Transcatheter Pulmonary Valve Implantation

Description

Transcatheter pulmonary valve implantation (TPVI) received approval from the U.S. Food and Drug Administration under a humanitarian device exception in January 2010 for patients with previous repair of congenital heart disease (CHD) and right ventricular outflow tract (RVOT) obstruction. Patients with prior CHD repair are at risk of needing repeated reconstruction procedures. TPVI has been proposed as a less invasive alternative to open surgical pulmonary valve replacement or reconstruction for RVOT obstruction.

Background

Description of Disease. Congenital heart disease, including tetrology of Fallot, pulmonary atresia, and transposition of the great arteries, is generally treated by surgical repair at an early age. This involves reconstruction of the right ventricular outflow tract (RVOT) and pulmonary valve by means of a surgical homograft or a bovine-derived valved conduit. These repairs are prone to development of pulmonary stenosis or regurgitation over long periods of follow-up.

As individuals with prior congenital heart disease repair are living longer into adulthood, the problem of RVOT dysfunction following initial repair has become more common. Calcification of the RVOT conduit can lead to pulmonary stenosis, while aneurysmal dilatation can result in pulmonary regurgitation. RVOT dysfunction can lead to decreased exercise tolerance, potentially fatal arrhythmias, and/or irreversible right ventricular dysfunction. 1

Interventions for RVOT dysfunction often require repeat open heart surgery, resulting in numerous open heart procedures in patients who live into adulthood. Treatment options for pulmonary stenosis, open surgery with valve replacement, balloon dilatation, or percutaneous stenting. (1) Interventions for pulmonary regurgitation are primarily surgical, either reconstruction of the RVOT conduit or replacement of the pulmonary valve through open surgery. The optimal timing of these interventions is not well understood. 2

Transcatheter pulmonary valve replacement offers a potentially less invasive treatment option for patients with prior surgery for congenital heart disease and RVOT dysfunction. It is possible that the use of less invasive valve replacement techniques can spare patients from multiple repeat open heart procedures over long periods of follow-up.
### Description of Technology

The Melody® transcatheter pulmonary valve and the Ensemble® Transcatheter Valve Delivery System are used together for percutaneous replacement of a dysfunctional pulmonary valve. The Melody valve consists of a section of bovine jugular vein with an intact native venous valve. The valve and surrounding tissue is sutured within a platinum-iridium stent scaffolding. The transcatheter delivery system consists of a balloon-in-balloon catheter with a retractable sheath and distal cup into which the valve is placed. The procedure is performed on the beating heart without use of cardiopulmonary bypass.

The Melody valve is first crimped to fit into the delivery system. It is introduced through the femoral vein and advanced into the right side of the heart and put into place at the site of the pulmonary valve. The inner balloon is inflated to open up the artificial valve, and then the outer balloon is inflated to position the valve into place.

The Edwards Sapien Transcatheter Heart Valve (Pulmonic) (Edwards Lifesciences), composed of a stainless steel frame with bovine pericardial tissue leaflets and available in 23-mm and 26-mm sizes, is CE-marked for use in Europe, but does not have Food and Drug Administration approval for use in the United States.

### Regulatory Status

The Melody® transcatheter pulmonary valve and the Ensemble® Transcatheter Valve Delivery System, manufactured by Medtronic Heart Valves, Inc (Santa Ana, CA), received FDA approval under the Humanitarian Device Exemption (HDE) Program on January 25, 2010. Approval was for use as an adjunct to surgery in the management of pediatric and adult patients with the following clinical conditions:

- Existence of a full (circumferential) RVOT conduit that was equal to or greater than 16mm in diameter when originally implanted; and
- Dysfunctional RVOT conduits with clinical indication for intervention, and either:
  - Regurgitation: ≥ moderate regurgitation; or
  - Stenosis: mean RVOT gradient ≥35mm Hg.

In 2015, approval of the Melody® device was amended to a premarket approval (PMA) because FDA determined that the device represented a breakthrough technology. The PMA was based, in part, on 2 prospective clinical studies, the Melody® TPV Long-term Follow-up Post Approval Study (PAS) and the Melody TPV New Enrollment PAS.

