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Transcatheter Pulmonary Valve Replacement With the Melody Valve in Small Diameter Expandable Right Ventricular Outflow Tract Conduits

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ABSTRACT

OBJECTIVES This study sought to evaluate the safety, feasibility, and outcomes of transcatheter pulmonary valve replacement (TPVR) in conduits ≤16 mm in diameter.

BACKGROUND The Melody valve (Medtronic, Minneapolis, Minnesota) is approved for the treatment of dysfunctional right ventricular outflow tract (RVOT) conduits ≥16 mm in diameter at the time of implant. Limited data are available regarding the use of this device in smaller conduits.

METHODS The study retrospectively evaluated patients from 9 centers who underwent percutaneous TPVR into a conduit that was ≤16 mm in diameter at the time of implant, and reported procedural characteristics and outcomes.

RESULTS A total of 140 patients were included and 117 patients (78%; median age and weight 11 years of age and 35 kg, respectively) underwent successful TPVR. The median original conduit diameter was 15 (range: 9 to 16) mm, and the median narrowest conduit diameter was 11 (range: 4 to 23) mm. Conduits were enlarged to a median diameter of 19 mm (29% larger than the implanted diameter), with no difference between conduits. There was significant hemodynamic improvement post-implant, with a residual peak RVOT pressure gradient of 7 mm Hg ($p < 0.001$) and no significant pulmonary regurgitation. During a median follow-up of 2.0 years, freedom from RVOT reintervention was 97% and 89% at 2 and 4 years, respectively, and there were no deaths and 5 cases of endocarditis (incidence rate 2.0% per patient-year).

CONCLUSIONS In this preliminary experience, TPVR with the Melody valve into expandable small diameter conduits was feasible and safe, with favorable early and long-term procedural and hemodynamic outcomes. (J Am Coll Cardiol Intv 2018;11:554–64) © 2018 by the American College of Cardiology Foundation.

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In 2010, the Melody transcatheter pulmonary valve (TPV) (Medtronic, Minneapolis, Minnesota) was granted HDE approval by the U.S. Food and Drug Administration for the treatment of dysfunctional right ventricular outflow tract (RVOT) conduits. In reports of trial patients and other cohorts, TPV replacement (TPVR) has been shown to restore pulmonary valve function and extend the life span of various surgical conduits and pulmonary valves (1–7). Until early 2017, the instructions for use for the Melody valve followed the U.S. investigational device exemption (IDE) trial in specifying that the RVOT conduit must have been ≥16 mm at the time of surgical implant (8). Accordingly, there are limited published data on TPVR into smaller RVOT conduits, which are generally embedded within larger series (4,9–11). Although the IDE trial required that conduit diameter measured 14 to 20 mm by sizing balloon after initial predilation (8), the instructions for use does not specify criteria for actual conduit size at the time of TPVR.

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This disparity is noteworthy, as the original size of the implanted conduit may or may not correspond to its diameter at the time of TPVR. As documented recently, many RVOT conduits, homografts, and valved bovine jugular vein conduits in particular become substantially narrowed in situ, whereas others may enlarge after implant (1,3). Moreover, homograft conduits tend to lose the mural structure and mechanical behavior of arteries and become less compliant over time, such that the originally implanted size may not reflect the expected capacity of the remodeled conduit to expand (12–14). Thus, it is not clear that small original conduit diameter should be an a priori exclusion criterion for TPVR. Considering these factors, the purpose of this multicenter study was to evaluate the procedural characteristics and outcomes of TPVR in patients with an expandable RVOT conduit that was ≤16 mm at the time of surgical implant to determine whether efficacy and safety were similar to published data on implants in larger conduits.

METHODS

PATIENTS. All patients with an expandable RVOT conduit who underwent percutaneous catheterization for intended TPVR at 9 participating institutions from January 2010 to March 2017 were reviewed, and those whose original (implanted) conduit diameter was reportedly ≤16 mm were analyzed for this study. Expandable conduits were defined as those composed of biological tissue without a rigid frame, specifically, homografts and valved bovine jugular vein (Contegra, Medtronic) conduits. Synthetic tube grafts, composite conduits, and stented pulmonary valves were excluded, as were any type of biological graft >16 mm at implant. Ring-supported Contegra conduits were considered eligible because the expandability is unknown.

Written informed consent was obtained for clinical percutaneous catheterization and TPVR. Institutional review board approval for retrospective data collection and analysis was obtained at each of the participating centers.

Pre-catheterization data included demographic, diagnostic, and historical information. Standard measures were recorded from pre- and post-implant imaging studies, including echocardiography and magnetic resonance imaging if applicable. Pulmonary regurgitation (PR) was evaluated qualitatively by spectral and color Doppler ultrasound, and categorized as either moderate-severe or mild or less. The underlying hemodynamic indication for TPVR was classified as PR (moderate or severe), stenosis (maximum Doppler gradient ≥50 mm Hg, mean Doppler gradient ≥35 mm Hg, or peak invasive gradient ≥30 mm Hg), or combined stenosis and PR. The narrowest angiographic conduit diameter in any projection was measured, and the degree of conduit calcification was graded as heavy (extensive, circumferential) or minimal or none. Acute post-implantation hemodynamic data and final conduit size were recorded. Longer-term outcomes, including death, RVOT reintervention, and endocarditis, were specifically ascertained, along with attributed causes. The mean Doppler RVOT gradient was not available as often as maximum gradient, so only the latter is reported.

TPVR PROCEDURE. TPVR was performed following general techniques that have well described (1,5,6), but specific technical measures were at the discretion of the implanting physician. The number and type of prestents implanted before TVPR were recorded. Ratios were calculated of balloon sizes to original implanted, narrowest angiographic, and final post-TPVR conduit diameters, and of angiographic or implanted and final or implanted conduit diameters. The narrowest angiographic/implanted diameter ratio was used as a marker of shrinkage from the time of surgical implant to catheterization, whereas balloon/angiographic or implanted diameter ratios and final post-TPVR/angiographic diameter ratios were indices of the aggressiveness of dilation and conduit expansion.

