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FOCUS ISSUE: STRUCTURAL HEART DISEASE

Clinical Research

Percutaneous Implantation of the Edwards SAPIEN Transcatheter Heart Valve for Conduit Failure in the Pulmonary Position

Early Phase 1 Results From an International Multicenter Clinical Trial

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Chicago, Illinois; Los Angeles and Irvine, California; Durham, North Carolina; London, United Kingdom; Charleston, South Carolina; Philadelphia, Pennsylvania; and New Haven, Connecticut

Objectives The purpose of this study was to evaluate the safety and effectiveness of the Edwards SAPIEN transcatheter heart valve (Edwards Lifesciences LLC, Irvine, California) in the pulmonary position in patients with moderate to severe pulmonary regurgitation with or without stenosis.

Background Transcatheter pulmonary valve replacement is evolving, but to date, experience has been limited to the Melody valve (Medtronic Inc., Minneapolis, Minnesota).

Methods Eligible patients with dysfunctional right ventricle-to-pulmonary artery conduits were screened if body weight was ≥35 kg and the in situ conduit diameter was ≥16 mm and ≤24 mm. Standardized implantation and follow-up protocols were used.

Results Thirty-six patients from 4 centers were recruited between April 2008 and May 2010. Mean body weight was 73.4 ± 22.9 kg. Successful valve deployment was achieved in 33 of 34 attempts (97.1%). Valve migration occurred in 3 patients, with 2 requiring surgical retrieval; however, 1 patient underwent successful perventricular valve implantation. Further intraprocedure complications included pulmonary hemorrhage (n = 2), ventricular fibrillation (n = 1), and stent migration (n = 1). Pullback gradient across the conduit decreased from 26.8 ± 18.4 mm Hg to 11.7 ± 8.0 mm Hg ($p < 0.001$). The right ventricular/aortic pressure ratio decreased from 0.6 ± 0.2 to 0.4 ± 0.1 ($p < 0.001$). Peak Doppler gradient across the right ventricular outflow tract decreased from 41.9 ± 27.9 mm Hg to 19.1 ± 13.3 mm Hg ($p < 0.001$). At 6-month follow-up, all patients were alive. The number of patients with New York Heart Association functional class I increased from 5 at baseline to 27 at follow-up. Pulmonary regurgitation was ≤2+ in 97% of patients. Freedom from reintervention was 97% with 1 patient undergoing elective placement of a second valve due to conduit-induced distortion of the initial implant.

Conclusions Transcatheter pulmonary valve replacement using the Edwards SAPIEN transcatheter heart valve is safe and effective in patients with dysfunctional right ventricle-to-pulmonary artery conduits. (J Am Coll Cardiol 2011; 58:2248–56) © 2011 by the American College of Cardiology Foundation

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Transcatheter pulmonary valve replacement (tPVR) provides a less invasive alternative to surgery in patients with right ventricular-to-pulmonary artery (RV-PA) conduit dysfunction. Since the original report using a bovine jugular vein within a balloon-expandable stent was described in an ovine model more than 10 years ago (1), several clinical trials using this valve (Melody valve, Medtronic Inc., Minneapolis, Minnesota) in both Europe and the United States have demonstrated effective immediate restoration of valvular competence with significant reductions in conduit pressure gradients (2,3). Concerns have been raised, however, regarding the performance of this device with early stent fracture rates leading to potential valve dysfunction in more than 25% of cases (4). The Edwards SAPIEN transcatheter heart valve (THV) (Edwards Lifesciences LLC, Irvine, California) was initially introduced as a transcatheter alternative to surgical valve replacement in elderly patients with severe aortic stenosis (5). Since then, favorable safety and efficacy have been reported in a large randomized clinical trial involving elderly inoperable patients and high-risk surgical patients with severe aortic valve stenosis (6). Reports describing implantation in the pulmonary position for right ventricular outflow tract conduit dysfunction, mirroring valve efficacy and durability in the aortic position have followed (7); however, to date, formal studies evaluating valve effectiveness in the pulmonary position have not been conducted.

The COMPASSION (COngenital Multicenter trial of Pulmonic vAlve regurgitation Studying the SAPIEN interventional) THV was designed as a prospective, nonrandomized, multicenter study to assess the safety and efficacy of the SAPIEN THV for the treatment of dysfunctional RV-PA conduits with moderate to severe pulmonary regurgitation with or without stenosis. In this paper, we report the results of phase 1 U.S. Food and Drug Administration–approved clinical trial, with particular emphasis on restoration of valve competency and impact on conduit stenosis. The institutional review board of each participating institution approved the trial.