On February 29, 2016 the Edwards SAPIEN XT™ Transcatheter Heart Valve (THV) the FDA expanded the premarket approval indications for relief of symptomatic heart disease due to severe native calcified aortic stenosis to include pulmonic valve implantation. Pulmonary valve implantation is indicated for use in pediatric and adult patients with a dysfunctional, non-compliant Right Ventricular Outflow Tract (RVOT) conduit with a clinical indication for intervention and:

- pulmonary regurgitation greater than or equal to moderate and/or
mean RVOT gradient greater than or equal to 35 mmHg.

The Compassion Trial, a clinical study to establish a reasonable assurance of safety and effectiveness of pulmonary implantation with the Edwards SAPIEN THV in patients with dysfunctional RVOT conduits were the basis for the PMA approval decision, performed by the manufacture in the U.S. under FDA Investigational Device Guidelines.

FDA product code: NPV

Related Policies

7.01.132 Transcatheter Aortic-Valve Implantation for Aortic Stenosis

Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Transcatheter pulmonary valve implantation using the Edwards SAPIEN XT™ Transcatheter Heart Valve is considered **not medically necessary** for use in pediatric and adult patients with a dysfunctional, non-compliant Right Ventricular Outflow Tract (RVOT) conduit and pulmonary regurgitation.

Implantation of the Melody® or the Ensemble® transcatheter pulmonary valves, when performed according to FDA-approved indications, is considered **medically necessary** for patients with prior repair of congenital heart disease and right ventricular outflow tract (RVOT) dysfunction, who are not good candidates for open repair due to one or more of the following conditions:

- High-risk for surgery based due to concomitant medical comorbidities; or
- Poor surgical candidate due to multiple prior thoracotomies for open heart surgery.

Transcatheter pulmonary valve implantation is considered **investigational** for all other non-FDA approved indications.

Rationale

The published literature on TPVI consists of small case series, which generally report on short-term outcomes. Some of the larger, representative publications are discussed in this literature review.

Studies Using FDA-Approved Valves

In February 2016, the FDA expanded the Edwards SAPIEN XT™ Transcatheter Heart Valve (THV) the premarket approval indications for relief of symptomatic heart disease due to severe native calcified aortic stenosis to include pulmonic valve implantation.4

SAPIEN XT-CONgenital Multicenter trial of Pulmonic vAlve regurgitation Studying the SAPIEN InterventIONal THV Trial. The "COMPASSION" trial was a prospective, non-randomized, multi-center clinical study to assess the safety and effectiveness of pulmonic implantation of the SAPIEN THV in
patients with dysfunctional Right Ventricular Outflow Tract (RVOT) conduits requiring treatment for moderate or severe pulmonary regurgitation (PR) by transthoracic echocardiography (TTE) and/or RVOT conduit obstruction with a mean gradient of ≥ 35 mmHg by TTE. It included 81 patients at 7 investigational sites.4 There were 69 patients available for analysis in the valve implant population at the completion of the study. The COMPASSION Trial demonstrated that patients implanted with the SAPIEN transcatheter heart valve for treatment of a dysfunctional, non-compliant RVOT conduit are free from device- or procedure-related death and/or reintervention at 1 year. At 5 years, the freedom from device- or procedure-related death and/or reintervention was 77.1%. Freedom from reintervention to 5 years for the valve implant population was:

- freedom from surgical pulmonic valve repair was 98.3% at 1 year and 91.8% at 5 years;
- freedom from transcatheter pulmonic valve implantation was 97.1% at 1 year and 85.8% at 5 years;
- freedom from balloon valvuloplasty was 100% at 1 year and 93.7% at 5 years; and
- freedom from other types of reintervention was 100% at 1 year and 97.9% at 5 years.

Additionally, freedom from Major Adverse Cardiac and Cerebrovascular Events (MACCE) at 6 months in the valve implant population was 94.1%. At 6 months, a decrease in pulmonary insufficiency to mild or less was observed in 96.2% of patients; improved pulmonary stenosis mean gradient was 93.8%; functional improvement in NYHA was 92.2%; and freedom from recurrent pulmonary stenosis was 100%. An improvement in conduit peak gradient was demonstrated, as it decreased from 37.2±25.5 mmHg at baseline to 18.7±15.0 mmHg at 30 days, 17.4 ± 12.1 mmHg at 1 year and 21.6±14.5 mmHg at 5 years. Moderate/severe pulmonic insufficiency decreased from 90% at baseline to 2% at 30 days, 4% at 1 year and 0% at 5 years. There was also significant improvement in NYHA class: 22% of the patients were in NYHA class 1 at baseline, 84% at 1 year and 94% at 5 years.