ABBREVIATIONS AND ACRONYMS

CI = confidence interval

IDE = investigational device exemption

OR = odds ratio

PR = pulmonary regurgitation

RVOT = right ventricular outflow tract

TPV = transcatheter pulmonary valve

TPVR = transcatheter pulmonary valve replacement

TABLE 1 Baseline Data in Patients Who Did and Did Not Undergo TPV Implant

	TPV Implant (n = 117)	No Implant (n = 23)
Pre-catheterization data		
Age, yrs	11.0 (3.5-35.0)	12.1 (3.5-18.0)
Weight, kg	34.0 (13.5-118.0)	35.0 (15.9-88.0)
Male	74 (63)	14 (61)
Diagnosis		
Tetralogy of Fallot	66 (56)	13 (56)
Pulmonary atresia	50 (43)	7 (30)
Pulmonary stenosis	12 (10)	5 (22)
Absent pulmonary valve	4 (3)	1 (4)
Truncus arteriosus	16 (14)	4 (17)
Left heart disease, Ross procedure	15 (13)	2 (9)
Other	20 (16)	4 (17)
Number of prior open heart surgeries	2 (1-6)	2 (1-3)
Prior history of endocarditis	5 (4)	0 (0)
Conduit age, yrs	9.5 (3.0-25.0)	9.2 (3.4-16.0)
Conduit type		
Homograft*	84 (72)	15 (65)
Aortic	26	8
Pulmonary	51	6
Contegra	33 (28)	8 (35)
Conduit size		
16 mm	46 (39)	5 (22)
15 mm	26 (22)	4 (17)
14 mm	20 (17)	8 (35)
12–13 mm	20 (17)	4 (17)
<12 mm	5 (4)	2 (9)
Existing conduit stent from prior procedure	23 (20)	6 (26)
Doppler maximum RVOT gradient, mm Hg	56 (5-122)	60 (15-102)
>50 mm Hg	65 (59)	16 (70)
Pulmonary regurgitation ≥moderate	92 (79)	19 (83)
Indication for implant		
Conduit stenosis	24 (21)	5 (22)
Conduit regurgitation	41 (31)	7 (30)
Mixed stenosis and regurgitation	52 (44)	11 (48)
Pre-implant catheterization data		
Narrowest angiographic conduit diameter, mm	11 (4-23)	10.2 (5-17)
Angiographic/surgical implant diameter ratio†	0.78 (0.25-1.58)	0.76 (0.36-1.13)
Conduit severely calcified	49 (42)	12 (52)
Peak RVOT gradient, mm Hg	26 (2-98)	32 (7-60)
Right ventricle/aorta systolic pressure ratio	0.66 (0.32-1.50)	0.65 (0.25-1.05)

Values are median (range) or n (%). *Homograft type unknown in 7 patients (6 implanted, 1 not implanted). †Implant diameter refers to the diameter of the conduit at the time of surgical implant; angiographic diameter refers to the narrowest angiographic diameter in the catheterization lab.

RVOT = right ventricular outflow tract; TPV = transcatheter pulmonary valve.

DATA ANALYSIS. Categorical data were presented as frequency (%), and continuous data were presented as median (range). The Wilcoxon signed rank test was used to compare continuous data between groups, and the Fisher exact or chi-square tests were used to compare categorical variables. Intergroup comparisons were performed according to RVOT conduit type and original conduit size. Factors associated with conduit calcification and conduit tears were also assessed. Odds ratios (ORs) are presented with 95% confidence intervals (CIs). Paired comparisons of pre- and post-implant hemodynamic data were performed using paired *t* test. Factors associated with categorical outcome measures on univariable analysis ($p < 0.05$) were considered for inclusion in multivariable logistic regression models built with forward stepwise selection. Kaplan-Meier curves were generated to estimate freedom from time-related outcomes, and log-rank testing or Cox regression analysis were performed to assess for factors associated with these outcomes. Statistical significance was defined as $p < 0.05$.

