 mm Hg, $P<0.001$) with no procedural complications.

Echocardiographic follow-up was 90.1% complete. On echocardiography, valvar competence was well maintained during follow-up; moderate PR was only seen in 2 patients in the context of endocarditis (Figure 3). PPVI was performed in 4 patients with pulmonary hypertension. Despite high diastol-

Table 4. Patients With Explanted Valves

Age, y	Primary Diagnosis	RVOT Anatomy	Outflow Tract, mm	Device Generation	Reason for Explantation	Freedom From DE, mo
13	ToF, pulm atresia	Carpentier-Edwards	18	1st	Outgrown conduit	37.7
10	ToF, pulm atresia	Hancock	18	1st	Outgrown conduit	70.8
10	ToF, pulm atresia	Hancock	18	1st	Outgrown conduit	69.76
11	ToF, absent pulm valve	Carpentier-Edwards	16	1st	Endocarditis	9.8
38	Aortic valve disease (Ross)	Homograft	21	1st	Hammock effect	28.8
18	Aortic valve disease (Ross)	Homograft	20	1st	Hammock effect, stent fracture	2.9
14	Aortic valve disease (Ross)	Homograft	U	1st	Hammock effect	2.4
15	TGA, Rastelli	Homograft	U	1st	Hammock effect/ext. compression	12.1
38	Isolated pulm stenosis	Homograft	23	2nd	Valve dislodgement	0
28	ToF, pulm stenosis	Homograft	23	2nd	Residual stenosis	28.9
30	ToF, pulm atresia	Homograft	22	2nd	Stent fractures, late embolization	8.6
9	ToF, pulm stenosis	Extended RVOT	17	2nd	Valve dislodgement	0
11	Truncus arteriosus	Homograft	17	2nd	Endocarditis	12.9
15	ToF, pulm stenosis	Homograft	21	2nd	Residual stenosis	12.4
13	ToF, pulm atresia	Hancock	18	2nd	Residual stenosis	5.5
11	TGA, Rastelli	Homograft	15	2nd	Residual stenosis	13.3
10	Truncus arteriosus	Homograft	16	2nd	Residual stenosis	15.1
11	Aortic atresia, mod Norwood	Homograft	15	2nd	Residual stenosis, hemolysis	0.7
9	DORV, Mustard	Homograft	18	2nd	LCA compression, emergency surgery	0
25	Aortic valve disease (Ross)	Homograft	U	2nd	Endocarditis	13
19	Truncus arteriosus	Homograft	12	2nd	Obstruction of RPA	0
14	ToF, pulm atresia	Homograft	18	2nd	Homograft rupture, emergency surgery	0
20	Truncus arteriosus	Homograft	21	2nd	Increasing gradient across mechanical AV	7.4

DE indicates device explantation; ToF, tetralogy of Fallot; pulm, pulmonary; U, unknown; TGA, transposition of the great arteries; Rastelli, Rastelli procedure; Mod Norwood, modified Norwood procedure using the left atrial appendix for reconstruction of the RVOT; DORV, double-outlet RV; LCA, left coronary artery; RPA, right pulmonary artery; and AV, aortic valve.

The last 5 rows represent patients whose valves were explanted who underwent implantation within the second cohort (patients 51 through 155).

ic PA pressures, all patients had mild or less PR at a median follow-up of 18.5 months.

In the cohort of patients who did not undergo reoperation or transcatheter reintervention, the peak velocity across the device increased slightly from 1 month to 36 months after the procedure ($P=0.07$). At 1, 6, 12, 36, and 70 months, peak RVOT velocity was 2.64±0.6 m/s (n=107), 2.7±0.59 m/s (n=86), 2.66±0.5 m/s (n=83), 2.89±0.74 m/s (n=25), and 3.7±1.31 m/s (n=3), respectively (Table 5). At a follow-up of 70 months, 2 patients who underwent PPVI at the age of 11.5±0.9 years were awaiting surgical RVOT revision owing to outgrown conduits.