Though the COMPASSION Trial is not a RCT and the sample size is small, this study established a reasonable assurance of safety and effectiveness of pulmonic implantation with the Edwards SAPIEN THV (as stated above) in pediatric and adult patients with dysfunctional RVOT conduits, who have moderate or greater pulmonary insufficiency. However, prospective registries with higher numbers of patients and longer follow up and/or RCT are needed to better evaluate safety and efficacy of the Sapien THV in the pulmonic position. The SAPIEN XT Pulmonic Post Approval Study (PAS) will be important in that the objective of this study is to evaluate longer-term safety and effectiveness of the SAPIEN XT THV in the pulmonic position for the intended patient population (especially pediatric) when used as indicated with all valve sizes. It is a single-arm, prospective, multicenter post-approval study using a performance goal based on the original COMPASSION trial.

In 2015, approval of the Melody® device was amended to a premarket approval (PMA) because FDA determined that the device represented a breakthrough technology.3 The PMA was based, in part, on 2 prospective clinical studies, the Melody® TPV Long-term Follow-up Post Approval Study (PAS) and the Melody TPV New Enrollment PAS.

US Melody TPV Trial. The multicenter U.S. Melody TPV trial was a multicenter, prospective uncontrolled trial designed to assess the safety, procedural success, and short-term effectiveness of the Melody Transcatheter Pulmonary Valve (TPV).2,5 It was the pivotal trial on which FDA approval of
the Melody valve was based. The investigators planned to follow 150 patients over a 5-year period. Eligibility criteria included a dysfunctional RVOT conduit or a dysfunctional bioprosthetic pulmonary valve, plus evidence of heart failure. For patients with New York Heart Association (NYHA) class I heart failure, a Doppler mean gradient of 40 mm Hg or greater or severe pulmonary regurgitation was required, and for patients with NYHA class II to IV heart failure, a mean gradient of 35 mm Hg or greater or moderate pulmonary regurgitation was required. These inclusion criteria generally were indications for pulmonary valve replacement. The primary outcomes were defined as procedural success, adverse events (AEs) from the procedure, and effectiveness, as measured by the proportion of patients with acceptable valve function at 6 months.

Trial results have been published in several reports.²,₅,₆ Short- and medium-term outcomes for 136 patients who underwent attempted TPVI were reported by McElhinney et al in 2010.² A total of 124 (91.2%) of 136 patients had successful implantation. In 12 patients, implantation was not possible due to anatomic or other intraprocedural findings. One (0.7%) death occurred as a result of the procedure, and serious AEs occurred in 8 (6%) of 136 patients. AEs included coronary artery dissection, conduit rupture/tear, wide complex tachycardia, respiratory failure, femoral vein thrombosis, and perforation of the pulmonary artery.

Ninety-four patients with successful implantation had reached the 6-month follow-up time point at the time of publication. Acceptable valve function, defined as mild pulmonary regurgitation or less on echocardiography, was present in more than 90% of patients. Right ventricular (RV) pressure and RVOT gradient improved following the procedure, and 71 (75.5%) of 94 were in NYHA class I heart failure at 6 months. During follow-up, stent fractures were diagnosed in 25 (20.2%) of 124 patients, and 9 (7.3%) of 124 required implantation of a second valve.

Cheatham et al reported on outcomes up to 7 years following TPVI for the 148 patients who received and were discharged with a transcatheter pulmonary valve (TPV) in the U.S. Melody TPV trial (of 171 patients enrolled).³ Of the 171 patients enrolled, 167 underwent catheterization, 150 had a Melody valve implanted, and 148 of those survived to discharge with the Melody valve in place. On echocardiogram at discharge, pulmonary regurgitation was absent/trivial or mild in 140 patients and 5 patients, respectively, which represented a significant improvement from baseline. Over a median follow-up of 4.5 years (range, 0.4-7.0 years), 4 deaths occurred. During the follow-up period, 32 patients required a reintervention on RVOT, 25 of which were TPV reinterventions. A total of 11 patients required Melody valve explantation. Among the 113 patients who were alive and free from reintervention at a median of 4.5 years postimplantation, the most recent RVOT gradient was unchanged from early after valve implantation. Functional outcomes generally improved during the study: before TPVI, 14% of patients were in NYHA class I and 17% were in class III or IV. At every postimplantation annual evaluation, at least 74% of patients were in class I and no more than 1% to 2% were in class III or IV.