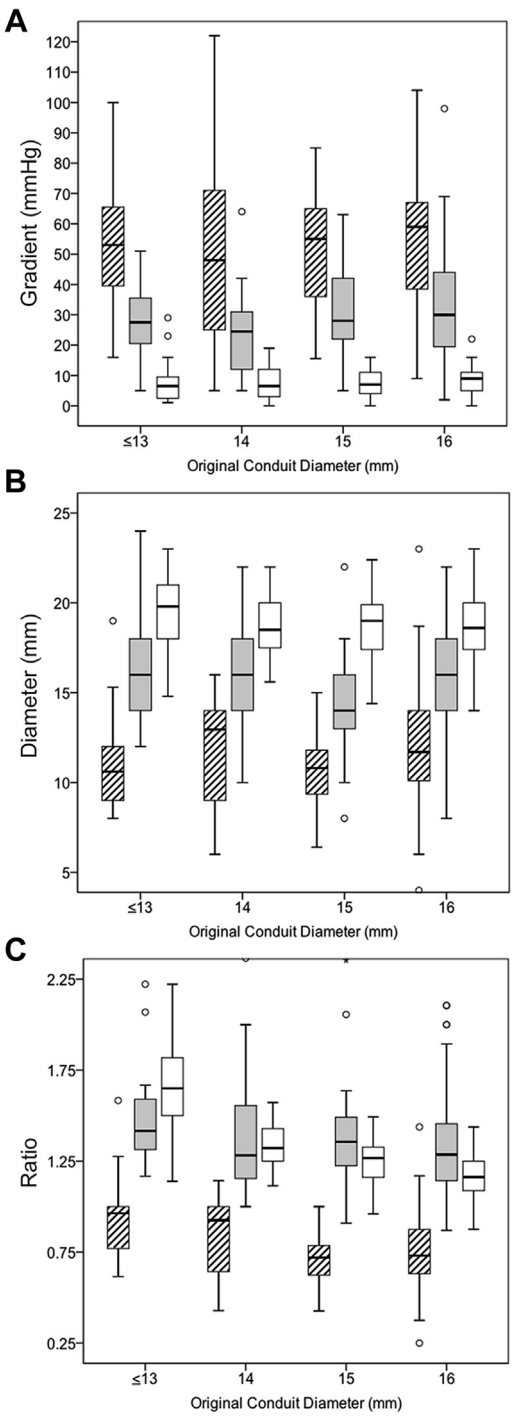
RESULTS

PATIENTS. Between January 2010 and March 2017, a total of 140 patients who met inclusion criteria underwent catheterization with the intent to perform TPVR, as detailed in Table 1. Of these, 117 (78%) patients had a Melody valve implanted. These 117 implants represented 20% of all Melody valve implants into expandable conduits at the 9 study centers during the study period, a frequency that ranged from 9% to 45% at the different centers. The median age and weight at the time of implant were 11 years and 34 kg, respectively, and 62% of patients were 10 years of age or older and 30 kg or larger. The median age of the conduit in the implanted group was 9.5 years (range: 3 to 25 years) versus 9.2 years (range: 3 to 16 years) in the nonimplanted cohort. Twenty-three of the 140 catheterized patients did not undergo TPVR due to coronary compression with test angioplasty (n = 6), satisfactory hemodynamics after conduit dilation or stenting alone (n = 6), operator discretion (n = 4), unfavorable conduit size or anatomy (n = 4), inability to advance the delivery system to the intended implant location through a percutaneous approach (n = 2), or hemodynamically unstable conduit rupture (n = 1). Five of these patients subsequently underwent surgical conduit replacement within a 1 year of attempted TPVR, and the others had no further RVOT interventions beyond angioplasty at the time of catheterization during a median follow-up of 3.1 years. Overall, patients who did not undergo TPVR had similar pre-procedural characteristics when compared with the TPVR cohort (Table 1).

In the majority of patients, the RVOT conduit was a homograft, most often a pulmonary homograft, whereas 28% had an unsupported Contegra. The median implanted conduit diameter was 15 mm (range: 9 to 16 mm) and was 13 mm or smaller in 20% of implanted patients and 26% of those who did not receive a TPV. In most patients, the narrowest

angiographic conduit diameter was smaller than the implanted diameter (median ratio 0.78), but 19 of 140 (14%) patients had a conduit that was larger than the reported implant diameter (11 pulmonary homografts, 5 unsupported Contegra, 3 aortic homografts).

FIGURE 1 Box Plots Demonstrating Conduit Outcomes



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Conduit-related factors, including gradients and diameters, are depicted according to the original implanted conduit diameter in Figure 1. Five patients in the implanted cohort (3 with a homograft conduit, 2 with a Contegra) had a previous history of endocarditis. In general, patient- and conduit-related factors were similar in the homograft and Contegra cohorts, although isolated stenosis was more common with Contegra conduits and PR more common with homografts (Table 2).

Almost one-half of the conduits were reported to have heavy calcification. Homografts and Contegra conduits were similarly likely to be calcified. Heavily calcified conduits had significantly larger implanted diameter (15 mm [range: 14 to 16 mm] vs. 14 mm [range: 13 to 16 mm]; $p = 0.001$) and smaller angiographic/surgically implanted diameter ratio than non- or mildly calcified conduits (0.72 [range: 0.43 to 1.14] vs. 0.87 [range: 0.38 to 1.43]; $p = 0.005$), and aortic homograft conduits were more likely to have heavy calcification than were pulmonary homografts (62% vs. 29%; OR: 2.1; 95% CI: 1.3 to 3.6; $p = 0.005$).

TPVR PROCEDURE. TPVR was performed through a femoral venous approach in 90% of patients and via the right internal jugular vein in 10%. The median first pre-dilation balloon diameter was 16 mm (range: 8 to 24 mm) and was 33% larger than the narrowest angiographic conduit diameter. Pre-stenting was performed in 105 of the implanted patients (90%) with 43 (37%) patients receiving more than 1 stent; 9 of the other 12 patients had an existing conduit stent from a prior procedure. In most cases, bare-metal stents were used—Palmaz XL P3110 (Cordis, Johnson and Johnson, Miami Lakes, Florida) in 64 patients,

FIGURE 1 Continued

(A) Box plots demonstrating right ventricular outflow tract gradients according to surgically implanted conduit diameter. **Hatched bars** indicate pre-transcatheter pulmonary valve replacement (TPVR) maximum Doppler gradient; **gray bars** indicate pre-TPVR peak gradient measured directly; **white bars** indicate post-TPVR peak gradient measured directly. **(B)** Box plots demonstrating the angiographic conduit diameter **(hatched bars),** the first pre-dilation balloon diameter **(gray bars)**, and the final conduit diameter after TPVR **(white bars)** according to surgically implanted conduit diameter. **(C)** Box plots demonstrating the minimum angiographic/implanted conduit diameter ratio **(hatched bars)**, the first balloon/angiographic conduit diameter ratio **(gray bars)**, and the **white bars** indicate final post-TPVR: implanted conduit diameter ratio according to surgically implanted conduit diameter. For box plots, the **dark line** within the box is the median, the **box** represents 25th to 75th percentiles, the **error bars** are the fifth and 95th percentiles, and **circles** represent outliers.

