Short-Term Performance of the Transcatheter Melody Valve in High-Pressure Hemodynamic Environments in the Pulmonary and Systemic Circulations

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Background—The Melody valve is approved for percutaneous pulmonary valve replacement in dysfunctional right ventricular outflow tracts. The function of this valve when subjected to high-pressure loads in humans is unknown. The aim of this study was to describe the immediate and short-term results of Melody valves implanted in a high-pressure environment.

Methods and Results—Definitions of a high-pressure system were established for Melody valves implanted in the systemic (ie, aortic or mitral position) and pulmonary (ie, right ventricular outflow tract conduit or tricuspid valve annulus) circulations. Implants in these environments were ascertained from databases of the 5 centers that participated in the US Investigational Device Exemption trial. Thirty implants met the inclusion criteria: 23 pulmonary circulation implants (all in the pulmonary position) systemic circulation implants (5 in the native aortic position, 1 in a left ventricle-to-descending aorta conduit, and 1 in the mitral annulus). All pulmonary circulation implants were performed percutaneously in the catheterization laboratory. A hybrid approach (surgical exposure for transcatheter implant) was used for 4 of the aortic implants. There were no procedure-related deaths. Three patients died of nonprocedure- and nonvalve-related causes. At 1 year, freedom from moderate to severe regurgitation was 100%, and freedom from mild regurgitation was 90%. Freedom from moderate to severe stenosis was 86% at 1 year.

Conclusions—Short-term performance of the Melody valve in high-pressure environments is encouraging, with good valve function in all patients. (Circ Cardiovasc Interv. 2011;4:00-00.)

Key Words: catheterization ▪ valves ▪ pediatrics ▪ hypertension pulmonary

The Melody valve (Medtronic Inc, Minneapolis, MN) was introduced more than a decade ago as a transcatheter alternative to pulmonary valve replacement for right ventricular outflow tract (RVOT) conduit dysfunction.1,2 Subsequent studies documented its acute and midterm benefit as a pulmonary valve implant.3–5 Because the Melody valve is manufactured using a venous valve (bovine jugular vein), there is concern about its suitability for use in high-pressure environments. There are limited published data on the performance of the valve under high pressure. The bovine jugular venous valve remained competent when placed in a high-pressure system in an experimental lamb model of acute aortic regurgitation, with preserved valve leaflet architecture in valves explanted up to 2 months after placement.6 A single case series has been published describing outcomes after Melody valve placement in 7 patients with pulmonary hypertension7; otherwise, it is unknown how the Melody valve will perform when subjected to higher pressure loads in humans, either acutely or over time. In this report, we describe 30 cases of Melody valve placement in human patients where the valve is subjected to a high transvalvar pressure gradient during valve closure.

Methods

Patients were from the 5 centers involved in the US IDE (Investigational Device Exemption) clinical trial of the Melody transcatheter pulmonary valve.6,8 All patients receiving the implant at these centers, both within and outside of the IDE trial, were eligible for inclusion in this study. Valves placed in the following locations were defined as being in a high-pressure system based on investigator consensus:

- Systemic circulation implants, including native aortic valve position (native valve or orthotopic prosthetic valve), heterotopic left
ventricle-to-aortic conduit, and mitral valve position in a systemic left ventricle.

- Pulmonary circulation implants, including RV-to-pulmonary artery (PA) conduit, bioprosthetic valve, or native/augmented RVOT (with high main PA pressure defined as a mean pressure >25 mm Hg) and tricuspid valve position, with a difference between the RV systolic pressure and mean right atrial pressure of >25 mm Hg.

**WHAT IS KNOWN**

- The Melody valve is approved for percutaneous pulmonary valve replacement in dysfunctional right ventricular outflow tracts.
- The functioning of this valve in a low-pressure environment is well established.

**WHAT THE STUDY ADDS**

- This initial small series describes the unique use of the Melody valve in the high-pressure environment of the aortic and mitral valves.
- Short-term follow-up of the Melody valve in a high-pressure environment demonstrates good valve function over 1 year.

Clinical information on results from diagnostic imaging modalities before and after placement of the valve was collected. Valve competence was assessed based on echocardiographic findings from the latest follow-up evaluation, according to the scale used in the US Melody valve trial. The IDE trial was conducted under an investigational device exemption (No. G050186), and all versions of and amendments to the protocol were approved by the Food and Drug Administration, the Center for Devices and Radiological Health, and the Institutional Review Board at each institution. The trial is registered at ClinicalTrials.gov (URL: http://www.clinicaltrials.gov; unique identifier: NCT00740870).