Methods

Patients. Between April 2008 and May 2010, 36 patients from 4 centers (3 in the United States and 1 in Europe) were recruited (Fig. 1). Patients with a dysfunctional RV-PA conduit, defined as ≥3+ pulmonary regurgitation by transthoracic echocardiography (TTE) or pulmonary regurgitant fraction ≥40% by cardiac magnetic resonance imaging (MRI) with or without stenosis, were considered eligible for inclusion in the trial provided that body weight was ≥35 kg and the in situ conduit diameter was ≥16 mm and ≤24 mm. After eligibility screening, informed consent was obtained from all potential subjects and/or their legal guardians. Pre-procedure baseline assessment included standard laboratory testing as well as computed tomography (CT) angiography and cardiac MRI. Exercise testing was also conducted using a standardized protocol. The primary endpoint for the trial was freedom from device failure or procedure-related death and/or reoperation at 1 year. Secondary endpoints included freedom from major adverse cardiac and cerebral events at 6 months and evidence of functional improvement as assessed by improvement in degree of pulmonary regurgitation and stenosis on TTE, pulmonary regurgitation on MRI, symptoms assessed by New York Heart Association (NYHA) classification, and exercise tolerance as assessed by cardiopulmonary exercise testing. Follow-up protocol included assessment at 30 days, 6 months, 1 year, and annually thereafter up to 5 years (Fig. 2). Standardized protocols for echocardiography, exercise testing, CT, and MRI were used. Cardiopulmonary exercise testing was performed using a ramp workload protocol. Anaerobic threshold was determined by use of the modified V-slope method. All study echocardiograms, MRI, and exercise stress tests were interpreted in centralized (Core) facilities.

Abbreviations and Acronyms

CT = computed tomography
MRI = magnetic resonance imaging
NYHA = New York Heart Association
RV-PA = right ventricle to pulmonary artery
THV = transcatheter heart valve
tPVR = transcatheter pulmonary valve replacement
TTE = transthoracic echocardiogram

Valve and delivery system. The SAPIEN Pulmonic THV is a radiopaque, stainless steel, balloon-expandable support structure (frame), with an integrated, unidirectional, trileaflet bovine tissue valve and a polyethylene terephthalate

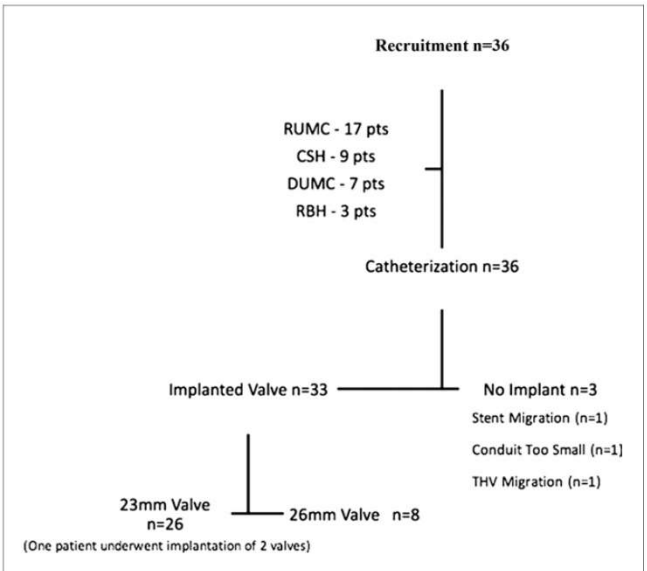

Figure 1 Flow Diagram Outlining Numbers of Patients Recruited and Subsequent Valve Implantation Outcome

CSH = Cedar Sinai Hospital; DUMC = Duke University Medical Center; RBH = Royal Brompton Hospital; RUMC = Rush University Medical Center; THV = transcatheter heart valve.

	Baseline	Discharge	30 Days	6 Months	12 Months	Annual
Physical Examination	✓	✓	✓	✓	✓	✓
Adverse Event Assessment		✓	✓	✓	✓	✓
NYHA Class Assessment	✓	✓	✓	✓	✓	✓
ECG	✓	✓	✓	✓	✓	✓
Chest X-Ray	✓	✓	✓	✓	✓	✓
TTE	✓	✓	✓	✓	✓	✓
Cardiopulmonary Exercise Testing	✓			✓	✓	✓
MRI Scan	✓			✓		
CT Angiogram	✓			✓	✓	✓

Figure 2 **Subject Schedule of Events**

Follow-up data are included at baseline, discharge, 30 days, and 6 months for this study. CT = computed tomography; ECG = electrocardiography; MRI = magnetic resonance imaging; NYHA = New York Heart Association; TTE = transthoracic echocardiography.

fabric cuff. The valve tissue is fabricated from 3 equal sections of bovine pericardium that have been preserved in low-concentration solutions of buffered glutaraldehyde to fully crosslink the tissue, while preserving its flexibility and strength. The THV is treated according to the Edwards ThermaFix process, which involves heat treatment of the tissue in glutaraldehyde and uses ethanol and polysorbate-80. The valve is available in 2 sizes: 23 mm (14-mm height) and 26 mm (16-mm height). Valve delivery was achieved using the Retroflex delivery system. These catheters consist of a balloon catheter and a deflectable guiding catheter, and require either 22- or 24-F hydrophilic sheaths for the 23- and 26-mm valves, respectively. A specialized manual crimping tool was used to symmetrically compress the valve onto a 30-mm-long valvuloplasty balloon that was presized to the final valve diameter. The primary operator verified the correct valve mounting and orientation after crimping onto the balloon.