TABLE 2 Baseline Data in TPVR Patients According to Surgical RVOT Conduit Type

	Total (n = 117)	Homograft (n = 84)	Contegra (n = 33)	p Value
Pre-catheterization data				
Age, yrs	11.0 (3.5-35.0)	10.4 (4.0-35.0)	11.4 (3.5-17.0)	0.65
Weight, kg	34.0 (13.5-118.0)	34.0 (15.5-118.0)	37.0 (13.5-69.0)	0.99
Male	74 (63)	53 (63)	21 (64)	0.96
Number of prior open heart surgeries	2 (1-6)	2 (1-6)	2 (1-6)	0.24
Prior history of endocarditis	5 (4)	3 (4)	2 (6)	0.62
Conduit age, yrs	9.5 (3.0-25.0)	9.0 (3.0-25.0)	9.9 (3.4-15.4)	0.86
Conduit size, mm	15 (9-16)	15 (9-16)	16 (12-16)	0.40
Existing conduit stent from prior procedure	23 (20)	18 (21)	5 (15)	0.61
Doppler maximum RVOT gradient, mm Hg	56 (5-122)	55 (5-105)	64 (10-122)	0.009
Pulmonary regurgitation ≥moderate	92 (79)	71 (87)	21 (66)	0.011
Indication for implant				0.011
Conduit stenosis	24 (21)	12 (14)	12 (36)	
Conduit regurgitation	41 (31)	34 (41)	7 (21)	
Mixed stenosis and regurgitation	52 (44)	38 (45)	14 (42)	
Pre-implant catheterization data				
Narrowest angiographic conduit diameter, mm	11.0 (4.0-23.0)	11.2 (6.0-23.0)	11.0 (4.0-19.0)	0.69
Angiographic (surgical implant diameter ratio*	0.78 (0.30-1.58)	0.79 (0.40-1.44)	0.75 (0.10-2.58)	0.58
Conduit severely calcified	49 (42)	33 (39)	16 (49)	0.36
Peak RVOT gradient, mm Hg	26 (2-98)	25 (2-69)	31 (5-98)	0.040
Right ventricle/aorta systolic pressure ratio	0.66 (0.32-1.50)	0.64 (0.32-1.40)	0.68 (0.32-1.50)	0.16

Values are median (range) or n (%). *Implant diameter refers to the diameter of the conduit at the time of surgical implant; angiographic diameter refers to the narrowest angiographic diameter in the catheterization lab.
RVOT = right ventricular outflow tract; TPVR = transcatheter pulmonary valve replacement.

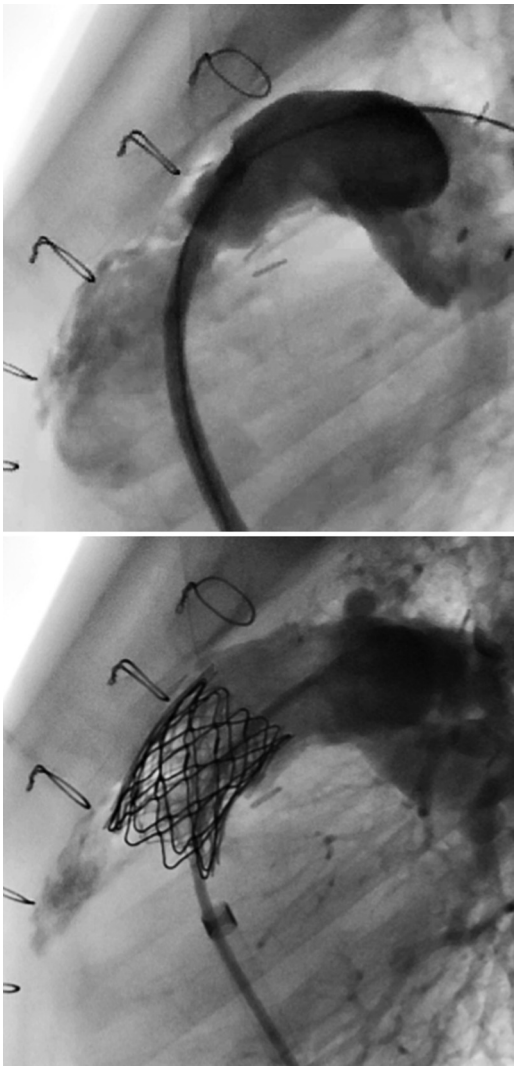
Palmaz XL P4010 in 15 patients, and ev3 MaxLD (Medtronic) in 6 patients—whereas 19 patients received a covered CP stent (NuMED, Hopkinton, New York) either prophylactically (n = 8) or for exclusion of a stable conduit tear (n = 11). The Melody valve was mounted on the 18-mm Ensemble delivery system in 44 (34%) patients, and 2 patients (both with Contegra conduits) underwent modified delivery on a 14- or 16-mm balloon. The Melody valve was successfully deployed at the intended location in all of the implanted patients (Figures 2 and 3). Concomitant pulmonary artery angioplasty or stenting was performed in 24 (21%) patients, and an atrial septal defect was closed in 4 patients. One patient underwent iliac vein stenting for a stenosis that was detected during the catheterization. Another patient underwent placement of an occlusion device for a contained tear of the main pulmonary artery.

EARLY OUTCOMES. There was a significant reduction in peak RVOT pressure gradient and RV to aortic systolic pressure ratio, and no significant PR, after TPVR, with no difference between homograft and Contegra groups (Table 3). The median final conduit diameter in the implanted cohort measured 19 mm (range: 14 to 23 mm), with no difference according to conduit type, and was a median of 29% larger than the implanted diameter. Post-implant conduit-related factors are depicted according to original conduit size in Figure 1. There were no significant differences in post-implant gradient or final conduit diameter according to original conduit type or size. Heavily calcified conduits were more likely to have multiple pre-stents placed than non/mildly calcified conduits (58% vs. 28%; OR: 3.6; 95% CI: 1.4 to 9.0; p = 0.006) and had a smaller final angiographic/surgically implanted diameter ratio (1.26 [range: 0.98 to 1.50] vs. 1.32 [range: 0.92 to 2.22]; p = 0.020). Although hemodynamic outcomes did not differ according to conduit type, patients with an aortic homograft were more likely to be implanted with an 18 mm or smaller delivery system (62% vs. 33%; OR: 1.9; 95% CI: 1.1 to 3.1; p = 0.015) and accordingly had smaller final angiographic/implanted surgical diameter ratio (1.21 [range: 0.91 to 2.13] vs. 1.31 [range: 0.92 to 2.22], p = 0.026) after implant than did those with a pulmonary homograft. Both groups had similar pre-implant diameters and degree of narrowing relative to the original conduit diameter.

