The first human transcatheter pulmonary valve (TPV) implant was reported in 2000, and since that time >6000 procedures have been performed worldwide. In 2010, after a multicenter trial comprising 150 patients, the Melody TPV (Medtronic Inc, Minneapolis, MN) was approved for use in the United States under a Humanitarian Device Exemption. Patients weighing <30 kg were excluded from the initial clinical trial and, as such, limited data exist regarding the feasibility, safety, and efficacy of this procedure in small children with dysfunctional right ventricle–pulmonary artery (RV-PA) conduits.

Methods

Study Design

This study was performed as a multicenter retrospective review designed to capture all patients <30 kg who underwent cardiac catheterization with intention to place a TPV at the initial 3 sites involved in the US Investigational Device Exemption (IDE) Melody valve trial (Boston Children’s Hospital, Miami Children’s Hospital, and Children’s Hospital of New York) through May 2011. Techniques for Melody valve implant in these smaller patients were generally similar to what has been reported previously. Any modifications, including vascular access site, were at the discretion of the operator and are reported in the Results section.

Data collected included demographic, preprocedural, procedural, and follow-up data. Patients were classified into 1 of 3 groups based on preprocedural findings: primary conduit stenosis, primary conduit regurgitation, mixed conduit stenosis, and regurgitation. Data were reviewed and analyzed to assess the feasibility of Melody valve implantation in this cohort of patients.

Conclusions

Percutaneous TPV replacement can be performed in small children with good procedural and early hemodynamic results in the majority of patients. (Circ Cardiovasc Interv. 2014;7:142-148.)

Key Words: cardiac catheterization ● congenital ● heart defects, congenital ● pulmonary valve
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Data Analysis
Descriptive and summary data are presented as percentage of total for count data, median (minimum to maximum) for continuous variables with non-normal distribution, and mean (SD) for continuous variables with normal distribution. Paired 2-tailed t-tests were used to compare continuous paired data (eg, pre-TPV versus post-TPV implant RV-PA gradient).

Results
Patient Characteristics
Between January 2008 and May 2011, a total of 25 children with a median age of 8 years (3.4–14.4 years) and median weight of 21.4 kg (13.8–29.0 kg; 10 patients <20 kg) underwent cardiac catheterization with intention to undergo TPV implantation for treatment of conduit dysfunction (Table 1). The majority of patients (72%) had an initial diagnosis of tetralogy of Fallot and had undergone ≥2 previous surgeries (84%). Most patients (84%) had a homograft RV-PA conduit, and in all but 4 patients the original conduit was ≥16 mm (the diameter specified in the instructions for use); in the other 4 patients, the original conduit diameter was reported to be 15 (n=3) or 12 mm (n=1; augmented surgically at previous reoperation).

Procedural Outcomes
Two patients who underwent cardiac catheterization did not undergo TPV implantation. In 1 patient, coronary artery compression was evident when selective coronary angiography was performed with simultaneous balloon inflation within the conduit, suggesting the patient would be at significant risk for coronary artery compression with TPV implantation. In another patient, who weighed 20 kg, the delivery system could not be advanced beyond the common femoral vein because of what seemed to be significant size mismatch between the delivery system tip and the vein. There were no cases in which TPV implant was abandoned once the delivery system reached the right atrium because of inability to advance the delivery system through the heart.

The remaining 23 patients underwent successful TPV implantation, with prestenting of the conduit with ≥1 bare metal stents at the same catheterization in 8 (3 other patients had existing bare metal stents in the conduit from a previous catheterization). The median largest predilation balloon diameter was 18 mm (14–22 mm), and the median largest predilation balloon diameter:implanted conduit diameter ratio was 1.0 (0.78–1.29). The Melody valve was mounted on the 18-mm

Data presented as number (% of total), median (minimum-maximum), or mean±SD. TPV indicates transcatheter pulmonary valve.

*In the 3 patients with bioprosthetic valves, the original valve sizes were 19 mm in 2 patients and 23 mm in 1 patient; the 12-mm homograft conduit was augmented surgically at previous reoperation.