Procedure. All procedures were performed with the patients under general endotracheal anesthesia with biplane fluoroscopic guidance. Pretreatment with intravenous antibiotics was given before valve implantation. Intraprocedure boluses of heparin were recommended to maintain activated clotting time longer than 200 s. Hemodynamic and angiographic assessment of the RV-PA conduit was performed to determine the baseline pressure gradient and degree of pulmonary regurgitation across the dysfunctional conduit. The minimum diameter of the conduit was also assessed from the angiograms in 2 orthogonal planes. Additionally, aortic root angiography or selective coronary angiography to assess for possible coronary compression was performed before right ventricular outflow tract intervention. In all cases, pre-stenting of the conduit with a bare metal stent was performed to provide a "landing zone" for the stented valve. This was either performed in a separate procedure (n = 12) in anticipation of the stented valve or during the valve implantation procedure (n = 24). This 2-step procedure allowed a greater margin of safety when positioning the relatively short valve prosthesis (14 to 16 mm) and increased the chance of the device maintaining a circular configuration in the long term. It also reduced the risk of distal or proximal obstruction in conduits that were generally significantly longer than the valve. The type and length of stent used for pre-stenting were left to the discretion of the operator, and the stent was deployed on a BiB (balloon-in-balloon) catheter (NuMED Inc., Hopkinton, New York) to a diameter of up to 2 mm less than the original conduit size in stenotic conduits or slightly larger in conduits without stenosis. Less aggressive dilation was acceptable in larger sized original conduits if there was no persisting pressure gradient across the stent. The final measurement used to guide the choice of SAPIEN THV was based on the diameter of the balloon at full inflation during pre-stenting. In conduits with stenosis, a 23-mm THV was used if the dilated conduit diameter was 21 to 23 mm, and a 26-mm THV was used if the dilated diameter was 23 to 26 mm. In conduits without stenosis and with a diameter of 19 to 21 mm, a 23-mm THV was used, and if the diameter was 21 to 23 mm, then a 26-mm valve was used. The SAPIEN valve was then crimped symmetrically using a specialized crimping device onto a 30-mm-long pre-sized balloon catheter (volume driven instead of pressure driven). The valve was delivered over a stiff guidewire across the pre-stented area and deployed with balloon inflation. After valve

Table 1 Demographic Data

Age, yrs	30.3 ± 15.1
Weight, kg	73.4 ± 22.9
Male/female	24/12
Diagnosis	
Tetralogy of Fallot	16
Ross procedure	11
Transposition of the great arteries	1
Other	8
NYHA functional class (baseline)	
I	5
II	17
III	12
IV	2
Open heart surgeries	1.94 (1–5)
RVOT conduit types	
Homograft	29
Other	7
Original RVOT conduit size, mm	23.4 ± 3.9
Primary indication	
Stenosis	15
Regurgitation	19
Mixed	2
RVOT pre-stenting	
Stent placed at time of procedure	24
Stent placed before day of procedure	12
Fluoroscopy time, min	38.2 ± 17.1

Values are mean ± SD, n, or n (range).
NYHA = New York Heart Association; RVOT = right ventricular outflow tract.

deployment, further pressure and angiographic assessments were performed to determine whether post-deployment high-pressure balloon dilation was necessary. At the end of the procedure, venous hemostasis was achieved with either 2 Perclose sutures (Abbott Vascular, Abbott Park, Illinois) placed at the beginning of the procedure or using a figure-of-8 suture (8). Protocol recommendation included pre-treatment with 81 mg of aspirin the evening before the procedure and continuation of this for the duration of the trial.

Statistical analysis. All adverse events were adjudicated by an independent clinical events committee. Summaries of echocardiography, cardiac MRI, and exercise data were based on the cohort of patients who had the study valve implanted. Unless otherwise noted, the mean ± SD were calculated for each continuous variable; the number and percentage of patients in each category were reported for each categorical variable.

A summary of baseline demographic and clinical risk data is presented in Table 1. Device success was defined as deployment of the valve to the target area and removal of the delivery catheter from the body and improvement in the regurgitation to mild or less (≤2+) per the earliest evaluable echocardiogram. Time to reoperation was calculated as the time from implantation to reoperation or last follow-up. Freedom from reoperation was calculated using Kaplan-Meier method (9). NYHA functional class was summarized at baseline, 30 days, and 6 months. Select echocardiographic, hemodynamic, cardiac MRI, and cardiopulmonary exercise data were summarized at baseline and at 6 months. A 2-sample nonpaired *t* test was used to analyze pulmonary regurgitant fraction and right ventricular end-diastolic volume as measured by MRI. No multiplicity adjustment was performed for this analysis. The Wilcoxon signed-rank test was used to investigate the difference from baseline to 6 months for paired data. The method of Holm (10) was used to adjust for multiplicity. Values of $p < 0.05$ were considered statistically significant.