PROCEDURAL ADVERSE EVENTS. Confined, hemodynamically stable conduit tears occurred in 16% of implanted patients, with a similar incidence in homograft and Contegra groups. Of the 19 confined tears, 11 were treated with a covered stent, and 8 were either excluded with the Melody valve or not treated. In addition, 3 nonimplanted patients had confined tears (no covered stents), and 1 had a conduit rupture that was treated with a covered stent and surgical conduit replacement. Three other patients had pulmonary artery injuries related to sheath advancement or guidewire perforation: 2 of these were treated with vascular occlusion devices, 1 of whom also had a chest tube placed for a single day. One patient developed a femoral artery pseudoaneurysm that was treated with compression, and 1 remained intubated for 24 h to facilitate femoral hemostasis. Other events included fracture and distal embolization of a small fragment of a long sheath in 1 patient, and embolization of a bare-metal pre-stent into the RV treated by stabilization with a second stent in 1 patient.

Among implanted patients, there were no differences in the incidence of conduit tear according to surgical conduit type or the severity of calcification. However, patients reported to have a conduit tear had

FIGURE 2 Angiograms of TPVR in 15-mm Aortic Homograft



These angiograms are from a 10-year-old, 27-kg patient with a 15-mm aortic homograft conduit. **(Top)** The conduit was heavily calcified along its entire length and had a focal narrowing (6.8 mm minimum) at the level of the valve, and a peak gradient in the catheterization lab of 41 mm Hg. **(Bottom)** The final lumen diameter after transcatheter pulmonary valve replacement (TVPR) was 15.6 mm. This case illustrates a conduit that was not substantially enlarged beyond its original diameter, but had no gradient after TPVR.

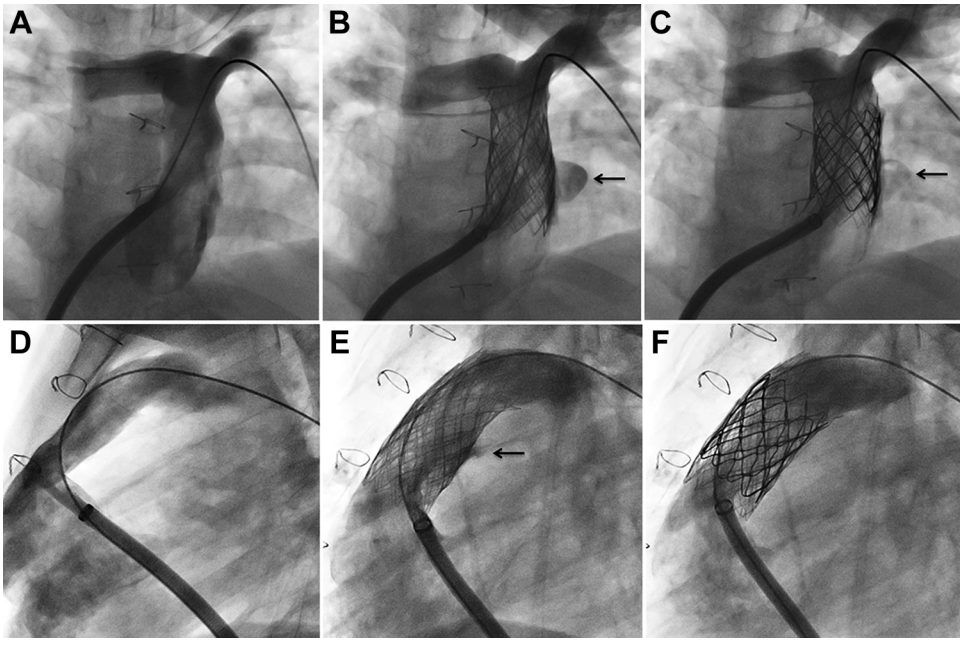
higher pre-TPVR mean Doppler gradient (median 65 mm Hg [range: 40 to 100 mm Hg] vs. 55 mm Hg [range: 5 to 122 mm Hg]; $p = 0.007$), higher pre-TPVR directly measured peak gradient (median 38 mm Hg [range: 22 to 59 mm Hg] vs. 25 mm Hg [range: 2 to 98 mm Hg]; $p = 0.001$), smaller angiographic diameter (9.0 mm [range: 6.8 to 14.0 mm] vs. 11.8 mm [range: 4.0 to 23.0 mm]; $p < 0.001$), smaller angiographic/surgically implanted diameter ratio (0.64 [range: 0.45 to 1.0] vs. 0.80 [range: 0.25 to 1.58]; $p = 0.008$), larger first balloon/angiographic conduit diameter ratio (1.50 [range: 1.17 to 2.97] vs. 1.31 [range: 0.87 to 2.75]; $p < 0.001$), and larger final balloon/angiographic conduit diameter ratio (2.00 [range: 1.50 to 2.97] vs. 1.54 [range: 1.07 to 3.50]; $p < 0.001$). There were no differences in outcomes between patients who did and did not have a conduit tear.