**Results**

Thirty patients met the inclusion criteria and comprised the cohort for this study. One of 2 patients who had a Melody valve implanted in the mitral valve position was described as a separate case report and was not included in this review (unpublished data). No tricuspid valve implants met the criteria for a high-pressure environment.

Twenty-nine valves were placed in the catheterization laboratory, 4 using hybrid surgical-transcatheter delivery and 1 implanted surgically. All valves were implanted successfully in the intended location.

**Pulmonary Circulation Implants**

A Melody valve was electively placed in the RVOT of 23 patients with pulmonary hypertension, as described in the inclusion criteria. Eleven of these patients underwent Melody valve implantation as part of the IDE trial. Ten implants were in valved homograft conduits, and 13 were in previously placed bioprosthetic valves or bioprosthetic valved conduits; the median size of the conduit or valve was 22 mm (minimum, 15 mm; maximum, 29 mm). The size of the delivery system used to deploy the Melody valve was 18 mm in 5 patients, 20 mm in 4, and 22 mm in 14. The majority of patients had tetralogy of Fallot with pulmonary atresia. The primary implant indication was pulmonary regurgitation in 9 patients, conduit stenosis in 5, and mixed stenosis and regurgitation in 9. The pre- and postimplant hemodynamics are shown in Figure 1. None of the Melody valves had more than mild regurgitation at a median follow-up of 12 months (minimum, 3 days; maximum, 3 years) (Figure 2). Four patients had moderate stenosis with Doppler echocardiography-derived maximum instantaneous gradients across the Melody valve between 41 and 55 mm Hg at latest follow-up, whereas mild stenosis (maximum gradient, 20–40 mm Hg) was present in 8 patients. Before implantation, 9 patients had significant clinical symptoms (New York Heart Association [NYHA] functional class III–IV); all of these patients were in NYHA class I or II at latest follow-up. Only 1 patient had deterioration of symptoms after Melody valve implantation, which was related to endocarditis in the context of intravenous drug use; this patient was in NYHA class II before implantation and deteriorated to NYHA class III. Patients with moderate to severe conduit regurgitation before Melody valve placement had significant acute increases in mean and
diastolic PA pressure (PAp) after Melody valve implant. The mean±SD PAp increased from 32±10 to 37±12 mm Hg (P=0.04), and the diastolic PAp increased from 19±4 to 24±8 mm Hg (P=0.04). Patients with trivial or mild regurgitation before implantation had no significant change in any PAp parameter after valve placement.

Systemic Circulation Implants
The Melody valve was placed in the native aortic valve position in 5 patients, in a left ventricle-to-descending aorta conduit in 1 patient, and in the mitral valve annulus in 1 patient (Table). All left-side heart implants were performed under compassionate or emergency use or outside of the Humanitarian Device Exemption-approved indications for use of the Melody valve. For the aortic implants, a portion of the wall of the vein was resected in the Melody valve sinuses to facilitate coronary blood flow (Figure 3). The procedure was performed urgently in 3 patients and electively in the others, who were poor candidate for surgical valve replacement. Transcatheter deployment of the Melody valve was performed in 6 patients, whereas surgical valve placement was performed in 1. A hybrid transcatheter approach was used in 4 patients, with a surgically exposed left ventricular apical approach adopted in 3 patients and access through cutdown on the innominate artery in 1. A percutaneous (femoral venous) antegrade transseptal approach was used to deploy the valve in 2 patients: the patient with the left ventricle-to-descending aorta conduit and the patient where the valve was implanted in the mitral valve annulus (Figure 4).

As depicted in Figure 2, none of the patients had more than mild Melody valve regurgitation at a median follow-up of 2.9 months (2 days–3 years). At latest follow-up, functional status was improved in all the living patients (NYHA class IV–II). In the aortic valve implant patients, there was a modest but statistically insignificant increase in systolic, mean, and diastolic aortic pressures and a decrease in pulse pressure after placement of a competent Melody valve.

