



Kansas City

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Transcatheter Pulmonary Valve Implantation

Policy Number: 7.01.131
Origination: 2/2012

Last Review: 2/2014
Next Review: 2/2015

Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for transcatheter pulmonary valve implantation when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered

Transcatheter pulmonary valve implantation, 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.

When Policy Topic is not covered

Transcatheter pulmonary valve implantation is considered **investigational** for all other indications.

Description of Procedure or Service

Transcatheter pulmonary valve implantation (TPVI) is an alternative to pulmonary valve replacement by open surgery. It is intended for patients who have previously had a pulmonary valve repair for congenital heart disease, in whom dysfunction of the repaired valve necessitates further intervention.

Background

Description of Disease. Congenital heart disease, including tetralogy 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 to 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.

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

Rationale

This policy was created in November 2011 and updated periodically with literature review. The most recent update with literature review covers the period from August 2012 through September 30, 2013. The published literature on transcatheter pulmonary valve implantation (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

The only device that currently has U.S. Food and Drug Administration (FDA) approval for transcatheter pulmonary valve implantation is the Melody™ valve (Medtronic Heart Valves, Inc., Santa Ana, CA). Approved indications include right ventricular outflow tract (RVOT) dysfunction, defined as pulmonic regurgitation (moderate or greater) or pulmonic stenosis (mean gradient of 35 mm Hg or higher). In addition, a circumferential RVOT conduit should exist that is equal to or greater than 16 mm in diameter when originally implanted.

US Melody TPV trial. The multicenter US Melody TPV trial is a prospective uncontrolled trial from 5 clinical sites that was designed to study the safety, procedural success, and short-term effectiveness of the Melody transcatheter pulmonary valve. (2, 3) This was the pivotal trial on which FDA approval for the Melody valve was based. The study was designed to follow 150 patients over a 5-year period. Eligibility criteria included a dysfunctional right ventricular outflow tract (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 equal to or greater than 40 mm Hg or severe pulmonary regurgitation was required, and for patients with NYHA class II-IV heart failure, a mean gradient of equal to or greater than 35 mm Hg 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 from the procedure, and effectiveness, as measured by the proportion of patients with acceptable valve function at 6 months.

Interim results from this trial have been published.(2,3) The most recent publication (2) reported on 136 patients who underwent attempted TPVI. A total of 124/136 patients (91.2%) had successful implantation. In 12 patients, implantation was not possible due to anatomic or other intraprocedural findings that precluded implantation. One death occurred as a result of the procedure (0.7%), and serious adverse events occurred in 8/136 patients (6%). Adverse events included coronary artery dissection, conduit rupture/tear, wide complex tachycardia, respiratory failure, femoral vein thrombosis, and perforation of the pulmonary artery.

A total of 94 patients had successful implantation and 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 greater than 90% of patients. Right ventricular pressure and right ventricular outflow tract gradient improved following the procedure, and 71/94 (75.5%) were in NYHA class I heart failure at 6 months. Over the course of follow-up, stent fractures were diagnosed in 25/124 (20.2%) patients, and 9/124 (7.3%) required implantation of a second valve.

A secondary publication from the US Melody TPV trial focused on the change in exercise function following TPVI.(4) Patients completed a standardized cardiopulmonary regimen 2 months prior to TPVI and 6 months following TPVI. Results of pre- and postexercise parameters were available for 94-114 patients, depending on the specific outcome. There were numerous physiologic outcome measures reported, with some of these showing a statistically significant change between the 2 time points, and others not showing a significant change. 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 study reports 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).