FOLLOW-UP. All patients were alive at most recent follow-up, a median of 2.0 years (range: 0.1 to 7.5 years; mean 2.2 years) after TPVR. Eight patients underwent reinterventions on the RVOT, the details of which are summarized in Table 4. Freedom from RVOT reintervention was 97 ± 2% at 2 years and 89 ± 5% at 4 years (Figure 4). No risk factors for shorter freedom from RVOT reintervention were identified, including original conduit type or size. Three patients underwent cardiac reinterventions not related to the Melody valve: heart transplant for persistent RV failure in 1, ventricular septal defect device closure in 1, and re-expansion of an RVOT stent (proximal to the Melody valve) and pulmonary artery stent in 1.

Five patients (2 conduits and 3 with homografts) were diagnosed with endocarditis, 4 with viridans group *Streptococcus* and 1 with *Hemophilus parainfluenza*, 1.2 to 6.5 years after TPVR None of these 5 patients had a prior history of endocarditis. Four of these patients underwent RVOT reintervention related to endocarditis, as detailed in Table 4. Freedom from endocarditis at 2 and 4 years was 97 ± 2% and 91 ± 4%, respectively, with an estimated endocarditis incidence rate of 2.0% per patient-year. No risk factors for development of endocarditis were identified.

Among patients who had the original Melody valve in place, the maximum Doppler gradient on most recent echocardiography ranged from 0 to 60 mm Hg (median 20 mm Hg) and was significantly lower than pre-implant. In the patient with a 60-mm Hg gradient, the obstruction was all subvalvar. All patients had no or trivial PR except for 2 in whom it was mild and 1 in whom it was moderate (3 years after implant). On multivariable analysis, smaller final conduit diameter (OR: 0.67; 95% confidence interval: 0.49 to 0.91; $p = 0.010$), higher post-implant gradient measured in the catheterization lab (OR: 1.11; 95% CI: 1.01 to 1.23; $p = 0.040$), and heavier weight at follow-up (OR: 1.06; 95% CI: 1.02 to 1.09; $p = 0.001$) were associated with follow-up maximum Doppler gradient ≥30 mm Hg.

FIGURE 3 Angiograms of TPVR in a 14-mm Unsupported Contegra Conduit



This series of angiograms are **(A to C)** frontal-cranial and the corresponding **(D to F)** lateral images from a 10-year-old, 25-kg patient who underwent transcatheter pulmonary valve replacement (TPVR) for mixed obstruction and regurgitation of a 14-mm unsupported Contegra conduit that had been implanted 9.5 years earlier. **(A, D)** There was anteroposterior narrowing (9.0 mm narrowest anteroposterior diameter, proximally, compared with 14 mm at the same level in lateral dimension; 12.4 mm narrowest diameter, distally) along the entire length of the conduit to the bifurcation. **(B, E)** After placement of 3 bare-metal stents extending the full length of the conduit, there was substantial enlargement and a contained tear along the leftward aspect of the conduit **(arrows)**. **(C, F)** After the Melody valve was implanted and post-dilated with a 20-mm high-pressure balloon, the conduit measured 19 mm at its narrowest. There was no residual gradient, and a small amount of residual flow entering the tear **(arrow)** around the proximal end of the Melody valve.

DISCUSSION

MELODY VALVE IMPLANT INTO SMALL DIAMETER EXPANDABLE CONDUITS. The U.S. IDE trial limited enrollment to patients with an implanted conduit diameter ≥16 mm and a sizing balloon waist ≥14 mm after pre-dilation (8), and the instructions for use specified that the Melody valve was indicated in patients with a conduit that was 16 mm or larger at implant. Even though 16 mm was within the inclusion criteria, it was a very small subset of the study cohorts with only 5% of patients in the original Melody valve trials had a 16-mm conduit (1,8,9,11). As this study shows, however, TPVR into homograft and Contegra conduits that were originally ≤16 mm is relatively common at some centers. Although a subset of these patients was small, most were >30 kg (the threshold for inclusion in the IDE trial) and >10 years of age, demonstrating that this cohort of patients with small conduits was not simply limited to young children.

In most patients, the conduit was enlarged beyond its original diameter, with a low post-implant gradient and no significant PR. Moreover, freedom from RVOT reintervention appeared comparable to reported data from other studies. These findings suggest that TPVR into small conduits may be an effective strategy even in larger patients and may not be limited to short-term benefit, even relative to surgical conduit replacement or revision (15,16). In the IDE trial, it was specified that conduit pre-dilation should not exceed 110% of the original conduit diameter (8), but the current study, as well as prior investigations of TPVR in general (3) and bare-metal stenting of smaller RVOT conduits (17), confirms that conduits can safely be enlarged substantially beyond that arbitrary threshold. Naturally, care should be taken in expanding conduits to that extent, with gradual dilation beginning at smaller diameters and progressively increasing balloon size after confirming conduit integrity with interval angiography.

There are limited published data from which to understand the prevalence of TPVR into small conduits beyond the centers included in this study. There have been several reports of TPVR in small patients, many of whom had concomitantly small conduits (9,10), and a series focused on Contegra conduits, some of which were <16 mm as well (2). A recent study reported 11 patients with conduits <16 mm, 10 of whom (those with an expandable conduit) were included in the present series (11). Those studies also found that TPVR into small patients and small conduits was feasible and yielded excellent outcomes, supporting the findings of this larger series.

However, also similar to this study, those reports were selected series that did not necessarily shed light on which small patients and small conduit should be considered for TPVR. Compared with a recent analysis of data from prospective Melody valve trials, which reported a median angiographic/surgically implanted conduit diameter ratio of 0.61 for homografts (3), the conduits treated in the current series were less constricted, with a median ratio of 0.79. Thus, patients in this series generally had conduits with relatively modest shrinkage from baseline. It is likely that there were many patients with small conduits who were not referred for potential TPVR at these study centers. Accordingly, this report should not be interpreted as advocating indiscriminant TPVR in patients with small conduits, but rather that some patients with small conduits can undergo TPVR with substantial enlargement of the conduit and durable improvement in RVOT hemodynamics. Although this study does not define completely which patients with implanted conduits ≤16 mm should and should not undergo TPVR, it is reasonable to recommend that those with a small conduit and primary PR be considered for TPVR, recognizing that it is often possible to enlarge the conduit 20% or more beyond its implanted diameter.