Mortality
Three patients in this series died, with cause of death unrelated to the Melody valve or implant procedure. Two of these patients had undergone Melody valve implant in the systemic circulation on a compassionate or emergency use basis because of high surgical risk, whereas 1 had a rightsided implant. One of the left-sided implant patients was a 3-year-old child with hypertrophic cardiomyopathy, severe left ventricular outflow tract obstruction, severe aortic regurgitation, and moderate mitral stenosis. Several hours after an attempt at dilating the mitral valve, the patient became hypotensive and bradycardic and had a cardiac arrest for which extracorporeal membrane oxygenator support was initiated. Repeated attempts at weaning from extracorporeal membrane oxygenator support failed, presumably because of severe aortic regurgitation leading to myocardial ischemia and left ventricular dysfunction. The patient also experienced an intracranial hemorrhage that complicated the prospect of a surgical aortic valve replacement on cardiopulmonary bypass.

Under these circumstances, a Melody valve was placed in the

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Table: Demographics of Patients Who Underwent Melody Valve Implant in a Systemic Heart Valve

<table>
<thead>
<tr>
<th>No.</th>
<th>Diagnosis</th>
<th>Age, y</th>
<th>Sex</th>
<th>Site</th>
<th>Valve</th>
<th>Implant Size, mm</th>
<th>Implant Method</th>
<th>Implant Condition</th>
<th>Implant Site</th>
<th>LVSP, mm Hg</th>
<th>LVEDP, mm Hg</th>
<th>SBP or LA a Wave, mm Hg</th>
<th>DBP or LA v Wave, mm Hg</th>
<th>Preimplant Regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>IAA, VSD s/p modified Konno LV</td>
<td>0.7</td>
<td>M</td>
<td>Aortic</td>
<td>Melody</td>
<td>12</td>
<td>Catheter-hybrid</td>
<td>Severe</td>
<td>Aortic</td>
<td>110</td>
<td>95</td>
<td>50</td>
<td>10</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>HCM with AS/AR</td>
<td>3</td>
<td>M</td>
<td>Aortic</td>
<td>Melody</td>
<td>12</td>
<td>Catheter-hybrid</td>
<td>Severe</td>
<td>Aortic</td>
<td>108</td>
<td>91</td>
<td>48</td>
<td>48</td>
<td>Severe</td>
</tr>
<tr>
<td>3</td>
<td>HLHS s/p Fontan with native AR</td>
<td>4</td>
<td>M</td>
<td>Aortic</td>
<td>Melody</td>
<td>14</td>
<td>Electrophys/scheduled</td>
<td>Severe</td>
<td>Aortic</td>
<td>69</td>
<td>13</td>
<td>13</td>
<td>13</td>
<td>Severe</td>
</tr>
<tr>
<td>4</td>
<td>HHHS s/p Fontan with native AR</td>
<td>13</td>
<td>M</td>
<td>Aortic</td>
<td>Melody</td>
<td>22</td>
<td>Electrophys/scheduled</td>
<td>Severe</td>
<td>Aortic</td>
<td>119</td>
<td>49</td>
<td>26</td>
<td>26</td>
<td>Moderate</td>
</tr>
<tr>
<td>5</td>
<td>Williams syndrome s/p MIV</td>
<td>23</td>
<td>M</td>
<td>Mitral</td>
<td>Melody</td>
<td>22</td>
<td>Electrophys/scheduled</td>
<td>Severe</td>
<td>Mitral</td>
<td>125</td>
<td>23</td>
<td>125</td>
<td>125</td>
<td>Moderate</td>
</tr>
<tr>
<td>6</td>
<td>AS s/p LV apex to descending aorta conduit</td>
<td>74</td>
<td>M</td>
<td>LV-aorta conduit</td>
<td>Melody</td>
<td>22</td>
<td>Electrophys/scheduled</td>
<td>Severe</td>
<td>LV-aorta conduit</td>
<td>168</td>
<td>38</td>
<td>168</td>
<td>38</td>
<td>Severe</td>
</tr>
</tbody>
</table>

AR indicates aortic regurgitation; AS, aortic stenosis; DPG, diastolic blood pressure; HCM, hypertrophic cardiomyopathy; HLHS, hypoplastic left heart syndrome; IAA, interrupted aortic arch; LA, left atrial; LV, left ventricular septal defect.
aortic valve and subaortic region on a 12-mm balloon through a surgically exposed left ventricular apical approach. There was immediate relief of aortic regurgitation and outflow tract obstruction, but because of deteriorating neurological status, care was withdrawn 2 days after placing the valve. There was no obstruction or regurgitation of the Melody valve. The other death was a 74-year-old patient who had undergone placement of a left ventricular apex-to-descending aortic

Figure 3. Images from patient 5 (see Table) who underwent placement of a Melody valve in the aortic position. A, Photograph demonstrating modifications to the Melody valve, specifically resection of vein wall tissue, to allow coronary flow through the sinuses. B, Ascending aortic angiogram after Melody valve implantation demonstrates a competent valve and filling of both coronary arteries. Echocardiographic images in systole (C) and diastole (D), demonstrating a broad jet of antegrade flow across the Melody valve and trivial regurgitation through the valve leaflets during diastole.