Table 1. Baseline Precatheterization Demographic and Diagnostic Information

<table>
<thead>
<tr>
<th>Patients</th>
<th>25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14</td>
</tr>
<tr>
<td>Female</td>
<td>11</td>
</tr>
<tr>
<td>Age, y</td>
<td>8.0 (3.4–14.4)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>21.4 (13.8–29.0)</td>
</tr>
<tr>
<td>Original diagnosis</td>
<td></td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>9 (36)</td>
</tr>
<tr>
<td>Tetralogy of Fallot with absent pulmonary valve syndrome</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Tetralogy of Fallot with pulmonary atresia</td>
<td>7 (28)</td>
</tr>
<tr>
<td>Truncus arteriosus</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Double-outlet right ventricle or transposition of the great arteries</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Aortic valve disease, previous Ross procedure</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Type of conduit</td>
<td></td>
</tr>
<tr>
<td>Pulmonary homograft</td>
<td>11 (44)</td>
</tr>
<tr>
<td>Aortic homograft</td>
<td>10 (40)</td>
</tr>
<tr>
<td>Contegra</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Bioprosthetic valve</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Conduit diameter at the time of implant, mm*</td>
<td>17 (12–23)</td>
</tr>
<tr>
<td>Number of previous surgeries</td>
<td>2 (1–5)</td>
</tr>
<tr>
<td>Primary indication for TPV replacement</td>
<td></td>
</tr>
<tr>
<td>Stenosis</td>
<td>5 (20)</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>7 (28)</td>
</tr>
<tr>
<td>Mixed stenosis and regurgitation</td>
<td>13 (52)</td>
</tr>
<tr>
<td>Conduit mean Doppler gradient, mm Hg</td>
<td>31±13</td>
</tr>
<tr>
<td>Stenotic cohort</td>
<td>42±12</td>
</tr>
<tr>
<td>Regurgitation cohort</td>
<td>16±14</td>
</tr>
<tr>
<td>Mixed stenosis and regurgitation cohort</td>
<td>32±5</td>
</tr>
<tr>
<td>Pulmonary regurgitation by echocardiography</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Trace</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Mild</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Moderate</td>
<td>5 (21)</td>
</tr>
<tr>
<td>Severe</td>
<td>15 (62)</td>
</tr>
</tbody>
</table>

WHAT IS KNOWN

• Transcatheter pulmonary valve replacement within dysfunctional right ventricle to pulmonary artery conduits is safe and effective in patients ≥30 kg.
• There is limited to no published data regarding the feasibility and effectiveness of percutaneous transcatheter Melody valve implantation in smaller children.

WHAT THE STUDY ADDS

• This is the largest and most substantial information regarding feasibility and short-term outcomes of transcatheter pulmonary valve replacement in children <30 kg.
• This article highlights the technical aspects of this procedure in smaller children.
• The results are encouraging and suggest that percutaneous Melody valve implantation in small children is safe and effective in the short term; more experience and follow-up are needed.

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Ensemble delivery system in 11 patients (48%), 3 of whom had an initial conduit diameter of 15 mm; the 20-mm delivery system was used in 9 patients (39%), 1 of whom had an initial conduit diameter reported to be 12 mm (this conduit seemed larger and in fact had been surgically augmented at a previous reoperation and was expanded and prestented to a diameter of 18–19 mm); and the 22-mm delivery system was used in 3 patients (13%). The median Ensemble delivery system size:implanted conduit diameter ratio was 1.06 (0.87–1.29).

The TPV was deployed via percutaneous access in all patients: through the femoral vein in 17 (74%), the right internal jugular vein in 4 (17%), and the left subclavian vein in 2 (9%; Figures 1–3). Notably, the 5 smallest patients in the series, who all weighed <18 kg, had the Melody valve deployed via superior (ie, jugular or subclavian) venous access. No modifications of the delivery system or crimping technique were reported.

There was significant reduction in conduit obstruction and pulmonary regurgitation after TPV implant (Table 2; Figure 4). Two patients had mild pulmonary regurgitation after TPV implantation because of a small paravalvar leak (n=1) or distortion of the proximal portion of the TPV secondary to encroachment of infundibular muscle (n=1); all other patients had trivial/absent pulmonary regurgitation.