Complications During Follow-Up

Endocarditis was diagnosed in 5 patients at a median of 4.93 (range 1.9 to 23.2) months after PPVI. In these patients, endocarditis occurred in the context of unprotected dental treatment (n=1), reactivation of previously treated fungal infection (n=1), and a septic wound after arm trauma (n=1). Two patients had histories of endocarditis treated medically before PPVI. Organisms were *Staphylococcus aureus*, *Streptococcus aurelius*, and *Candida albicans*. Endocarditis led to valve explantation in 3 patients; 2 patients were successfully treated medically, which led to moderate PR on echocardiography 1 year after diagnosis.

After technically successful valve implantation into a 15-mm homograft, 1 patient developed hemolysis within hours after the procedure. This was attributed to a significant residual gradient (60 mm Hg) in a rather small homograft in addition to external compression of the RVOT, which necessitated device explantation.

One patient who underwent PPVI for RV-to-PA conduit stenosis after Rastelli repair experienced an out-of-hospital arrest 3.5 years after the procedure. Ventricular tachycardia was documented at resuscitation, and she was resuscitated successfully without neurological sequelae. At latest follow-up, 2.3 months before the event, echocardiography had revealed a competent valve with a peak velocity across the valved stent of 3.0 m/s. On ventricular stimulation during electrophysiological studies, no arrhythmia could be induced, and an implantable defibrillator was inserted. Although benign in the majority of cases,[24] stent fractures led to stent embolization into the right PA in 1 patient, who required surgical explantation of the percutaneous pulmonary valve.

Mortality

Four of 155 patients who underwent PPVI died. Survival at 83 months was 96.6%. Two of the patients who died had presented in cardiogenic shock and multiorgan failure, and PPVI was performed as a palliative strategy. The first patient

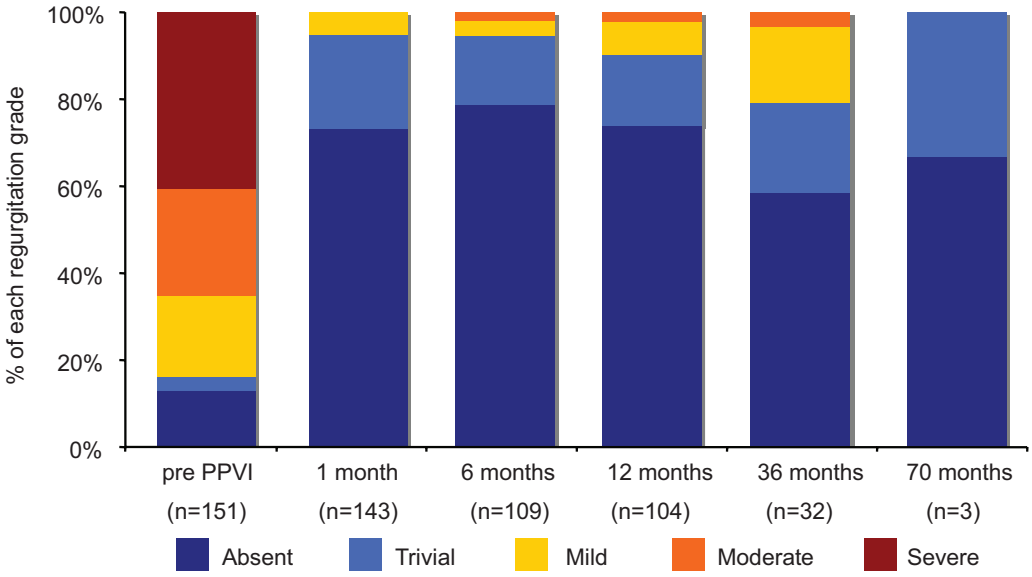

Figure 3. Valvar competence during follow-up assessed on echocardiography. PR was graded as absent, trivial, mild, moderate, or severe and expressed as a percentage before valve implantation and at 1, 6, 12, 36, and 70 months after PPVI.

had a history of 5 previous operations, deteriorated 6 weeks after a technically successful PPVI, and died of a chest infection. The second presented in multiorgan failure and severe fluid overload with critical recoarctation and RVOT obstruction. Despite successful PPVI and dilation of severe recoarctation, the patient died of pulmonary edema 24 hours after the procedure.