Figure 4. These images are from patient 6 (see Table) who underwent placement of a Melody valve in the mitral position. A, A transesophageal echocardiogram showing the mitral valve during diastole demonstrates narrow and turbulent antegrade flow through the stenotic valve before Melody valve implantation. B, A fluoroscopic image in an oblique anteroposterior projection showing a Melody valve being placed in the mitral position. The delivery system was introduced through the inferior vena cava and right atrium, across the atrial septum into the left atrium, and then across the mitral valve; the guidewire was advanced through the left ventricle and aortic valve and was exteriorized through the femoral artery. Transesophageal echocardiogram images in systole (C) and diastole (D), demonstrating mild regurgitation through the Melody valve leaflet and a broad, nonturbulent antegrade flow through the valve.
conduit (aortic homograft attached in series to a 22-mm bioprosthetic valved conduit). During covered stent treatment of a false aneurysm near the origin of the conduit from the left ventricular apex, the conduit became severely regurgitant. Being a poor surgical candidate, the patient was taken to the catheterization laboratory, and a Melody valve was implanted in the conduit on a 22-mm delivery system. The patient was successfully discharged from the hospital and lived another 2 years but then died of a nonvalve-related cause. At most recent follow-up, the valve was functioning normally without any significant stenosis or regurgitation.

The patient in the right-sided implant group who died was a 43-year-old with tetralogy of Fallot and pulmonary atresia who had a complete repair at age 13 with a Hancock valved conduit and who experienced severe pulmonary hypertension. A Melody valve was placed across the conduit to relieve stenosis and regurgitation. The patient died 8 months later of a drug overdose. The valve had normal function at the latest follow-up before death.

**Major Adverse Events**

One of the patients with an aortic implant had transient occlusion of the left coronary artery. This 8-month-old had interrupted aortic arch type B and multiple ventricular septal defects and developed a subaortic membrane after an initial complete repair. A modified Konno procedure with intraoperative aortic valve balloon dilation was performed. The patient then developed progressive aortic regurgitation and severe left ventricular dysfunction. Given the severe left ventricular dysfunction, the patient was deemed a poor surgical candidate for aortic valve repair and replacement. Because this was a very-high-risk procedure, the neck vessels were exposed for possible extracorporeal membrane oxygenator cannulation before placing the Melody valve. A hybrid procedure (surgical exposure of the left ventricular apex) was performed in the catheterization laboratory, with surgical exposure of the left ventricular apex, introduction of a sheath through a pursestring suture in the apex, and delivery of the Melody valve on a 10-mm balloon. The valve was seated slightly lower than the ideal position. Postimplant dilation of the valve was performed using a 12-mm balloon, after which left coronary artery occlusion was observed, apparently because of native aortic valve leaflet entrapment in the left sinus. Because of hypotension, cardiopulmonary resuscitation was initiated, and preparations were made to cannulate the neck vessels for extracorporeal membrane oxygenator support. The patient recovered within 5 minutes of initiation of resuscitation, and it was noticed that the Melody valve stent had moved approximately 1 mm toward the left ventricular apex, and flow to the left coronary artery was reestablished. The patient was transferred to the cardiac intensive care unit in stable condition, with a dramatic decrease in the degree of aortic regurgitation. The left ventricular dysfunction persisted, and the patient was successfully bridged to transplant 1 month later. In 1 patient, surgical femoral venoplasty was performed after removal of a ruptured balloon catheter.

**Discussion**

Our experience with these 30 patients who underwent Melody valve placement in a high-pressure system, including the pulmonary valve position in patients with pulmonary hypertension, the aortic position in 6 patients with severe aortic regurgitation or mixed obstruction and regurgitation, and the mitral valve position in 1 patient with mixed stenosis and regurgitation, is encouraging. Implantation of the valve was successful in all patients, with only 1 case of implantation-related complication and no valve-related mortality.