Results

Successful valve implantation was achieved in 33 of 34 attempts (97.1%). Eight patients underwent implantation of a 26-mm SAPIEN valve. Comparative echocardiographic, MRI, and exercise stress test data at baseline and 6-month follow-up are presented in Table 2. Valve deployment was not attempted in 2 patients due to inappropriate conduit size in 2 and stent embolization (used for pre-stenting) requiring surgical retrieval in another. In 3 patients, THV

Table 2 Comparative TTE, MRI, and CPET Data at Baseline and 6-Month Follow-Up

	Baseline	6 Months Post-Procedure	p Value
Transthoracic echocardiography			
Conduit peak gradient, mm Hg	41.9 ± 26.2	19.1 ± 13.3	<0.001
Conduit mean gradient, mm Hg	24.0 ± 15.0	12.0 ± 8.8	<0.001
Estimated RV pressure, mm Hg	67.3 ± 20.6	49.3 ± 11.1	0.005
Magnetic resonance imaging*			
Pulmonary regurgitant fraction, %	28.64 ± 18.0	3.47 ± 5.40	<0.001
RV end-diastolic volume, ml/m^2	130.9 ± 62.6	86.9 ± 19.6	0.02
Cardiopulmonary exercise testing			
Peak Vo_2, ml/kg/min	22.1 ± 9.4	23.1 ± 8.0	0.09
RQ at peak exercise	0.9 ± 0.1	0.9 ± 0.2	0.23

Values are mean ± SD. *No multiplicity adjustment was performed for MR data, and the p values are based on a *t* test of nonpaired baseline and 6-month follow-up data.
CPET = cardiopulmonary exercise testing; MRI = magnetic resonance imaging; RQ = respiratory quotient; RV = right ventricular; TTE = transthoracic echocardiography.

Table 3 Intraprocedure Hemodynamic Data Pre- and Post-Pulmonary Valve Implantation

	Pre-Implantation	Post-Implantation	p Value
RV systolic pressure, mm Hg	55.3 ± 18.2	42 ± 13.2	<0.001
RV diastolic pressure, mm Hg	10.5 ± 4.0	9.2 ± 4.3	0.036
Mean PA pressure, mm Hg	16.0 ± 5.2	30 ± 8.2	0.001
Diastolic PA pressure, mm Hg	9.3 ± 3.1	12.4 ± 5.5	<0.001
RV/aortic pressure	0.6 ± 0.2	0.4 ± 0.1	<0.001
RV-PA pressure gradient, mm Hg	26.8 ± 18.4	11.7 ± 8.0	<0.001

Values are mean ± SD.
PA = pulmonary artery; RV = right ventricular.

migration occurred after deployment. In 2 of these, surgical retrieval was performed; however, in one, further transcatheter valve implantation was performed via a perventricular approach (delivery through a catheter placed in the wall of the right ventricular outflow tract) after the migrated valve was removed under inflow occlusion without cardiopulmonary bypass (11). In another patient, the THV was deployed without complication in the inferior vena cava with subsequent successful deployment of a further valve. Device success, therefore, using the intention-to-treat criteria mentioned was achieved in 31 of 36 patients (86.1%).

Intraprocedure hemodynamics are outlined in Table 3. The mean procedure time was 144 ± 60 min with a mean fluoroscopy time of 38.2 ± 17.1 min. Twenty-four patients underwent pre-stenting of the RV-PA conduits during the same procedure. Pullback systolic peak-to-peak gradient across the conduit decreased from 26.8 ± 18.4 mm Hg to 11.7 ± 8.0 mm Hg ($p < 0.001$). The pre-interventional right ventricle/descending aorta pressure ratio was reduced from 0.6 ± 0.2% to 0.4 ± 0.1% ($p < 0.001$), with a significant reduction in both the absolute systolic (from 55.3 ± 18.2 mm Hg to 42 ± 13.2 mm Hg [$p < 0.001$]) and diastolic (from 10.5 ± 4.0 mm Hg to 9.2 ± 4.3 mm Hg [$p = 0.036$]) right ventricular pressures. There was also a significant increase in the pulmonary artery diastolic pressure (from 9.3 ± 3.1 mm Hg to 12.4 ± 5.5 mm Hg [$p < 0.001$]), likely related to establishment of pulmonary valve competence. On post-procedure angiography, pulmonary regurgitation was graded trivial or less in 31 of 33 successful percutaneous implants.