A secondary publication from the U.S. Melody TPV trial focused on the change in exercise function following TPVI.⁷ Patients completed a standardized cardiopulmonary regimen 2 months before TPVI and 6 months after TPVI. Results of pre- and postexercise parameters were available for 94 to 114 patients, depending on the specific outcome. Numerous physiologic outcome measures were reported, with some showing a statistically significant change between the 2 time points, and others not. For
example, there was a significant increase in the percent predicted maximal workload from 65.0% at baseline to 68.3% at follow-up (p<0.001) and a significant decrease in the ratio of minute ventilation to co2 production from 30.8 at baseline to 29.1 at follow-up (p<0.001). In contrast, there were no significant changes in peak oxygen consumption or in spirometric measures of pulmonary function. This trial reported modest benefits in exercise parameters for patients treated with TPVI. The results are limited by the lack of a control group and by the large number of patients who did not have completed exercise results available (approximately one-third of total).

**Melody TPV Long-term Follow-up Post Approval Study**

Armstrong et al published 1-year follow-up results of the Melody TPV Long-term Follow-up Post Approval Study (PAS), a prospective study designed to evaluate the short-term hemodynamic changes following device implantation. The study used historical controls from the Melody pivotal investigational device exemption (IDE) trial described above to investigate whether the short-term effectiveness of the device was noninferior to results shown in the IDE trial. PAS enrolled 120 subjects, 101 of whom underwent attempted TPVI. Patient selection was based on the criteria used in the IDE trial, but did not include the age (≥5 years of age) and weight (≥30 kg) limitations. Procedure-related significant AEs occurred in 16 patients (13.3% of total cohort; 15.8% of those who had an attempted TPVI), the most common of which was a confined conduit tear. Procedural success occurred in 99 subjects (98% of those with an attempted TPVI). At 1-year follow-up, the proportion of patients in NYHA class I heart failure increased from 35% at baseline to 89%. Of the 99 patients implanted for at least 24 hours, 87 had acceptable TPV hemodynamic function confirmed at 6 months (96.7% of those with evaluable echocardiographic data, 87.9% of entire cohort) and 82 had acceptable TPV hemodynamic function at 1 year (94.3% of those with evaluable echocardiographic data, 82.8% of the entire cohort). Following the procedural period, serious device-related AEs occurred in 8%, most commonly endocarditis (n=3 patients).

Gillespie et al evaluated results of TPVI after a Ross procedure in a retrospective review of pooled findings from the U.S. Melody TPV trial and PAS and an additional European registry, the manufacturer-sponsored Melody TPV Post-Market Surveillance Study conducted in Canada and Europe (NCT00688571). In the pooled sample (total N=358 patients), 67 (19%) had a prior Ross procedure. A Melody valve was successfully implanted in 56 (84%) of 67 Ross patients who underwent catheterization with intent for TPVI. Six (9%) patients had symptomatic coronary artery compression after TPVI or did not undergo implantation due to the risk of compression. RV hemodynamics generally improved after TPVI, but RVOT reinterventions were required in 12 of 55 patients discharged from the implant hospitalization with the Melody valve in place.

**Additional Noncomparative Studies**

A number of publications have reported on series of patients treated with TPVI. Some of the larger series are discussed in detail.

Lurz et al reported on 163 patients who underwent attempted TPVI from 4 clinical centers in Europe. Eligibility for the procedure included elevated RV systolic pressure, increased RVOT dimensions, and either symptoms or evidence of severe RV dysfunction. Procedural success was achieved in 155 (95.1%) of 163 patients. Procedural complications occurred in 12 (7.4%) of 163, 8 of which were considered serious and 5 of which required open surgery. Median follow-up was 28.4 months. During
follow-up, 4 (2.6%) of 155 patients died, and an additional 5 (3.2%) developed infective endocarditis. At 12-month follow-up, more than 90% of patients had absent or mild valve dysfunction as measured by echocardiography.

Eicken et al reported on 102 consecutive patients (mean age, 21.5 years) undergoing TPVI at 2 centers in Germany. Eligibility for the procedure included RVOT dysfunction with evidence of RV compromise or increased RV pressure. One (1.0%) death occurred as a result of compression of the left coronary artery. Two (2.0%) patients had evidence of stent fracture immediately postprocedure and 1 (1.0%) other patient developed infective endocarditis at 6-month follow-up. At a median follow-up of 357 days, there was a significant decrease in the RVOT gradient from a median of 36 to 15 mm Hg (p<0.001). However, there was no significant change in exercise capacity as measures by maximal oxygen uptake.