Two patients died suddenly at 8 and 35 months after PPVI. In both cases, autopsy revealed the valved stent appropriately seated in the RVOT. At latest follow-up, echocardiography showed good valvar competence of the device with a peak velocity across it of <3 m/s. The deaths were presumed to be due to arrhythmia.

Impact of the Learning Curve on Outcome

Freedom from reoperation in the first series of 50 patients was significantly shorter than in the subsequent patient population (log-rank test $P<0.001$; Figure 4A). In addition, residual gradients measured invasively after PPVI were associated with higher rates of reoperation (log-rank test $P=0.01$; Figure 4B) and transcatheter reintervention (log-rank test $P=0.008$).

Of the first 50 patients, 16 patients underwent device explantation compared with 5 patients in the second cohort. The incidence of a residual gradient of >25 mm Hg was higher in the first cohort of patients (n=16 of 50 versus 5 of 105 patients in the second cohort). Freedom from transcatheter reintervention did not differ significantly in the 2 cohorts on time-dependent analysis (n=13 versus n=9; log-rank test $P=0.18$). This is due to the fact that reinterventions were performed predominantly due to stent fractures, a complication that was not affected by the learning curve. The incidence of procedural complications fell from 6% in the first cohort to 2.9% in the second cohort of patients (n=3 of 50 versus 3 of 105 patients).

Discussion

Percutaneous interventions on the RVOT have been performed to avoid multiple open heart operations in patients with repaired congenital heart disease. Balloon dilation and bare-metal stenting of the outflow tract have successfully achieved relief of obstruction; however, these procedures compromise valvular function.[8–10,25] In contrast, PPVI represents a percutaneous technique to treat both pulmonary stenosis and regurgitation. We report our current experience of 155 patients who underwent transcatheter pulmonary valve implantation. This experience constitutes the longest and largest single-operator experience in percutaneous insertion of a heart valve. We have demonstrated that PPVI is an effective treatment for RVOT dysfunction. Device deployment was successful with very few exceptions and led to a marked improvement in hemodynamics. This was achieved with a very low complication rate and mortality.

Table 5. Peak Velocity Across the RVOT During Follow-Up Assessed by Echocardiography

	Before PPVI*	1 Month After PPVI	6 Months After PPVI	12 Months After PPVI	36 Months After PPVI	70 Months After PPVI
Reoperated/recatheterized patients	3.94±0.87 (39)	3.4±0.67 (36)	3.77±0.63 (23)	3.9±0.69 (21)	4.16±0.42 (7)	...
Patients without any intervention after PPVI	3.58±0.83 (112)	2.64±0.6 (107)	2.70±0.59 (86)	2.66±0.50 (83)	2.89±0.74 (25)	3.70±1.31 (3)†
Total patient population	3.67±0.85 (151)	2.84±0.7 (143)	2.93±0.74 (109)	2.91±0.74 (104)	3.17±0.86 (32)	3.70±1.31 (3)

Values are expressed as mean±SD (n). Velocity was measured in meters per second.

*In 4 patients, echocardiographic assessment of the RVOT was not possible owing to the retrosternal position of the RV-to-PA conduit.

†Two patients were awaiting surgical RVOT revision due to outgrown conduit.