Seven significant adverse events occurred in 7 patients, 4 of which were considered major. There were 5 confined conduit tears, none of which were associated with hemodynamic compromise or hemothorax, and none were managed surgically. Two of the tears were considered major and were treated with placement of a covered stent before further conduit rehabilitation, and the other 3 were considered minor and simply covered with the TPV. In 1 patient, a small, self-limited abdominal hematoma developed presumably secondary to trauma from an attempt to pass the delivery system across a small common femoral-inferior vena cava junction. This patient underwent successful TPV implantation from a jugular venous approach and required a single blood transfusion before discharge 48 hours after the procedure. Another patient had a guidewire-induced peripheral PA branch perforation during the TPV implant procedure, which was self-limited.

There were no deaths related to the TPV implant procedure. One patient with mixed conduit disease underwent TPV placement whereas, on extracorporeal membrane oxygenation, 1 day after having a left PA laceration during PA angioplasty, in an effort to improve hemodynamics and possible weaning from mechanical support. This patient ultimately died from complications related to the initial adverse event.

In addition to the aforementioned events, we encountered the need for unexpected additional vascular access in 5 patients (weight 15.6–25 kg) because of size mismatch between the relatively large Melody valve delivery system and venous structures. This size mismatch prevented TPV implantation in 1 of these patients, who subsequently underwent successful treatment of severe conduit stenosis with bare metal stents. In the remaining 4 patients, the TPV was successfully implanted after switching to an alternate access vein: the contralateral femoral vein in 2 patients and the right internal jugular vein in 2 patients.

**Follow-Up**

The patient at risk for coronary compression underwent successful surgical conduit replacement. The patient in whom size mismatch between the delivery system and femoral vein prevented successful TPV implantation underwent successful bare metal stenting and is awaiting recatheterization for planned TPV implantation.
Variables after initial implant. One patient underwent elective conduit treatment with a second TPV implant 2.1 years and 7 months later. Two of the patients without a prestented conduit implant were followed for a median of 16 months (1–39 months). During follow-up, 4 patients underwent conduit reintervention. One patient with a 17-mm aortic homograft and regurgitant at the time of catheterization, 3.5 years after it was implanted, was substantially contracted and both stenotic and regurgitant at the time of catheterization, 3.5 years after surgery. After prestenting with 2 bare metal stents and TPV implant on a 20-mm delivery system through a femoral venous approach, the conduit obstruction was reduced from 37 mm Hg (peak) to 6 mm Hg, and the regurgitation was eliminated.

The 22 patients who were discharged after successful TPV implant were followed for a median of 16 months (1–39 months). During follow-up, 4 patients underwent conduit reintervention. One patient with a 17-mm aortic homograft continued to exhibit significant conduit stenosis after TPV implant and was referred for elective conduit replacement 16 months later. Two of the patients without a prestented conduit developed a clinically significant Melody valve stent fracture associated with moderate restenosis and were successfully treated with a second TPV implant 2.1 years and 7 months after initial implant. One patient underwent elective conduit replacement after medical therapy for bacterial endocarditis because of the presence of a mobile vegetation (the valve was functioning well, with no progression of obstruction or regurgitation), 1.6 years after TPV implant. Another patient was treated medically for presumed bacterial endocarditis without TPV involvement (8 months after implant) and maintained a well-functioning Melody valve. There were no reported subacute access site complications, development of TPV dysfunction, or other adverse events during follow-up.

On the most recent follow-up visit and echocardiogram (before reintervention, if applicable), there was no significant progression in the degree of TPV obstruction or regurgitation. Specifically, the average Melody valve mean Doppler gradient was $12.9\pm 9$ mm Hg, while regurgitation was mild in 2 patients and absent or trivial in the rest.

### Discussion

Melody valve implantation has been shown to be a safe and effective adjunct to surgery for the treatment of dysfunctional RV-PA conduits in older patients.8,9 Importantly, one inclusion criterion for the US IDE trial was weight ≥30 kg. In the initial European experience with TPV replacement, Khambadkone et al7 reported excellent results in 58 patients whose median age and weight were 16 years (9–43 years) and 56 kg (25–110 kg), respectively. Although an inclusion criterion for this cohort was weight ≥20 kg, the smallest patient was 25 kg, and the overwhelming initial reported European experience with TPV replacement has been with larger patients.8,9