Other case series reported on smaller numbers of patients, with a range of 7 to 64 patients. These series generally reported similar results as the larger series, with high procedural success and relatively low rates of serious complications. The longest follow-up was reported by Borik et al, who evaluated 51 patients who underwent TPVI with the Melody valve at a single institution. Over a mean follow-up of 4.5 years (range, 0.9-6.9 years), freedom from any reintervention was 87% and 68% at 3 and 5 years, respectively, and freedom from surgery was 90% at 5 years. Overall, RV functional parameters did not change with longer follow-up.

Section Summary: Studies Using Valves Approved by the U.S. Food and Drug Administration
The evidence for the use of TPVI with the Melody valve consists of the prospective, interventional, noncomparative pivotal study on which the device’s FDA approval was based, along with a postapproval registry study and a number of additional case series. Overall, the evidence suggests that TPVI is associated with high rates of short-term technical success and improvements in heart failure-related symptoms and hemodynamic parameters. Studies with follow-up extending to a maximum of 7 years postprocedure have suggested that the functional and hemodynamic improvements are durable, with a number (20%-30%) requiring reintervention on the pulmonary valve.

Non-FDA-Approved Uses of TPVI
A variety of potential off-label uses of TPVI have been reported in the literature. They include use of devices that are not FDA-approved, and use of approved devices for non-FDA-approved indications.

Non-FDA-Approved Devices
A small number of retrospective, comparative studies have compared outcomes of the Edwards Sapien and the Melody valves. Bosshoff et al described the off-label uses in 21 patients treated with the Melody valve and 2 patients treated with the Edwards Sapien pulmonic valve. Use has included native RVOT obstruction, in conduits smaller than the FDA-labeled indications, and large RVOT with a dynamic outflow aneurysm. No deaths or major procedural complications were reported for these patients. Clinical outcomes data were lacking or very limited in this publication.

Faza et al reported on 20 patients who underwent successful implantation of the Edwards Sapien pulmonic valve at 1 clinical center. There were no peri-procedural deaths, and all but 1 patient had no or trivial pulmonic regurgitation on latest follow-up. A comparison of hemodynamic parameters in these
20 patients was made with 13 patients treated with the Melody valve. Immediately postprocedure, transvalvular gradients were similar between groups. At last follow-up, mean residual transvalvular gradient was higher for patients receiving the Sapien valve (18.4 mm Hg vs 11.2 mm Hg, p=0.016), but this difference was disappeared when patients were matched for length of follow-up.

A few other small case series reporting on the use of the Edwards Sapien pulmonic valve for RVOT obstruction have been published. For example, Kenny et al reported on a phase 1 multicenter study of the Sapien valve in 36 patients from 4 clinical centers. Procedural success was reported in 97% of patients. Procedural complications occurred in 19% (7/36) of patients, including valve migration (n=3), pulmonary hemorrhage (n=2), ventricular fibrillation (n=1), and stent migration (n=1). At 6-month follow-up, there were no deaths and 75% (27/36) of patients were in NYHA class I, compared with 14% at baseline. Freedom from reintervention at 6 months was 97%.

Non-FDA-Approved Indications
Analysis of data from the Valve-in-Valve International Database (VIVID) multicenter registry evaluated the off-label use of transcatheter aortic and TPVI prostheses for tricuspid valve-in-valve implantation (TVIV). One hundred fifty of 156 patients in the registry had successful TVIV with a Melody (n=93) or a Sapien (n=57) valve. During a median 13.3-month follow-up, 22 (15%) patients died, all with NYHA class III or IV. There were 10 (6.6%) tricuspid valve reinterventions and 3 (2%) other patients who had significant recurrent dysfunction of the valve. Preintervention, 71% of patients were NYHA class III or IV; at follow-up, 77% of surviving patients were NYHA class I or II (p<0.001).

A few case series have been reported on use of the Melody valve in patients with clinical characteristics that do not correspond to FDA-approved indications. These indications have included use of valves in positions other than pulmonic, patients with conduit sizes not corresponding to the FDA indications, and patients with prior congenital heart repair surgery not involving construction of a RVOT conduit. In general, these case series have reported high rates of procedural success with low rates of periprocedural complications, but evidence on longer term outcomes is lacking.