Italian Society of Pediatric Cardiology Registry.(5) Butera et al. published outcomes of 63 patients who were enrolled in this prospective, multicenter registry. Implantation was successful in 97% (61/63) of patients. There was one early death following TPVI, and peri-procedural complications occurred in 14% (9/63). Two complications were considered major, these were stent migration requiring reintervention and ventricular fibrillation treated with external cardioversion. The median right ventricular systolic pressure was reduced from 80 at baseline to 20 ($p < 0.001$) following the procedure, and 60% (38/63) of patients had either grade 0 or grade 1 pulmonary regurgitation. At a median follow-up of 30 months, an additional 3 patients died and 6 patients had major complications. These complications included Melody valve endocarditis ($n=2$), stent fracture requiring reintervention ($n=2$), and herpes virus encephalitis ($n=2$). There were also 8 patients (13%) who had stent fractures that did not require intervention. Freedom from valve failure or reintervention at last follow-up was estimated to be 81.4%.

Lurz et al. (6) This publication reported on 163 patients who underwent attempted TPVI from 4 clinical centers in Europe. Eligibility for the procedure included elevated right ventricular (RV) systolic pressure, increased RVOT dimensions, and either symptoms or evidence of severe RV dysfunction. Procedural success was achieved in 155/163 patients (95.1%). Procedural complications occurred in 12/163 (7.4%), 8 of which were considered serious and 5 of which required open surgery.

The median follow-up was 28.4 months. Over the course of follow-up, 4/155 patients (2.6%) died, and an additional 5/155 patients (3.2%) developed infective endocarditis. At 12 months' follow-up, greater than 90% of patients had absent or mild valve dysfunction as measured by echocardiography.

Eicken et al.(7) This study reported on 102 consecutive patients (mean age, 21.5 years) undergoing transcatheter pulmonary valve implantation at 2 centers in Germany. Eligibility for the procedure included RVOT dysfunction with evidence of RV compromise or increased RV pressure. There was one death (1.0%) that occurred as a result of compression of the left coronary artery. Two patients (2.0%) had evidence of stent fracture immediately postprocedure, and 1 additional patient (1.0%) 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 ($p<0.0001$). However, there was no significant change in exercise capacity as measured by maximal oxygen uptake.

Other case series reported on smaller numbers of patients, with patient populations ranging from 7-59.(8-12) These publications reported generally similar results as the larger series, with high procedural success and relatively low rates of serious complications. One of these trials reports follow-up for up to 2 years; no studies were identified that provide longer follow-up data.

Non-FDA Approved Uses of TPVI

There are a variety of potential off-label uses of TPVI that have been reported in the literature. These include use of devices that are not FDA-approved, and use of approved devices for non-FDA-approved indications.

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.(13,14) These have included use in valves other than the pulmonic position, patients with conduit sizes that do not correspond to the FDA indications, and patients with prior congenital heart repair surgery that did not involve construction of a right ventricular outflow tract (RVOT) conduit. In general, these case series have reported high rates of procedural success with low rates of peri-procedural complications, but evidence on longer term outcomes is lacking.

A small number of retrospective, comparative studies have compared outcomes of the Edwards SAPIEN® pulmonic valve with the Melody® pulmonic valve. Boshoff 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.(14) These included use in native RVOT obstruction, in conduits that were smaller than the FDA-labeled indications, and in large RVOT with a dynamic outflow aneurysm. There were no deaths or major procedural complications reported for these patients. Clinical outcome 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 one clinical center.(15) 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 who were treated with the Melody valve. Immediately following the procedure, the transvalvular gradient was similar between groups. At last follow-up, the 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 no longer present 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.(16-18) For example, Kenny et al. reported on a Phase I multicenter study of the Sapien pulmonic valve in 36 patients from 4 clinical centers.(17) Procedural success was reported in 97% of patients. Procedural complications occurred in 19% of patients (7/36), 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% of patients (27/36) were in NYHA class I, compared to 14% at baseline. Freedom from reintervention at 6 months was 97%.

Adverse Events

In addition to the adverse events reported in the case series, several publications have focused on adverse events following TPVI.