TABLE 3 Procedural and Post-Implant Data in TPVR Patients According to Surgical RVOT Conduit Type

	Total (N = 117)	Homograft (n = 84)	Contegra (n = 33)	p Value
Procedural data				
First pre-dilation balloon diameter, mm	16 (8–24)	16 (8–22)	18 (8–24)	0.028
First balloon/angiographic diameter ratio*	1.33 (0.87–3.00)	1.30 (0.87–2.70)	1.34 (0.96–3.00)	0.10
Coronary compression testing performed	75 (64)	57 (68)	18 (55)	0.20
Confined conduit tear	19 (16)	14 (17)	5 (15)	0.84
Pre-stent before TPVR	105 (90)	74 (88)	31 (94)	0.52
More than 1 pre-stent placed	43 (37)	33 (39)	10 (30)	0.36
Covered stent placed	19 (16)	14 (17)	5 (15)	0.84
Delivery system 18 mm or smaller	46 (39)	35 (42)	11 (33)	0.41
TPV post-dilated	50 (43)	31 (37)	19 (58)	0.048
Largest balloon/surgical implant diameter ratio*	1.25 (0.88–2.20)	1.23 (0.88–2.20)	1.29 (0.88–2.00)	0.35
Post-implant data				
Final angiographic conduit diameter, mm	19 (14.0–23.0)	19 (14.4–23–0)	19 (14.0–23.0)	0.58
Final angiographic/surgical implant diameter ratio*	1.29 (0.88–2.20)	1.29 (0.91–2.20)	1.25 (0.88–1.90)	0.98
Peak RVOT gradient, mm Hg	7 (0–29)	7.5 (0–29)	6 (0–22)	0.76
Right ventricle/aorta systolic pressure ratio	0.39 (0.23–1.10)	0.39 (0.23–1.10)	0.39 (0.27–0.64)	0.56

Values are median (range) or n (%). *Implant diameter refers to the diameter of the conduit at the time of surgical implant; angiographic diameter refers to the narrowest angiographic diameter in the catheterization lab; first balloon refers to the first pre-dilation balloon; and largest balloon refers to the largest balloon used to expand the conduit/valve, whether delivery balloon or post-dilation balloon.

Abbreviations as in Table 2.

CONDUIT-RELATED FACTORS AND OUTCOMES. Despite the well-known tendency of homograft

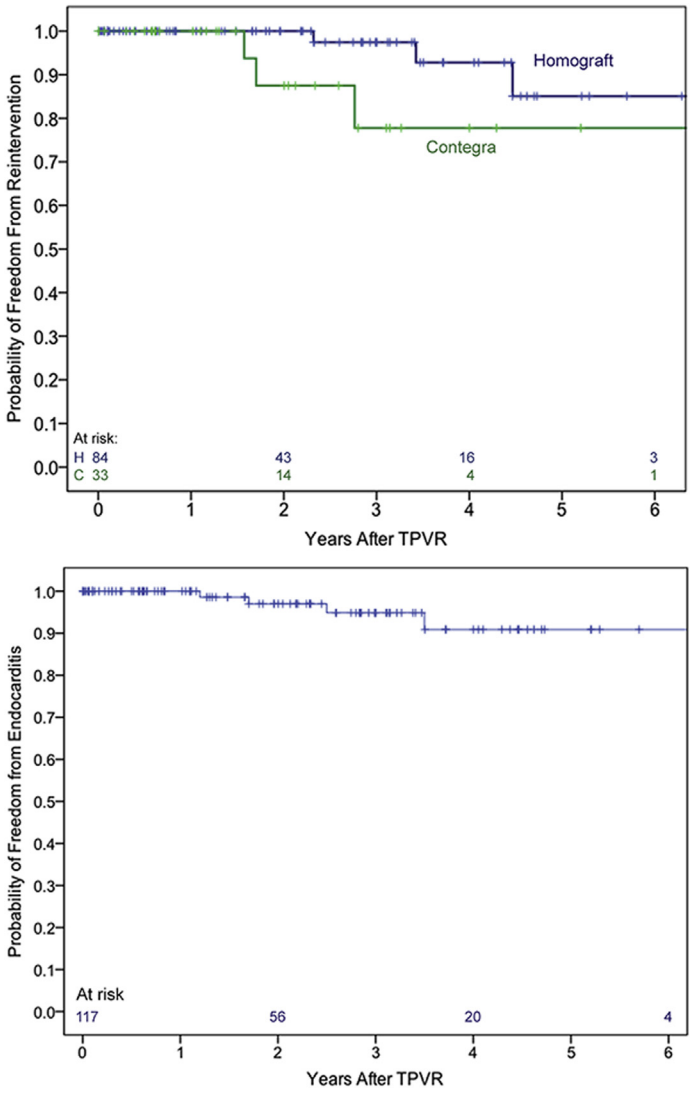
TABLE 4 Details of RVOT Reinterventions in 8 Patients

Age at TPVR (yrs)	Weight at TPVR (kg)	Conduit Type	Original Conduit Diameter (mm)	Final/Implanted Conduit Diameter Ratio	Post-Implant Peak Gradient (mm Hg)	Duration After TPVR (yr)	Intervention	Indication
10.5	27.0	Homograft (Ao)	15	1.04	0	4.5	Balloon dilation	Suspected stenosis*
15.7	60.0	Homograft (Ao)	16	1.25	5	6.6	Balloon dilation†	Endocarditis, stenosis
11.7	24.0	Homograft (Ao)	15	1.15	4	3.4	Stent†	Endocarditis, stenosis
10.5	32.0	Contegra	16	1.13	16	7.2	Redo TPVR	Stenosis
15.0	84.4	Homograft (P)	14	1.36	15	2.3	Redo TPVR	Stent fracture, stenosis
9.5	37.0	Contegra	16	1.25	12	1.7	Conduit replacement	Endocarditis, stenosis
10.5	29.8	Contegra	14	1.43	15	2.8	Conduit replacement	Endocarditis
15.0	48.3	Contegra	16	1.08	22	1.6	Conduit replacement	Stenosis

*Stenosis suspected by echocardiography but only mild at catheterization. Conduit/TPV still dilated, reducing peak gradient from 20 mm Hg to 8 mm Hg. †These patients underwent transcatheter intervention acutely, followed 6-8 weeks later by conduit replacement.