Although most studies have evaluated the use of TPVI in patients with a constructed RVOT conduit, a few have evaluated TPVI with either the Melody valve or the Edwards Sapien Transcatheter Heart Valve in a native RVOT or RVOT without a circumferential conduit. Meadows et al reported results from a retrospective, 5-center review of patients who underwent TPV placement in a nonconduit RVOT, with native tissue comprising at least part of the circumference. Thirty-one patients were included, with indications for RVOT intervention including primarily valvular insufficiency in 14 (45%), obstruction in 3 (10%), and mixed obstruction and insufficiency in 14 (45%). TPVI was successful in all patients, but serious complications occurred in 2 (6%). At a median follow-up of 15 months (range, 1 month to 3.8 years), all patients were alive, and none had greater than mild pulmonary regurgitation. Among the 19 patients with adequate imaging at follow-up, 6 (32%) had evidence of stent fracture. Three patients were treated for endocarditis or bloodstream infection. Malekzadeh-Milani reported outcomes for 34 patients with a native or patched noncircular RVOT who underwent Melody TPV insertion at a single center. The procedure was technically successful in all patients, although early complications occurred in 8.8%. At a mean follow-up of 2.6 years, no patients had stent fracture or migration, and 32 (94.1%) of 34 had no or trivial pulmonary regurgitation.
Several other small case series by Demkow et al (N=10) and Odemis et al (N=7) have reported on the use of the Edwards Sapien pulmonary valve for noncircumferential RVOT patch and large-diameter conduits, respectively. The authors reported high rates of successful valve implantation, but no long-term follow-up.

### Adverse Events

In addition to the AEs reported in the case series, several publications have focused on AEs following TPVI. FDA reviewed results from the U.S. Melody TPV trial as part of its approval process and reported data on complications from the procedure. At that time, data were available for 99 patients enrolled between January 2007 and December 2008. Ninety patients were deemed suitable for implantation following catheterization, and 87 of them had successful implantation. There was 1 (1.1%) procedure-related death. Table 1 is adapted from the FDA summary of safety and probable benefit.

#### Table 1. Device-Related Adverse Events (N=89 Subjects)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Subjects With Event, n (%)</th>
<th>Freedom From Event at 12 Months (SE)</th>
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<tbody>
<tr>
<td>Stent fracture (all)</td>
<td>16 (18%)</td>
<td>77.1% (7.5%)</td>
</tr>
<tr>
<td>Minor$^a$</td>
<td>11 (12%)</td>
<td>84.1% (6.7%)</td>
</tr>
<tr>
<td>Major$^a$</td>
<td>5 (6%)</td>
<td>90.6% (5.2%)</td>
</tr>
<tr>
<td>Valve stenosis</td>
<td>6 (7%)</td>
<td>90.5% (4.8%)</td>
</tr>
<tr>
<td>Worsening tricuspid regurgitation</td>
<td>1 (1%)</td>
<td>100% (−)</td>
</tr>
<tr>
<td>Reintervention$^b$</td>
<td>6 (7%)</td>
<td>93.5% (4.3%)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>1 (1%)</td>
<td>98.6% (2.2%)</td>
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</table>

$^a$ Stent fractures that did not require intervention were defined as minor; those that required reintervention were defined as major.

$^b$ Reinterventions were balloon angioplasty in 1 patient; repeat implantation of a second transcatheter pulmonary valve in 5 patients.

There were 64 patients in the FDA analysis who reached 6 months of follow-up. Of these, 56/64 (87.5%) had acceptable hemodynamic function of the valve by Doppler echocardiography. At 6 months, approximately 75% of patients were in NYHA class I, and 25% were in NYHA class II. Pulmonary regurgitation that was mild or worse was present in 6.2% of patients.

Another publication focusing on AEs from the U.S. Melody TPV trial was published in 2011. This report assessed AEs at a median follow-up of 30 months in 150 patients. Stent fracture occurred in 26% (39/150) of patients. The estimated freedom from stent fracture was 77% at 14 months and 60% at 39 months. Freedom from reinterventions for all patients was estimated to be 86% at 27 months, and freedom from reinterventions for patients with stent fracture was estimated at 49% at 2 years.