Seven patients (20.5%) experienced adverse events (Table 4). Of those, 3 required surgery for migration of the THV (n = 2) and stent embolization (n = 1). In all 3 cases, surgery was uneventful with no damage to the intracardiac structures noted as a consequence of the attempted THV implantation. In another patient, the valve migrated toward the right ventricle after balloon inflation, and it was deployed without complication in the inferior vena cava. Mild intraprocedure pulmonary hemorrhage developed in 2 patients, thought to be related to the position of the stiff guidewire in the distal pulmonary vascular bed; neither required any specific treatment. Two episodes of ventricular fibrillation occurred in 1 patient during the procedure, but the patient was cardioverted to sinus rhythm on both occasions with a single asynchronous shock. Mean post-procedure hospital stay was 2.1 ± 2.0 days.

During 6-month follow-up, 1 patient required a repeat THV implantation. At discharge, this patient was noted to have moderate residual estimated gradient across the stented valve with estimated peak gradient across the right ventricular outflow tract of 69 mm Hg and mild pulmonary regurgitation as assessed by TTE. It was not clear whether optimal functionality of the THV was impeded by acute renarrowing of the valved conduit, and therefore the patient was brought back to the catheter laboratory for further high-pressure ballooning of the conduit. A decision was made at this time to implant a second 23-mm Edwards SAPIEN THV to ensure that dysfunction of the valve system was not contributing to these findings. The procedure was uncomplicated, with peak residual gradient of 25 mm Hg measured at the end of the procedure by direct pullback. However, the gradient at discharge from the hospital as measured by TTE was found to be 69 mm Hg with 2+ regurgitation. On the 30-day follow-up TTE, the peak gradient had increased to 89 mm Hg with 3+ pulmonary regurgitation. There were no further adverse events on follow-up reported. No stent fractures were seen on the chest radiograph or CT scan at 6-month follow-up. Significant improvements in NYHA functional class (Fig. 3), echocardiographic right ventricular outflow tract peak gradient (Fig. 4), and degree of pulmonary regurgitation (Fig. 5) persisted at 30-day and 6-month follow-up compared with baseline.

Interpretable nonpaired follow-up MRI data were available for 13 patients (38%). These demonstrated significant improvements in right ventricular volumes (from 130.0 ± 62.9 ml/m^{-2} to 86.9 ± 19.6 ml/m^{-2}, $p = 0.02$) and pulmonary regurgitant fraction (from 28.6 ± 18.0% to 3.5 ± 5.4%, $p < 0.001$) after valve implantation (Table 2). No significant changes in variables measured at cardiopulmonary exercise testing were noted; however, the majority of patients did not reach the anaerobic threshold, and direct

Table 4 Intraprocedure Adverse Events

Patient #	Adverse Event	Outcome
1	THV migration	Surgical removal and surgical PVR
2	THV migration	Surgical removal and transapical delivery of 26-mm Edwards SAPIEN THV
3	THV migration	Successful deployment within the inferior vena cava
4	Stent embolization to right ventricle	Surgical removal and surgical PVR
5	Pulmonary hemorrhage	Spontaneous resolution without need for blood transfusion
6	Pulmonary hemorrhage	Spontaneous resolution without need for blood transfusion
7	Ventricular fibrillation (2 episodes)	Successful immediate direct current cardioversion

PVR = pulmonary valve replacement; THV = transcatheter heart valve.

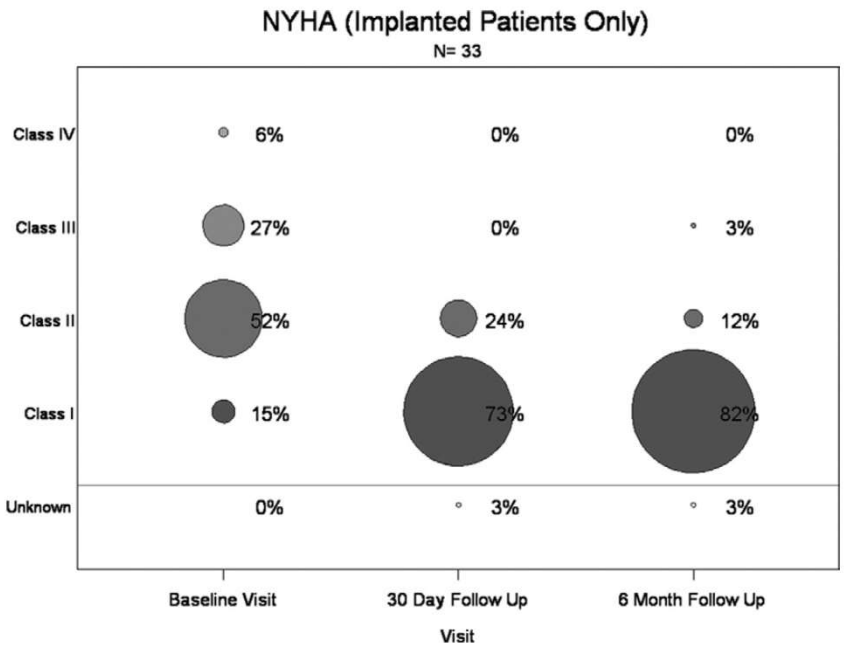

Figure 3 New York Heart Association Functional Classification at Baseline and Follow-Up