The FDA reviewed results from the US Melody TPV trial as part of the FDA approval process and reported detailed data on complications from the procedure.(19) At that time, data were available for 99 patients enrolled between January 2007 and December 2008. A total of 90 patients were deemed suitable for implantation following catheterization, and 87/90 patients had successful implantation. There was one procedural-related death (1.1%). The following table is adapted from the FDA summary of safety and probable benefit:

Device-Related Adverse Effects (N=89 Subjects)

Event	Subjects With Event	Freedom From Event at 12 Months (SE)
Stent fracture (all)	16 (18%)	77.1% (7.5)
Minor ^a	11 (12%)	84.1% (6.7)
Major ^a	5 (6%)	90.6% (5.2)
Valve stenosis	6 (7%)	90.5% (4.8)
Worsening tricuspid regurgitation	1 (1%)	100% (--)
Reintervention ^b	6 (7%)	93.5% (4.3)
Reoperation	1 (1%)	98.6% (2.2)

^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 one patient; repeat implantation of a second TPV 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 adverse events in the US Melody TPV trial was published in 2011.(20) This publication reported on adverse events 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 reported rates of infective endocarditis from 3 prospective cases series enrolling a total of 311 patients followed for a median of 2.5 years.(21) There were a total of 16 patients (5.1%) diagnosed with endocarditis at any location and 6 patients (1.9%) who had endocarditis at the pulmonic valve location. This corresponded to an annualized rate of pulmonic valve endocarditis of 0.88%/patient-year.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

In response to requests for clinical vetting in 2011, input was received from 5 academic medical centers. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

Overall response to whether TPVI was investigational was mixed, with 2 of 5 reviewers indicating they agree with the investigational status, and 3 reviewers who indicated it was a split decision. The majority of reviewers (4/5) indicated in their written response that there was a subpopulation of patients who were high risk for surgery or who were not candidates for surgery, in whom there were no other available options. These reviewers felt that TPVI was a viable alternative that offered potential benefit for these patients.

Summary

Transcatheter pulmonary valve implantation received FDA approval under the Humanitarian Device Exception program in January 2010 for patients with previous repair of congenital heart disease and right ventricular outflow tract (RVOT) obstruction. There is currently a lack of high-quality evidence evaluating outcomes of this procedure for the indicated population. No randomized controlled trials (RCTs) have been performed, and there are no controlled trials that compare transcatheter valve implantation to available alternatives. The available evidence consists of case series of patients with RVOT dysfunction who require intervention.

The results of the case series indicate that there is a high rate of procedural success and low procedural mortality. The rate of serious procedural adverse events reported in these series ranges from 3.0-7.4%. At 6 to 12 months of follow-up, there is evidence that the majority of valves demonstrate competent functioning by Doppler echocardiography, with most patients in NYHA functional class I or II. Complications at 6 month follow-up, such as stent fractures and the need for reinterventions, were reported by the 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 the majority of stent fractures have not required reintervention. There is no direct evidence to demonstrate that TPV implantation leads to a reduction in future open heart procedures.

In patients who are not candidates for open surgery, or who are at high-risk for surgery due to other medical comorbidities, alternative treatment options are limited. Clinical vetting received in 2011 indicated near uniform support for use of TPVI in patients who were not candidates for open repair or who were at high risk for open surgery. Based on this clinical vetting and the evidence on short-term success, TPVI can be considered medically necessary for patients who are not candidates for open repair or who are high risk for open repair.

There is very 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. For these off-label uses, TPVI is considered investigational.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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Billing Coding/Physician Documentation Information

0262T Implantation of catheter-delivered prosthetic pulmonary valve, endovascular approach

Additional Policy Key Words

N/A

Policy Implementation/Update Information

2/1/12 New policy; considered medically necessary for patients who are high risk for open surgery and are poor surgical candidates due to multiple prior thoracotomies for open heart surgery. Considered investigational for all other indications.

- 2/1/13 Medically necessary statement amended to include “when performed according to FDA-approved indications”.
 - 2/1/14 No policy statement changes.
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