Because the initial international experience with TPV replacement was encouraging, widespread distribution and use of the Melody valve has followed. To date, a publication has evaluated the use of the Melody valve specifically in the young.10 In that cohort, Vezmar et al10 included 28 adolescents with a median age of 14.9 years and a median weight of 57.7 kg, but the smallest patient weighed 40 kg. Although those data, along with the experience of Lurz et al,11 support the effectiveness of TPV replacement in younger patients, they do not necessarily reflect the feasibility or clinical impact of TPV placement in smaller patients. Therefore, although preliminary, the current study of patients <30 kg, including 10 patients <20 kg, provides the most substantial information about the feasibility and outcomes of Melody valve therapy in small children. Based on this limited experience, it seems that similar acute and short-term hemodynamic results can be achieved with TPV replacement in small children as in previously reported, older and larger populations.6–11

The deleterious effects of conduit dysfunction on the RV have been well reported.12–16 As we have learned more about the effects of chronic volume and pressure overload on the RV,15,16 the optimal point at which to intervene for RV outflow tract dysfunction remains a moving target. However, there seems to be a trend toward earlier intervention at many centers,17–19 and there is some evidence that earlier RV outflow tract intervention may provide a tangible benefit.20 A likely contributing factor affecting this trend is the ability to restore conduit function with less invasive modalities, namely TPV placement. It would seem reasonable to intervene earlier in these patients if the risk benefit balance supports it. With time, this will hopefully include clearer and widely accepted

### Table 2. Acute Hemodynamic Changes (n=23)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline Hemodynamics</th>
<th>Postimplantation</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV systolic pressure, mm Hg</td>
<td>65.2±23.5</td>
<td>46.8±15.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RV/aortic pressure ratio</td>
<td>0.75±0.27</td>
<td>0.45±0.16</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RV-PA gradient, mm Hg</td>
<td>29.4±15.7</td>
<td>8.8±6.0</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

PA indicates pulmonary artery; and RV, right ventricle.
indications for TPV placement, leading to improved patient selection for this application.

Although the results of the study are encouraging, it is important to acknowledge that the technical aspects of TPV replacement in small children can make this a more challenging procedure. Although assessing and preparing the conduit with balloon angioplasty and bare metal stents can be performed routinely from the femoral venous approach, the size of the Melody valve delivery system may preclude deploying the valve from this approach for several reasons. An important potential limitation is passing the 22 Fr delivery system through the smaller lower extremity venous system as it was in some patients in this series, but it is not the only consideration. When loaded with a Melody valve, the distal portion of the delivery system has a relatively long section that is stiff, which can be prohibitive when trying to negotiate the tight sinuous catheter course that is required with femoral venous access through a small heart. Also, conduits and proximal branch PA segments are often relatively small and short in this patient population, sometimes with acutely angled branch PA origins and existing stents. These factors may limit the ability to obtain stable guidewire position or may otherwise complicate advancement of the delivery system tip sufficiently out into the PA system to deliver and deploy the TPV in the intended location.

In the present cohort, there was a relatively frequent unanticipated need for additional vascular access to achieve successful TPV replacement, which occurred most often in smaller patients. The inability to deliver the Melody valve successfully through the initial access site in these cases was most likely related to incompatibility of the relatively large delivery system with small femoral veins. Although this may reflect one of the existing limitations of the current technology, it also speaks to the need to consider alternate access sites for delivery of the valve. Empirically, it is our sense that delivery from a superior approach, either jugular or left subclavian vein, is not only feasible, but offers certain advantages in small patients, as a natural loop can be formed instead of the relatively tight sinuous catheter course when coming from the femoral venous approach. The 5 smallest patients in this cohort underwent TPV replacement from a superior approach, including 2 through left subclavian venous access, establishing this as a viable alternative access for TPV implant. Although navigation of the large, stiff delivery system through the heart and into the PAs is a potentially limiting factor, it did not prevent TPV implant in any patients in this series.

If Melody valve use is going to be expanded in this population of small patients, it may be important to further characterize the venous size requirements and necessity for preprocedural vascular imaging to better plan what access is appropriate in a given patient, or even if a percutaneous approach is feasible. We cannot make firm recommendations about precatheterization or intracatheterization evaluation of access vessels based on the present study, but it seems reasonable to perform a femoral venous angiogram if femoral access is obtained, to ascertain venous stenoses that might be at risk for disruption, particularly in patients who have been catheterized previously. In patients <20 kg, it may be worthwhile to consider a jugular venous approach, which was able to accommodate the delivery system in patients as small as 13.4 kg in this series, and generally provides a favorable catheter course. In some small children, hybrid implantation may be a good option, particularly if there is difficult anatomy or access limitations, or if it seems likely to improve the chances of successful implantation and outcome.21,22