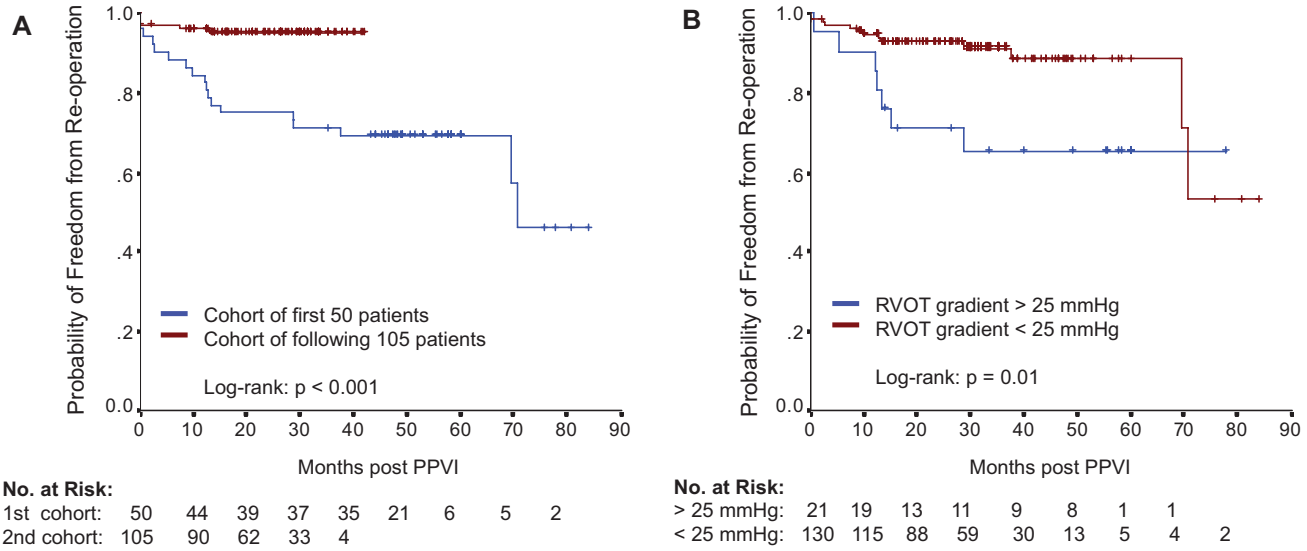

Figure 4. A, Kaplan–Meier plots comparing freedom from reoperation in the cohort of the first 50 patients (blue line) and the cohort consisting of the following 105 patients (red line). B, Freedom from reoperation in patients with an invasively measured postprocedural gradient >25 mm Hg (blue line) and <25 mm Hg (red line).

PPVI was performed with the aim to prolong the lifespan of the valved conduit, thus delaying surgery. Needless to say, the longevity of immediate and early results is crucial to the success of this technique. During follow-up over months, the hemodynamic improvement was sustained in the majority of patients.

Although reoperation and transcatheter reintervention were required in some patients during follow-up due to recurrence of stenosis, none required reinterventions for valvular incompetence in the absence of endocarditis. Initially, early restenosis was caused by the hammock effect,[15] which was resolved by altering the device design. Occurrence of stent fracture during follow-up led to an increase in RVOT gradient and RV pressures.[24] This was treatable with a second device, which proved to be a safe and successful approach.

Procedures were performed over a time frame of >6 years. In this period, the device design has been altered, the delivery system has improved, and the operator's confidence has grown. Therefore, we clearly identified a learning curve in our results. Freedom from reoperation was significantly longer in the second cohort of patients (51st through 155th) who underwent PPVI. Several factors contributed to this improvement. First, the incidence of residual gradients was reduced. A postprocedural gradient >25 mm Hg was associated with shorter freedom from reoperation. Incorrect patient selection, including patients with small conduits, and the reluctance to postdilate implanted valves led more frequently to postprocedural pressure gradients >25 mm Hg in the first cohort. In the second cohort, patients with residual gradients after PPVI were postdilated with high-pressure balloons with no demonstrable negative impact on valvar function. Second, patient selection improved with better understanding of the implantation site. Thus, device dislodgement at the time of PPVI was seen only in the first group. Careful assessment of conduit type, RVOT morphology,[19,26] and distensibility[24] has resulted in appropriate case selection for PPVI. This led us to understand that PPVI should generally not be attempted in patients with patch reconstruction of the RVOT and very distensible homografts, in the absence of an RV-to-PA gradient (seen in both patients in whom device dislodgement occurred). Third, strategies to deal with device failures changed: patients underwent a second PPVI in the latter experience rather than a reoperation. Finally, most procedural complications occurred within the series of the first 50 patients and, in our opinion, represent the learning curve. Despite clear progress, we have not found any strategies to predict or avoid homograft rupture. Further investigation is necessary to identify patients at risk of this complication.