In patients with moderate to severe pulmonary regurgitation before valve implantation, mean and diastolic PAP increased and systolic PAP decreased after implant. This finding can be explained by the change in forward stroke volume after placement of a competent valve and alleviation of regurgitation. This finding supports the data reported by Lurz et al. who showed in a larger cohort preservation of valve competence despite near-systemic PAP in 7 implant cases. Eight patients receiving implants in the present series had severe pulmonary hypertension with a mean PAP of ≥40 mm Hg. Only 4 valves had moderate stenosis at latest follow-up that lasted as long as 3 years. At 1-year postimplant and beyond, freedom from moderate to severe regurgitation was 100%, and freedom from mild regurgitation was 90% (Figure 2). In several follow-up studies of the Contegra conduit (Medtronic Inc), an unstented surgical conduit comprising a valved segment of bovine jugular vein, high PAP was reported as a risk factor for conduit dilation and subsequent regurgitation, leading to conduit replacement. It is unknown whether the added support of the stent, which prevents dilation and failure of valve coaptation, will allow better long-term performance of the Melody valve in patients with high PAP.

Transient occlusion of the left coronary artery in 1 of the aortic implant patients was related to the implantation technique. Because of concern about coronary ostial occlusion during previous cases, the Melody valve aortic implant was partially expanded above the ideal landing zone and then drawn back, with the expectation that the native valve leaflets would be retracted away from the coronary orifices. This technique seemed to result in successful placement of the Melody valve without any disturbance in coronary flow. Careful review of the angiograms in the patient who developed transient coronary occlusion demonstrated that because of placement of the Melody valve in a lower-than-ideal position, native aortic valve tissue was distorted and covered the coronary ostium. The native leaflets then moved away from the ostium during cardiopulmonary resuscitation and subsequently shifted the valve.

Since its introduction and subsequent approval for implantation in dysfunctional RVOT conduits ≥16 mm in diameter at the time of the surgical placement, transcatheter pulmonary valve placement has gained recognition as an alternative to surgical pulmonary valve replacement in some patients with dysfunctional RV-PA conduits. Because the valve is a jugular venous valve, however, its function in a high-pressure hemodynamic system is a source of concern. Originally intended to be placed in a low-pressure system (RV-PA conduits in patients with normal PAP), the Melody valve has shown excellent function over the short term when placed in a small cohort of patients with pulmonary hypertension, as well as in the descending aorta in an animal model of acute aortic
regurgitation and transvalvar gradients of 50 mm Hg at valve closure.6

Although transcatheter valves used in adults (predominantly in the aortic annulus) have shown excellent valve function under high pressure,11,12 these valves are larger than the Melody valve, which may limit their use in the pediatric population. As shown in the present series, the Melody valve was implanted over a wide range of sizes (12–22 mm) and maintained its competence.

Limitations

The inclusion criteria for this study were based on a general consensus among the centers in defining conditions where a valve was subjected to high pressure. This definition can be debated, particularly for the right-sided implants. The predominant pressure gradient that valve leaflets face is during diastole when placed in a semilunar valve position and systole when placed in an atrioventricular valve position, and the dynamics of these 2 types of loads differ. The case definition was more intuitive for left-sided implants because the valve is subjected to systemic systolic and diastolic pressures. The use of a mean PAp of >25 mm Hg for inclusion of RVOT implants primarily was based on conventional definitions of pulmonary hypertension. Depending on PA impedance and pulse pressure and RV compliance and diastolic pressure, peak and mean pressure gradients across the closed valve leaflet can vary considerably. Which of these (peak or mean pressure gradient) is most important in assessing the stress on and functional durability of a prosthetic valve is unclear.

This experience with the Melody valve in high-pressure settings and these findings are preliminary. Additional clinical studies will be necessary to better understand the functioning of this valve under high transvalvar gradients.

Conclusions

Despite its original biological origin as a bovine jugular venous valve, in this preliminary experience, the Melody valve has demonstrated satisfactory performance under a variety of high closing pressure situations. The Melody valve may provide a reasonable option for transcatheter therapy in pediatric patients who are poor candidates for surgical valve replacement in high-pressure systems.

Disclosures

Drs McElhinney, Cheatham, Vincent, Hellenbrand, Jones, and Zahn act in consultant roles for Medtronic Inc, the manufacturer of the Melody valve, and all authors except Drs Hasan and Brown act as investigators or proctors.

References

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