McElhinney et al reported rates of infective endocarditis from 3 prospective case series enrolling 311 patients followed for a median of 2.5 years. Sixteen (5.1%) patients were diagnosed with endocarditis at any location and 6 (1.9%) patients had endocarditis at the pulmonic valve location. This corresponded to an annualized rate of pulmonic valve endocarditis of 0.88% per patient-year. Malekzadeh-Milani et al evaluated patients with right-sided infective endocarditis at a single center to compare endocarditis rates in patients who had TPVs with those who had surgically paced pulmonary valves. Thirty-one patients with right-sided endocarditis and pulmonary valve implantation for congenital heart disease were included. Rates of endocarditis were 1.2 and 3.9 cases/100 person-years in patients with surgically implanted valves and TPVs, respectively (p=0.03).
Boudjemline et al conducted a prospective observational study to evaluate predictors of conduit rupture during the preparation of the RVOT for TPVI in a cohort of patients older than age 5 years with RVOT obstruction, pulmonary regurgitation, or mixed lesions, who underwent transcatheter therapies, including balloon dilatation, bare metal stent placement, or TPV placement. Ninety-nine patients were included, 56 of whom were adults. Of the total cohort, 83.8% underwent Melody TPVI. Conduit rupture occurred in 9 (9.09%) patients. In 2 of the 9 patients, conduit rupture was angiographically obvious and severe with extension, causing hemodynamic instability. All conduit ruptures occurred during balloon dilatation and occurred in patients with RVOT obstruction. Heavy calcification and the presence of a homograft were associated with conduit rupture risk.

Coronary artery compression during balloon angioplasty or stent placement in the RVOT conduit is considered a relative contraindication to TPV placement. Several studies have evaluated the incidence of coronary artery compression. Morray et al reported the incidence of coronary artery compression in a 4-center series of 404 patients who underwent attempted TPVI. Three hundred forty-three (85%) patients underwent TPVI, and 21 (5%) patients had evidence of coronary artery compression. Most (n=19) patients with coronary artery compression did not undergo TPV placement. Using the same cohort reported in the Boudjemline study, Fraisse et al reported the incidence, diagnosis, and outcome of coronary compression among patients treated with transcatheter RVOT interventions for RVOT obstruction, pulmonary regurgitation, or mixed lesions. All patients underwent balloon dilatation and coronary assessment with angiography, which was followed by TPV placement if RVOT dysfunction was ongoing. Of 100 patients evaluated, 83% had implantation of a Melody TPV. Coronary artery compression occurred in 6 cases, all of which could be diagnosed by selective coronary angiogram and/or aortic root angiogram during balloon dilation of the RVOT. No specific risk factors for coronary artery compression were identified.

Van Dijck et al compared rates of infective endocarditis between transcatheter pulmonary valves and surgically implanted pulmonary valves in a retrospective, single-center study that included 677 patients (738 conduits). Patients who underwent procedures from 1989 to 2013 were included. A total of 107 Melody conduits were implanted in 107 patients. A total of 577 pulmonary valve cryopreserved homografts were implanted in 517 patients, and 54 Contegra grafts were implanted in 53 patients. Freedom from infective endocarditis at 5 years by Kaplan-Meier analysis was 85%, 88%, and 99% for patients with Melody conduits, Contegra grafts, or cryopreserved homografts, respectively.

Malekzadeh-Milani et al reported on the incidence of infective endocarditis among 86 prospectively enrolled consecutive patients who underwent TPVI with the Melody valve. Over a mean follow-up of 23.6 months (range, 2.6-28.3 months) after Melody implantation, 5 patients developed infective endocarditis (5.8%; 95% confidence interval [CI], 0.9% to 10.7%). Factors related to demographics, conduit type, procedural success, residual gradient, and duration of Melody valve implantation did not differ significantly between patients who did or did not develop infective endocarditis. Patients with infective endocarditis were more likely to have undergone invasive procedures after TPVI without antibiotic prophylaxis (odds ratio, 13.69; 95% CI, 1.98 to 94.52; p=0.014), and aspirin use was preventive for infective endocarditis (relative risk, 20.1; 95% CI, 3.34 to 120.9; p=0.001), although confidence intervals around risk estimates for both factors were wide.
Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<tr>
<td>Ongoing</td>
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<tr>
<td>NCT00676689a</td>
<td>Implantation of the SAPIEN Transcatheter Heart Valve (THV) in the Pulmonic Position</td>
<td>70</td>
<td>Nov 2019</td>
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<tr>
<td>NCT00740870a</td>
<td>Implantation of the Medtronic Melody Transcatheter Pulmonary Valve in Patients With Dysfunctional RVOT Conduits: A Feasibility Study</td>
<td>150</td>
<td>Jan 2020</td>
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</table>

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.