This demonstrates the majority of patients with NYHA (New York Heart Association) functional class I at 6-month follow-up.

comparisons of oxygen consumption in this setting are difficult to interpret. Subanalysis of circularity index of the valve (defined as ratio of maximal and minimal valve diameters measured in orthogonal planes) in 15 patients as assessed by CT at 6 months demonstrated good maintenance of valve symmetry with a mean circularity index of 0.89 ± 0.15.

Discussion

This study demonstrates excellent short-term functionality and durability of the Edwards SAPIEN THV when deployed in patients with dysfunctional RV-PA conduits (regurgitation with or without stenosis). The procedure was highly effective at reducing immediate pressure gradients across the conduit with continued effectiveness noted at 6-month follow-up. This is particularly pertinent in light of recent data suggesting that conduit stenosis relief is associated with improved exercise capacity in the setting of pulmonary valve replacement, whereas relief of pulmonary regurgitation is not (12). The peak gradient across the conduit was reduced from 41.9 ± 26.2 mm Hg pre-procedure to 23.0 ± 13.8 mm Hg at discharge. There was a further reduction at 6 months with a mean peak SAPIEN THV gradient of 19.1 ± 13.3 (Fig. 4A). Considering the reported impact of flow turbulence on valve calcification in the setting of native semilunar valves (13), this continued early reduction in valve gradient is relevant. Another factor known to affect recurrent transvalvular pressure gradients is stent fracture. This complication was not encountered in our cohort; however, fractures have been reported with the only other currently available transcatheter pulmonary valve (Medtronic Melody valve). In recent reports describing experience with the Melody valve, stent fractures were seen in as many as 30% of patients (2,3) with 8% detected within 6 months of valve implantation (3). Pre-stenting of the conduit may reduce the risk of Melody valve stent fractures; however, this is still considerable at 1 year, with rates as high as 18% reported (14). All patients undergoing THV implantation in this study had pre-stenting performed. It is likely that this contributed to early stent valve durability; however, the absence of pre-stenting support has not affected valve integrity in more than 300 patients with SAPIEN valve implants in the aortic position, with no fractures reported at 1-year follow-up (6,15).

The durability of the Edwards SAPIEN valve was also evident when assessing valvular competence. No cases of acute valve failure were seen, and at 6 months, the Edwards valve maintained effective pulmonary competence (≤2+) in 97% of patients. This is in contrast to previously reported surgical series of pulmonary valve replacement. Acute pulmonary conduit failure requiring reoperation after surgical replacement was reported in 2 of 71 patients by Oosterhof et al. (16). Frigola et al. (17) demonstrated a pulmonary regurgitant fraction of 30% or greater in 7% of patients after surgical valve replacement as assessed by MRI at 1-year follow-up. One patient in our study was noted to have progressive pulmonary regurgitation and valve gradient at discharge. This was thought to be secondary to the asym-

