Technology Brief: Update

Percutaneous Pulmonary Valve Implantation

February 2012
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This brief was commissioned by Queensland Health, in its role as the Secretariat of the Health Policy Advisory Committee on Technology (HealthPACT). The production of this brief was overseen by HealthPACT. HealthPACT comprises representatives from health departments in all States and Territories, the Australian and New Zealand governments and MSAC. It is a sub-committee of the Australian Health Ministers’ Advisory Council (AHMAC), reporting to AHMAC’s Clinical, Technical and Ethical Principal Committee (CTEPC). AHMAC supports HealthPACT through funding.

This brief was prepared by the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S)
REGISTER ID
WP074

NAME OF TECHNOLOGY
PERCUTANEOUS PULMONARY VALVE IMPLANTATION

PURPOSE AND TARGET GROUP
PATIENTS WITH CONGENITAL HEART DEFECTS INVOLVING MALFORMATION OF THE RIGHT VENTRICULAR OUTFLOW TRACT (RVOT)

STAGE OF DEVELOPMENT (IN AUSTRALIA)

☑ YET TO Emerge
☐ Experimental
☐ Investigational
☐ Nearly established
☐ Established
☐ Established but changed indication or modification of technique
☐ Should be taken out of use

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐ Yes
☒ No
☐ Not applicable

INTERNATIONAL UTILISATION

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2012 SAFETY AND EFFECTIVENESS ISSUES

Study description

A total of two case series studies evaluating the safety and efficacy of percutaneous pulmonary valve implantation (PPVI) were included in this update (Eicken et al 2011 and Asoh et al 2010).

The study by Eicken et al (2011) aimed to assess the safety and efficacy of PPVI performed at two large tertiary paediatric cardiological referral units (level IV intervention evidence). Patients were included in the study if they were more than 5 years of age, weighed more than 20 kg, and were diagnosed with right ventricular outflow tract (RVOT) dysfunction resulting in significant pulmonary regurgitation with evidence of right ventricular dysfunction and/or an RVOT obstruction with right ventricular systolic pressures being at least 2/3 systemic. Patients were excluded from the study if the conduit size exceeded 22 mm in diameter.

A total of 102 consecutive patients (40 females and 62 males) who were scheduled for PPVI at the two centres between December 2006 and July 2010 were included in the study. The median age of patients was 21.5 years (range 16.2–30.1 years), and the median weight was 63 kg (range 54.2–75.9 kg). The leading lesion in 36 patients was a stenosis, in 18 patients it was regurgitation, and in the remaining 48 patients it was a combination of both. In terms of diagnoses, 61 patients had undergone surgical correction of a tetralogy of Fallot/pulmonary atresia with VSD, 14 had a common arterial trunc, 9 had a transposition of the great arteries after a Rastelli-operation/arterial switch OP, 8 patients with aortic stenosis after a Ross operation had early homograft dysfunction, and 10 patients had a range of other cardiac lesions. Patients had undergone an average of three previous cardiac operations (range 1-5).

The PPVI procedure was performed under general anaesthesia or deep sedation, and the Melody™ transcatheter pulmonary valve was used. All patients underwent a clinical examination, a posterior–anterior and a lateral chest X-ray, a standard 12-lead ECG, a trans-thoracic echocardiography, and a cardiac MRI study between 2 and 3 days after the PPVI procedure, before discharge from hospital. These examinations together with an exercise test were repeated 6 months after the procedure, and then annually. The median follow-up time was 357 days (range 99–388 days).

Asoh et al (2010) reviewed the early results of PPVI in children who had a previously implanted bioprosthetic valve (level IV intervention evidence). The authors suggest that PPVI provides an option for non-surgical management of RVOT dysfunction in paediatric patients whose previously implanted bioprosthetic valves have begun to degenerate. In this study, the medical and cardiac catheterisation records of all
children who underwent PPVI in one institution from October 2005 to February 2008 were retrospectively reviewed. Indications for the procedure included right ventricular pressure (RVP) overload from outflow tract obstruction (RVP-to-systemic pressure ratio >0.66), significant pulmonary insufficiency, RV dilation, or RV failure. Patients who had received a valve implantation in anything other than a bioprosthetic valve were excluded from the study.