Practice Guidelines and Position Statements

**Society for Cardiovascular Angiography and Interventions et al**

In 2015, the Society for Cardiovascular Angiography and Interventions, American Association for Thoracic Surgery, American College of Cardiology (ACC) and the Society of Thoracic Surgeons published a consensus-based report on operator and institutional requirements for TPVI.40 Recommendations to qualify for a TPVI program included 150 catheterizations/year, association with a surgical program, submission of all cases to a national registry, and, for patients, 80% freedom from re-intervention at 1 year.

**American Heart Association and American College of Cardiology**

In 2014, American Heart Association (AHA) and ACC issued guidelines for the management of patients with valvular disease.41 These guidelines do not make specific recommendations on the treatment of primary pulmonary valve disease (stenosis or regurgitation), but instead refer to the 2008 guidelines for the management of adults with congenital heart disease.

In 2008, the AHA and ACC (in collaboration with other medical societies) issued guidelines for the management of adults with congenital heart disease.42 For patients with isolated valvular pulmonary stenosis, the guidelines make recommendations on balloon valvulotomy or surgical intervention; however, TPVI is not addressed.

**U.S. Preventive Services Task Force Recommendations**

Transcatheter pulmonary valve implantation is not a preventive service.

**Summary of Evidence**

For individuals who have a history of congenital heart disease (CHD) and current right ventricular outflow tract (RVOT) obstruction who receive transcatheter pulmonary valve implantation (TPVI) with
an Food and Drug Administration (FDA)–approved device and indication, the evidence includes 1 prospective, interventional, noncomparative study and multiple prospective and retrospective case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity and mortality. Results of the case series indicate that there is a high rate of procedural success and low procedural mortality, although the rates of serious procedural adverse events reported ranges from 3.0% to 7.4%. Most valves demonstrate competent function by Doppler echocardiography at 6- to 12-month follow-up, but complications (eg, stent fractures, need for reinterventions) were reported in an FDA analysis to occur at rates of 18% and 7%, respectively. Other publications with longer follow-up have reported stent fractures in up to 26% of patients; however, most stent fractures have not required reintervention. Studies with follow-up extending to a maximum of 7 years postprocedure have suggested that the functional and hemodynamic improvements are durable, but a relatively high proportion of patients (20%-30%) require reintervention on the pulmonary valve. No comparative studies were identified, and there is no direct evidence that TPVI leads to a reduction in future open heart procedures. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have a history of CHD and current RVOT obstruction who receive TPVI with a non-FDA-approved device or indication, the evidence includes case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity and mortality. There is currently limited published evidence on the off-label use of TPVI, including implantation of a non-FDA-approved valve, or use of an approved valve for a non-FDA-approved indication. The published relatively small case series are heterogeneous in terms of the device used and the indications for TPVI. The evidence is insufficient to determine the effects of the technology on health outcomes.

Medicare National Coverage

There is no national coverage decision.

References


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<thead>
<tr>
<th>Policy History</th>
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<tbody>
<tr>
<td>September 2012</td>
<td>New Policy</td>
<td>Policy updated with literature review; references added: 4, 5, 13-15, 17. Medically necessary statement amended to include: “when performed according to FDA-approved indications”. Non-</td>
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approved FDA indications are investigational.

March 2014 Update Policy Policy updated with literature review. References 13-14, 16, 18, 21 added. No change to policy statement.


September 2016 Update Policy Policy updated with literature review through September 19 2016; references 3-5, 7-8, 16, 19, 26, 36-37 and 39 added. Policy statement revised adding " SAPIEN XT THV is not medically necessary for use in pediatric and adult patients with a dysfunctional, non-compliant Right Ventricular Outflow Tract (RVOT) conduit and pulmonary regurgitation."

Keywords

Pulmonary valve prosthesis, endovascular implantation
Transcatheter pulmonary valve
Ensemble Transcatheter Valve Delivery System
Melody

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 16, 2016 and is effective October 15, 2016.

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