The success of PPVI has significant implications for the timing of interventions for RVOT dysfunction. In clinical practice, timing of operation is often biased by the patient's and physician's reluctance to commit to multiple open heart surgeries, thereby exposing the RV to an increasing duration of abnormal loading conditions. Although reduction of RV diastolic and systolic volumes can be achieved even when patients are treated late,[27] studies have shown a lack of improvement in RV ejection fraction and exercise performance after surgical valve implantation.[28–31] The availability of PPVI might lead to better patient acceptance and therefore promote earlier intervention before irreversible ventricular dysfunction occurs. Although the optimal timing for intervention remains controversial, PPVI can allow for postponement of surgery after restoration of an acceptable RV loading condition.

Study Limitations

Because this is a midterm analysis of results after PPVI, long-term valvar performance is still unknown. It is likely that valvar degeneration, as seen in surgically implanted biological valves, will occur in this device. In the present series, however, we have not seen valvar degeneration leading to stenosis or regurgitation in the absence of endocarditis. Although PPVI led to a significant reduction in RV pressure and RVOT gradient, a small residual gradient was still

present in the majority of cases after the procedure. The long-term effects of low outflow tract gradients are unknown. Again, longer follow-up is necessary to address this question. Results of PPVI were not compared with surgical pulmonary valve implantation. However, transcatheter implantation of a valve in the pulmonary position was performed to prolong a surgical result after conduit placement rather than as a surrogate for open heart surgery. Therefore, we chose to assess the potential of PPVI to delay surgery by applying the same criteria for reintervention as for initial treatment, which were based on surgical indications.

Conclusions

PPVI improves RV outflow hemodynamics and delays surgery by prolonging conduit lifespan. Our experience represents the impact of evolving technologies in medicine, with progressive improvement in clinical results by device and technique modification. PPVI should reduce the number of operations and the cumulative hemodynamic burden on the RV over the total lifetime of children and young adults, potentially improving the life expectancy of patients with congenital heart disease that involves the RVOT.

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Disclosures

Dr Bonhoeffer is a consultant to Medtronic and NuMed and has received honoraria and royalties for the device described. Drs Taylor and Khambadkone are consultants to Medtronic and have received honoraria. The remaining authors report no conflicts.

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CLINICAL PERSPECTIVE

After the first transcatheter valve implantation in 2000, a new field in interventional cardiology developed. New techniques evolved rapidly, with significant improvement in outcomes. We assessed our results after percutaneous pulmonary valve implantation over a time frame of 6 years from the first to the 155th patient. The aim of percutaneous pulmonary valve implantation was to prolong the lifespan of conduits, which were surgically placed from the right ventricle to the pulmonary artery. Because of the limited longevity of conduits, the majority of patients with right ventricular outflow tract dysfunction traditionally undergo multiple open heart operations for conduit replacement. We show that percutaneous pulmonary valve implantation successfully restores conduit function with a low procedural complication rate. Explantation-free survival 5 years after percutaneous pulmonary valve implantation is >70%. This prolonged conduit lifespan should reduce the number of multiple open heart operations over the total lifespan of children and young adults with congenital heart disease and potentially improve life expectancy of these patients. As with all new procedures, whether surgical or interventional, the impact of the learning curve on a novel technique must be recognized. Therefore, we divided our patient population into a cohort consisting of the first 50 patients and a second cohort representing the later experience of 105 patients. In our experience, explantation-free survival was significantly longer in patients who underwent percutaneous pulmonary valve implantation in the second cohort. The impact of a learning curve on clinical results of new interventional procedures is of importance, especially if interventions and devices are compared with conventional therapies.