Follow-up was obtained on all children in 2008 and was 100% complete. Of the 30 patients who underwent PPVI during the specified time period, 14 patients (7 males and 7 females) had a previously implanted bioprosthetic valve and were included in this study. The mean age of patients was 15.4 ± 2.0 years (range 13.0–19.0 years) and mean weight was 56.8 ± 7.5 kg (range 42.2–71.1 kg). The most common intracardiac lesion was Fallot’s tetralogy or one of its variants. The mean time from prosthetic valve implantation to PPVI was a 10.4 ± 4.0 years (range 3.7–18.2 years). Valve dysfunction was categorised as predominantly stenotic in 2 patients, predominantly regurgitant in 2 patients and mixed in 10 patients. In two children with a Symbion™ valve, one was stented and the other balloon dilated at an earlier procedure.

All PPVI procedures were performed under general anaesthesia, and used the Melody™ transcatheter pulmonary valve. In all patients, echocardiography was performed before and within 24 hours after PPVI, with peak instantaneous pressure gradients reported. The RVP was calculated from the tricuspid regurgitant jet, and the grade of pulmonary regurgitation (PR) was determined by the appearance of the regurgitant jet on colour-flow Doppler mapping. The severity of PR was classified as follows: 0=none or trivial, 1=mild, 2=moderate and 3=severe. Right ventricular (RV) and left ventricular (LV) dimensions were measured echocardiographically, with all echocardiograms reviewed by single investigator.

2012 Safety

In the study by Eicken et al (2011), complications were reported in 8 patients (7.8%). One patient exhibited severe compression of the left coronary artery. In this patient, the Melody valve was replaced with a Contegra graft, following which the coronary artery was shown to be patent; however, despite this, the patient could not be weaned from a left ventricular assist device (LVAD) and died 2 weeks later. Another patient experienced complete AV block during the PPVI procedure, although sinus rhythm recurred 21 days later without the need for pacemaker implantation. Stent fracture occurred in 5 patients. In two of these patients, stent fracture was identified on chest X-ray before discharge from hospital, and occurred in one or more struts with no loss of stent integrity (type-1 fracture). These stent fractures were without
haemodynamic relevance, and the patients were able to be discharged from hospital. The other 3 patients developed stent fractures with a loss of stent integrity (type-2 fracture) during repeated balloon dilatation at a second catheterisation for significant residual RVOT obstruction; however, a successful valve-in-valve procedure was performed in all 3 patients. The Melody valve was surgically removed and replaced with a homograft valve in one patient who developed endocarditis with \textit{Staphylococcus aureus} 6 months after the PPVI procedure.

Asoh et al (2010) reported that following the procedure, one child (7.1%) was found to have a femoral artery pseudoaneurysm. The patient was managed with a thrombin injection and remained in hospital for 3 days. No other complications, including stent fractures, were reported, and the authors stated that all other children were discharged from hospital within 2 days of the procedure.

\textit{2012 Effectiveness}

Eicken et al (2011) reported that pre-stenting of the RVOT was performed in 96 (94\%) patients, while post-PPVI dilatation was performed in 75 (73\%) patients using a high-pressure balloon. Immediately after the PPVI procedure, the systolic gradient between the right ventricle and the pulmonary artery was reduced from a median value of 37 mmHg (range 29–46 mmHg) to 14 mmHg (range 9–17 mmHg) \((P<0.0001)\), while the ratio between systolic right ventricular and aortic pressure was decreased from a median value of 62\% (range 53–76\%) to 36\% range (30–42\%) \((P<0.001)\). Similarly, when assessed by MRI, pulmonary regurgitation was reduced from a median value of 16\% (range 5–26\%) to 1\% (range 0–2\%) \((P<0.001)\), while the right ventricular end-diastolic volume index decreased from a median value of 106 mL/m\(^3\) (range 93–133 mL/m\(^3\)) to 90 mL/m\(^3\) (range 71–108 mL/m\(^3\)) \((P<0.001)\).