Ao = aortic homograft; P = pulmonary homograft; other abbreviations as in Table 2.

FIGURE 4 Kaplan-Meier Curves for Freedom From Reintervention



These Kaplan-Meier curves depict **(top)** freedom from reintervention after transcatheter pulmonary valve replacement (TPVR) for patients with homograft and Contegra conduits ($p = 0.24$ by log-rank testing), and **(bottom)** freedom from endocarditis after TPVR.

conduits to degenerate over time, there have been few analyses evaluating the degree of conduit shrinkage or narrowing or calcification and few comparative assessments of these processes in pulmonary homograft, aortic homograft, and Contegra conduits (18-20). In the current selected cohort of patients with sufficient dysfunction to recommend intervention, there was no gross difference in the frequency of major fluoroscopic calcification, and no difference in the relative narrowing from implant to catheterization between conduit types. There were, however, notable correlations between conduit obstruction and calcification, irrespective of conduit type, with smaller angiographic or surgically implanted conduit diameter ratios in more severely calcified conduits. This corresponded to a modestly reduced capacity for conduit expansion, as heavily calcified conduits had a smaller final or surgically implanted conduit diameter ratio. Notably, there was no association between severity of calcification and conduit tears, which should help dispel the common misconception that heavier conduit calcification imparts a greater risk of rupture during dilation.

The frequency of confined conduit tears and conduit rupture in this series was similar to previous studies of TPVR and isolated conduit angioplasty or stenting (21,22). In IDE trial reports, the incidence of conduit tear or rupture was lower than the 19% frequency in this series, but the IDE trial and others did not routinely report self-limited conduit tears that did not lead to subsequent intervention. When appropriate comparison cohorts are considered (21,22), there is no evidence that conduit tears are more common in small conduits or small patients. Pooled estimates from the reported literature on TPVR, which did not include patient-level data or establish consistent definitions of tear or rupture, underestimated the frequency of conduit tears (23). Aside from the issues of frequency and severity, the mechanisms of conduit wall injury are not entirely clear, although all were observed during conduit preparation rather than after Melody valve implant. Notably, neither the severity of calcification or the original conduit diameter were associated with the likelihood of conduit tear. However, conduit tears were associated with smaller angiographic diameter and angiographic/surgically implanted diameter ratio, and with more aggressive initial angioplasty (i.e., larger first balloon/narrowest angiographic conduit diameter ratio). None of the confined tears in this cohort progressed to rupture, and their significance, aside from implantation of covered stents in some patients, appeared to be minimal, as hemodynamic and clinical outcomes were similar to patients without tears. Nevertheless, conduit rupture, although uncommon, remains a potentially serious complication, and ongoing surveillance and analysis will be necessary to provide insight into factors associated with this outcome.

Although most conduits were the same size or smaller than at implant, 14% were measured to be larger than the original implanted diameter, and 4% were at least 20% larger. A majority of these were pulmonary homografts. This phenomenon is known to occur, although the frequency and associated factors are not known, and there did not appear to be

any increased risk of conduit injury in this subset of patients. On the basis of the frequency of this finding and outcomes in these patients, the original implanted diameter alone should not be a reason to exclude patients from consideration for TPVR. Rather, patients should be evaluated on the basis of clinical status, hemodynamics, anatomic appearance of the conduit, and prospect of benefit.

STUDY LIMITATIONS. This study suffers from the limitations intrinsic to a retrospective review with relatively few adverse outcomes. The decisions to send patients to the catheterization lab for potential TPVR, and to perform TPVR, were discretionary and cannot be generalized beyond this cohort. Fluoroscopic assessment of conduit calcification and conduit tears was determined by each investigator, and may not have been consistent across the cohort. However, the grading was binary for each of these measures, which should minimize the implications of minor differences. Similarly, we did not perform detailed morphological assessment of conduit tears, limiting assessment of potential mechanistic differences and of risk factors.

CONCLUSIONS

In this preliminary experience, TPVR with the Melody valve into expandable small diameter conduits was feasible and safe, with favorable early and long-term procedural and hemodynamic outcomes. Adverse procedural outcomes and durability of the results did not appear to differ dramatically from published series in larger conduits and valves. Studies with more patients and longer follow-up will be needed to confirm these encouraging findings and to provide deeper insight into factors associated with the ability to enlarge conduits substantially beyond the original diameter or with significant conduit wall injury. However, it is reasonable to conclude from this study that TPVR should be considered as an option for treatment of some dysfunctional RVOT conduits that were ≤16 mm at the time of implant.

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PERSPECTIVES

WHAT IS KNOWN? The Melody valve is approved for the treatment of dysfunctional RVOT conduits ≥16 mm in diameter at the time of implant.

WHAT IS NEW? TPVR with the Melody valve into expandable small diameter conduits ≤16 mm was feasible and safe, with favorable early and long-term procedural and hemodynamic outcomes.

WHAT IS NEXT? Studies with more patients and longer follow-up will be needed to confirm these encouraging findings and to provide deeper insight into factors associated with the ability to enlarge conduits substantially beyond the original diameter or with significant conduit wall injury.

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