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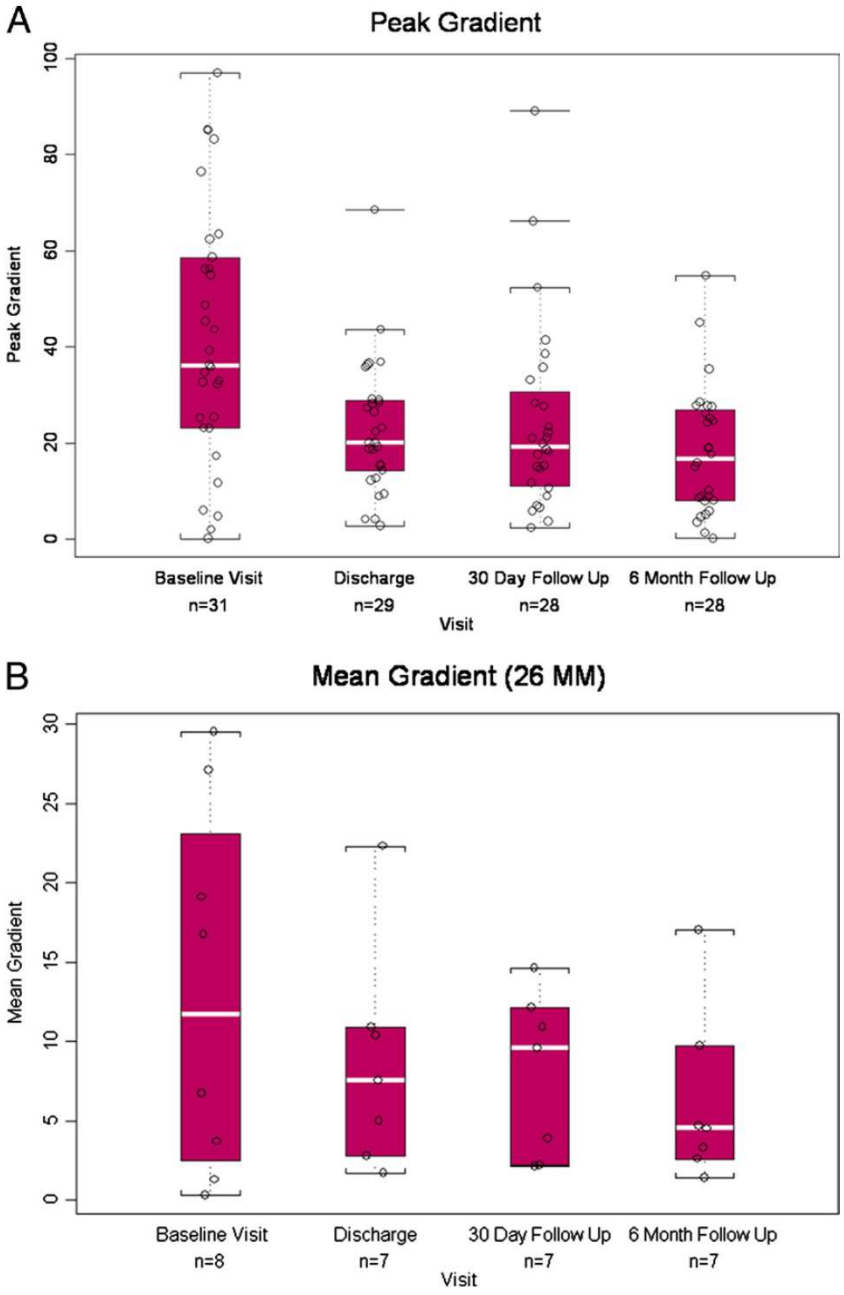

Figure 4 **Box Plots Demonstrating Changes in Echocardiographically Derived Gradients at Baseline and Follow-Up**

(A) Estimated peak pressure gradient across the pulmonary outflow assessed by transthoracic echocardiography (TTE) at baseline and follow-up.
(B) Reduction in mean pressure gradient across the pulmonary outflow assessed by TTE at baseline and follow-up in patients after implantation of a 26-mm valve.

metrical configuration of the valve despite pre-stenting, which may have had an impact on valve function. The patient underwent further valve balloon dilation and valve implantation 2 days after the original procedure; however, the residual pressure gradient and pulmonary regurgitation persisted, suggesting that dysfunction of the original valve was not contributory. This prompted a subanalysis of valve symmetry in 15 patients at 6 months as assessed by CT scan to determine the effect of potential asymmetry on valve function. This demonstrated excellent maintenance of valve circularity with a mean circularity index of 0.89 ± 0.15. In 2 patients with indices <0.8, pulmonary incompetence was described as trivial or none. It is noteworthy that the patient who underwent a second percutaneous valve implantation required surgical removal of the 2 valves and placement of a 25-mm Freestyle valve (Medtronic Inc.) 8 months later (outside the 6-month follow-up window of this study). However, 5 months after this surgery, a TTE revealed the presence of severe conduit ob-

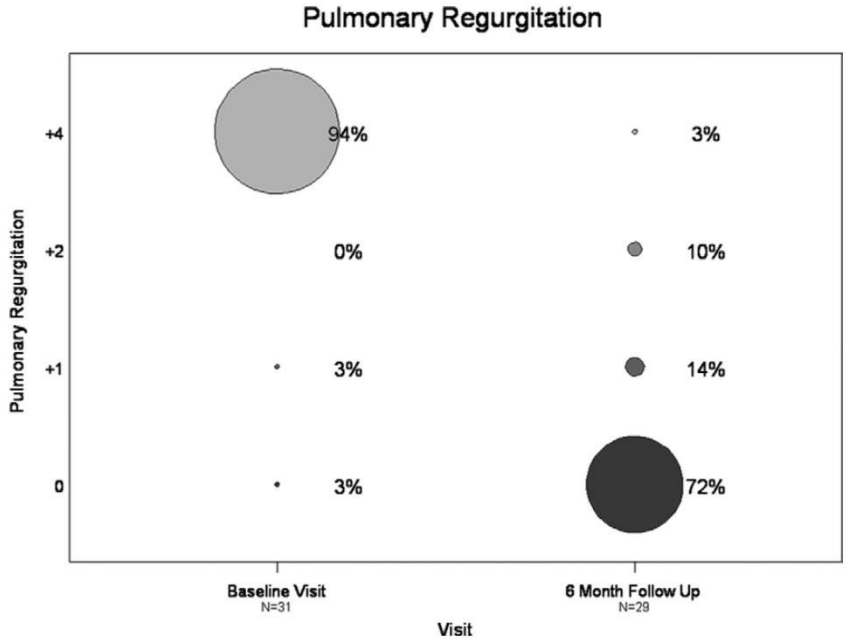

Figure 5 Severity of Pulmonary Regurgitation Assessed by TTE at Baseline and Follow-Up