Patients were discharged home at a median of 2 days after the PPVI procedure.

At the time of publication, a total of 9 (9\%) patients had required repeated catheterisation due to a peak systolic Doppler gradient >50 mmHg between the RV and the pulmonary artery. One of these 9 patients had experienced a partial occlusion (90\%) of the origin of the right pulmonary artery (RPA) following PPVI, which on re-catheterisation was dilated with an 18 mm balloon, leading to free flow to the RPA. In the other 8 patients, a repeated balloon dilatation was performed. In 4 of these 8 patients, redilatation of the valve adequately improved the haemodynamic result; however, in the other 4 patients (3 of which experienced longitudinal stent fractures during redilatation), valve-in-valve procedures were required in order to achieve adequate gradient relief.

At the latest follow-up examination (median 357 days, range 99–388 days), the Doppler gradient in the RVOT decreased from a median value of 36 mmHg (range
26–44 mmHg) before the PPVI procedure, to a median value of 15 mmHg (range 12–20 mmHg) after the procedure (P<0.0001). In addition, exercise testing showed that VO_{2max} remained unchanged with a median value of 22.4 mlO_{2}/kg/min before the PPVI procedure compared with 22.8 mlO_{2}/kg/min following the procedure.

The study by Asoh et al (2010) reported that PPVI procedures were successful in all 14 patients. Following the procedure, RVP fell from 62.2 ± 21.1 mmHg (range 34.0–110.0 mmHg) to 42.4 ± 11.4 mmHg (range 29.0–60.0 mmHg) (P<0.005), while RVOT pressure gradients fell from 36.7 ± 19.4 mmHg (range 7.0–81.0 mmHg) to 12.9 ± 7.3 mmHg (range 2.0–32.0 mmHg) (P<0.05). Similarly, the ratio of RVP to aortic pressure (AoP) fell from 72 ± 19% (range 47–113%) to 45 ± 10% (range 32–61%) (P<0.001). However, no significant change in RV end-diastolic pressure was observed following PPVI [9.8 ± 4.8 mmHg (range 4.0–22.0 mmHg) to 9.3 ± 2.9 mmHg (range 4.0–14.0 mmHg), P=0.6]. Angiography in the main pulmonary artery following the procedure showed that pulmonary regurgitation had improved.

The results of echocardiograms performed within 24 hours of the procedure showed that RVP fell from 82.2 ± 15.6 mmHg (range 50.0–110.0 mmHg) to 61.0 ± 10.0 mmHg, (range 48.0–80.0 mmHg) (P<0.01), while RVOT pressure gradients fell from 59.6 ± 26.8 mmHg (range 19.0–106.0 mmHg) to 41.0 ± 19.1 mmHg (range 21.0–96.0 mmHg) (P<0.05). In addition, there was a significant improvement in the grade of pulmonary regurgitation following PPVI, from 3.6 ± 0.8 to 0.6 ± 0.9 (P<0.001). Patients were discharged home at a median of 2 ± 0.4 days after the PPVI procedure.

Echocardiographic estimates of RVP and RVOT pressure gradients were shown to fall gradually (P<0.001) with time, and at the latest follow-up (mean 12.9 ± 9.8 months), the mean RVP, RVOT gradient and RVP/AoP ratio were 52.1 ± 14.4 mmHg, 28.9 ± 12.7 mmHg, and 48 ± 15%, respectively. In addition, an increase in aortic valve annulus diameters (P<0.001) and LV end-diastolic dimensions (P=0.01) were also observed; however, no change in the degree of pulmonary regurgitation was observed compared with the immediate postoperative period.

A total of 2 patients required balloon dilation for an obstructed implant at 0.99 and 1.9 years respectively. This resulted in an adequate reduction in the RVOT pressure gradient in one patient; however, the other patient had outgrown the maximal outflow diameter that could be achieved, and required surgical replacement. Freedom from re-intervention was reported to be 92% and 82% at 25 and 32 months, respectively.