**Figure 4.** Line graphs demonstrating the acute hemodynamic response in (A) systolic right ventricle (RV) pressure and (B) RV-pulmonary artery systolic gradient to transcatheter pulmonary valve (TPV) replacement for each subject in the cohort based on the primary indication for TPV replacement: square indicates stenosis; triangle, mixed; and circle, regurgitation.
The current Food and Drug Administration approval for Melody valve includes a recommendation for use in RV-PA conduits that were ≥16 mm in diameter at time of initial implant. Although the current cohort reflects a smaller patient population, 19 of the 23 patients who underwent successful TPV replacement met this recommendation. Of the remaining 4 patients, 3 patients had a conduit that was 15 mm in diameter at the time of initial implantation and 1 patient had a 12-mm diameter conduit (which had been augmented surgically and was expanded to 18–19 mm). The 1 patient who died secondary to complications of a previous PA laceration had a 15-mm conduit. The remaining 3 patients with a conduit diameter <16 mm all had a well-functioning Melody valve at last follow-up.

The US IDE trial incorporated a guideline not to expand the conduit beyond 110% of its initial diameter during the initial balloon dilation/assessment.6 We agree that this guideline should generally be observed, particularly when the mechanism of conduit dysfunction is stenosis with or without conduit shrinkage, but consideration for careful balloon expansion beyond this 110% guideline may be reasonable in some cases, given that occasional conduits may naturally enlarge with time.21 Although the initial size of the existing conduit will usually play a limiting role in the maximal achievable Melody valve diameter, it is possible that once a Melody valve is implanted in a small child at a diameter that is not large enough for an adult, it can be expanded further (and potentially larger than the originally placed conduit) as the patient grows, although we do not have data to this effect.

The incidence of major adverse events in the US IDE trial was 6%.2,6 In this cohort of small patients, 7 patients experienced significant procedural adverse events, 4 of which were considered major (16%). In the IDE trial, conduit rupture or dissection, typically associated with hemotherax and treated either with surgery or a covered stent, was considered a serious adverse event in that trial, but confined conduit tears were not specifically tracked. Of the 5 conduit tears in this series, all were confined, and none were associated with hemodynamic compromise or hemothorax: 3 conduit tears were thought to be minor, and 2 conduit tears were deemed more significant. Although we consider all of these events to be important, they may not be directly comparable with the IDE trial or other studies because of differences in reporting. Three of the 4 major adverse events (the 2 conduit tears and 1 self-limited PA perforation) have been reported in cohorts of larger patients5,6,7 and do not seem to occur at a substantially higher incidence in small patients. The only adverse event in this series that can be clearly linked to patient size was a hematoma at the femoral vein-inferior vena cava junction that required a blood transfusion postprocedure and no further interventions.

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Conclusions
TPV placement can be performed successfully in children <30 kg with good procedural and early hemodynamic results. However, alternative access sites, including the jugular or subclavian vein, were used frequently for Melody valve deployment, often because of inability to pass the delivery system through the femoral venous system. Technical considerations, including vascular access and wire position required for Melody valve delivery, should be considered carefully when planning TPV implant in small patients. Procedural adverse events were relatively common in this limited sample, but there were no procedural deaths related to the Melody valve implant or complications requiring surgery. Although this preliminary experience is encouraging, more experience and longer follow-up are needed before TPV replacement can be routinely recommended in small children.

Acknowledgments
We acknowledge and thank James E. Lock, MD, for his clinical contributions to this article.

Disclosures
Drs McElhinney, Hellenbrand, Vincent, and Zahn serve as proctors and consultants for Medtronic.

References


Feasibility and Short-Term Outcomes of Percutaneous Transcatheter Pulmonary Valve Replacement in Small (<30 kg) Children With Dysfunctional Right Ventricular Outflow Tract Conduits
Darren P. Berman, Doff B. McElhinney, Julie A. Vincent, William E. Hellenbrand and Evan M. Zahn

_Circ Cardiovasc Interv._ 2014;7:142-148; originally published online February 25, 2014; doi: 10.1161/CIRCINTERVENTIONS.113.000881
_Circulation: Cardiovascular Interventions_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-7640. Online ISSN: 1941-7632

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