Two patients' initial transthoracic echocardiography (TTE) assessment of pulmonary regurgitation (0+ and 1+ above) were performed before pre-stenting.

struction with a peak gradient of >75 mm Hg, which may reflect a tendency toward abnormally accelerated bioprosthetic valve degeneration in this particular substrate.

Seven patients experienced procedure-related adverse events. Three of these required operative interventions for either stent or THV migration, and this is similar to operative interventions after initial experience with the Melody valve (2). Two of these patients underwent traditional surgical pulmonary valve replacement without complication. In another in whom the THV had migrated proximally after deployment, it was possible to remove the migrated valve and place another valve as discussed previously (11). One further patient had the SAPIEN valve deployed in the inferior vena cava due to proximal stent migration on balloon inflation with further successful transcatheter SAPIEN valve implantation during the same procedure. The potential causes for valve migration include suboptimal valve positioning within the pre-stented RV-PA conduit. This underscores the importance of optimal valve deployment, in the middle of the deployed stent. Pre-stenting will certainly abolish any residual conduit valve competence leading to significant alternating flows also potentiating valve instability during inflation. As the SAPIEN valve is mounted on a single balloon, operator experience is important in countering these factors to maximize optimal valve positioning. Other technical aspects relating to implantation of the SAPIEN valve in the pulmonary position have been previously reported (7). It is worth pointing out that valve size did not affect the safety or efficacy of the procedure. Eight patients had successful implantation of a 26-mm valve with sustained significant reduction in RV-PA conduit valve pressure gradients at 6 months (Fig. 4B). In 2 of these patients, the minimum conduit diameter was 23 mm, which exceeds the recommended diameter for implantation of the Melody valve. The 26-mm valve thus extends the number of patients eligible for transcatheter valve implantation without affecting durability at 6 months. No further post-procedure complications including conduit aneurysm formation or pulmonary embolism were seen on 6-month follow-up CT scan.

A significant improvement in functional class was noted at 6 months post-procedure compared with baseline (Fig. 3). Previous studies have sought to objectively define improvement in exercise tolerance (due to a predominant lack of symptoms in many patients with pulmonary regurgitation) with cardiopulmonary exercise testing; however, in most studies to date, little or no difference has been shown (3,4,17). The majority of patients in this study failed to reach the anaerobic threshold, and therefore changes in peak oxygen consumption were difficult to interpret because many confounding variables affecting these values, particularly physical deconditioning, may be present. This represents one of the limitations of this study; however, similar difficulties have been experienced in previous studies assessing tPVR, and the benefits of cardiopulmonary exercise testing with continued difficulties in data interpretation in this setting must be questioned. Difficulties also arose when assessing MRI data with <50% of the initial cohort with interpretable ventricular volumes and regurgitant fractions, and this represents another limitation with our data. Pre-

stenting of the entire RV-PA conduit with stainless steel stents may lead to radiofrequency shielding within the stented area (18), exacerbating problems with direct assessment of pulmonary regurgitant fraction. This may not have been such an issue with the Melody valve due to the initial absence of pre-stenting, and less artifact maybe seen with platinum stents (18), although valid MRI data even in the absence of presenting with this valve has been reported to be as low as 48% (2). Indeed, MRI in this setting was initially described in patients undergoing surgical pulmonary valve replacement to evaluate right ventricular volumes above which the right ventricle may not normalize (16,17,19). Patients undergoing tPVR are more likely to have mixed stenosis/regurgitation, and indexed right ventricular volumes at the time of intervention have been significantly less than those reported in the cited surgical series, with predominant regurgitant lesions (3,20). It remains to be seen whether early surveillance to confirm pulmonary valve competence and reduction in right ventricular volumes with MRI will continue to be necessary in the setting of tPVR.

Conclusions

The 6-month follow-up data have demonstrated the Edwards SAPIEN THV to be safe and effective when used in patients with significant pulmonary regurgitation with or without stenosis in RV-PA conduits between 16 and 24 mm in size. Significant improvements in pressure gradients, pulmonary regurgitation, and symptoms were noted. Extended application of this valve in the pulmonary position with ongoing follow-up is required to determine whether these results are sustainable over a longer time period and broader population.

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Key Words: conduit ■ pulmonary valve replacement ■ SAPIEN ■ stent ■ transcatheter.