**2012 Cost Impact**

Two studies were identified that evaluated the cost impact of PPVI (Gatlin et al 2011 and Raikou et al 2011).
The purpose of the study by Gatlin et al (2011) was to compare the costs of PPVI to the more established surgical pulmonary valve replacement (PVR) procedure, in one institution. The total hospital costs of PPVI were compared to the costs of PVR, and a midterm cost-savings analysis was then modelled over 5 years using initial costs and reintervention rates. The authors derived the reintervention rates for PPVI and PVR from the published literature (5-year freedom from reintervention was assumed to be 53% for PPVI and 90% for PVR). The cost of the Melody valve and delivery device ($US 30,500) was higher than the cost of the porcine freestyle valve used in PVR ($US 8,700); however, overall procedural costs for both techniques were very similar, at just under $US 50,000 for each procedure. After taking into consideration the increased need for reintervention in patients with Melody valves, the authors reported that there was a mid-term cost saving of $US 19,928 per patient for PVR compared to PPVI.

Raikou et al (2011) aimed to assess the costs of PPVI and PVR using a cohort simulation model applied to the UK population. The authors stated that this was not a cost-effectiveness study, but rather was intended to provide an indication of the levels of cost which could be expected in a cohort of patients faced with a choice of treatment with PPVI or surgery. The cohort simulation model used in the study assessed the costs of PPVI and surgical PVR using a hypothetical population of 1,000 individuals with RVOT dysfunction starting when their first valved biological conduit was surgically placed and following them for a period of 25 years, assuming that (1) PPVI was not available as a treatment option and (2) that PPVI was available for those eligible for it. This model estimated that over the 25-year period of analysis, the mean cost per patient when PPVI is unavailable as a treatment option would be £5,791, compared with £8,734 when PPVI is available. After a sensitivity analysis was performed, the mean per patient cost difference in implementing PPVI over 25 years when compared to PVR was somewhere between £2,041 and £3,913. The authors concluded that this analysis showed that PPVI is associated with a relatively small increase in treatment management costs over a long period of time. It is important to note that Medtronic, the manufacturer of the Melody transcatheter pulmonary valve, funded this study through an educational grant, and that one of the authors was an employee of the company.

2012 ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS
No issues were identified from the retrieved material.

2012 OTHER ISSUES
The studies by Eicken et al (2011) and Asoh et al (2010) both reported that none of the authors had any conflicts of interest to declare.
Searches of clinical trial registers indicate that there are currently 4 ongoing clinical trials evaluating PPVI using the Melody™ transcatheter pulmonary valve (Table 1).

Table 1: Ongoing and currently recruiting clinical trials involving PPVI

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<td>NCT00740870 (ongoing but not recruiting)</td>
<td>USA</td>
<td>Case series of 150 patients undergoing PPVI with the Melody transcatheter pulmonary valve. Five year follow-up period.</td>
<td>August 2015</td>
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<td>NCT00688571 (ongoing but not recruiting)</td>
<td>Canada Denmark Germany Italy Netherlands Spain</td>
<td>Prospective, multicentre, case series of 63 patients undergoing PPVI with the Melody transcatheter pulmonary valve. Five year follow-up period.</td>
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<td>NCT01186692 (recruiting)</td>
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<td>Case series of estimated 100 patients undergoing PPVI with the Melody transcatheter pulmonary valve. Five year follow-up period.</td>
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<td>NCT01250327 (recruiting)</td>
<td>France</td>
<td>Prospective, non-randomised comparative study evaluating the cost of PPVI with the Melody transcatheter pulmonary valve compared with conventional techniques. Two year follow-up period.</td>
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2012 SUMMARY OF FINDINGS

A case series of over 100 patients demonstrated that PPVI is feasible, and improves the haemodynamics of patients suffering from congenital heart defects involving malformation of the RVOT. Specifically, significant reductions in the peak systolic RVOT pressure gradient, the ratio between systolic RV and aortic pressure, pulmonary regurgitation and RV end-diastolic volume were observed immediately after the PPVI procedure. In addition, at 1 year follow-up the mean Doppler gradient in the RVOT was significantly reduced when compared with pre-PPVI values. The rate of complications in this study was low; however, one death during the procedure was reported. Similar improvements in patient haemodynamics were observed up to 1 year after the procedure in a small case series study of 14 patients which assessed the safety and efficacy of PPVI in children previously implanted with a bioprosthetic valve. A low rate of complications was also observed in this study.

2012 HEALTHPACT ASSESSMENT

PPVI appears to be a safe and effective treatment for selected patients with dysfunctional conduits in the RVOT. However, the current evidence for PPVI is limited by the lack of long-term follow-up data, which is needed in order to determine whether the procedure can reduce the number of operations that a
patient undergoes. A number of clinical trials with scheduled follow-up periods of up to 5 years are currently ongoing. Therefore, HealthPACT wish to monitor the technology, which will be reviewed in 24 months time.

**2012 INCLUDED STUDIES**

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the following link on the HealthPACT web site.

Total number of studies 2
Level IV case series evidence 2

**2012 REFERENCES**


PRIORITISING SUMMARY 2010

REGISTER ID S000102

NAME OF TECHNOLOGY PERCUTANEOUS PULMONARY VALVE IMPLANTATION

PURPOSE AND TARGET GROUP PATIENTS WITH CONGENITAL HEART DEFECTS INVOLVING MALFORMATION OF THE RIGHT VENTRICULAR OUTFLOW TRACT (RVOT)

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2010 IMPACT SUMMARY

Percutaneous pulmonary valve implantation (PPVI) is an alternative to stenting for the treatment of a dysfunctional right ventricle to pulmonary artery conduit. The use of PPVI can potentially treat conduit dysfunction without sacrificing valvular competence, and may reduce the need for subsequent surgical repair.
2010 BACKGROUND
Obstruction of blood flow from the right ventricle to the pulmonary artery, the right ventricular outflow tract (RVOT), is a common feature of a number of congenital heart diseases. In patients with an impaired RVOT, the heart has to work harder than normal to pump blood and is less efficient at returning deoxygenated blood to the lungs. Surgical reconstruction of the RVOT is an integral part of treatment and is one of the most commonly performed operations in patients with congenitally malformed hearts. The repair is usually performed by sewing a cadaveric pulmonary or aortic graft (homograft), a porcine aortic conduit or a bovine jugular vein between the right ventricle and the pulmonary artery to increase the blood flow to the lungs. Dysfunction of the pulmonary valve, which results in pulmonary stenosis and/or backflow of blood (regurgitation), is relatively common post-surgery. Thus, even though surgical placement of conduits is associated a very low mortality rate, the conduits have a relatively short lifespan (less than 10 years) (Lurz and Bonhoeffer 2008). Consequently, patients often require multiple operations during their lifetime to prevent or reverse valvular incompetence or obstruction (Bove et al 1985, Eyskens et al 2000).

In an effort to reduce the need for reoperation, clinicians have utilised percutaneous dilation and stenting (bare-metal stenting [BMS]) to treat degenerated conduits. Although BMS relieves the obstruction to blood flow, it also results in pulmonary valve regurgitation. This was previously thought to be well tolerated in patients, at least in the early stages. However, research has shown that chronic volume overload of the right ventricle as a result of pulmonary valve regurgitation can cause significant right ventricular dysfunction, exercise intolerance and arrhythmia, with the added risk of sudden death (Gatzoulis et al 2000, Frigola et al 2004).

In 2000, the first pulmonary valve was implanted percutaneously in a 12-year old boy with a dysfunctional RVOT conduit (Bonhoeffer et al 2000). Following this, there has been interest in PPVI as an alternative to BMS. Percutaneous implantation of valves is a rapidly growing field in cardiology; PPVI is similar to percutaneous aortic valve replacement, which was assessed in an earlier prioritising summary written in February 2007. At the time of writing, the only commercially available valve utilised for PPVI is the Melody™ Transcatheter Pulmonary Valve (TPV) (Medtronic Inc., Minneapolis, MN, United States). The Melody valve is a bovine jugular vein valve mounted on a platinum iridium stent that is welded together with gold. The stent is 34 mm long and can be crimped down to a diameter of 6 mm. When expanded, the competence of the tri-leaflet valve is maintained at a large range of diameters, from 12 mm to 22 mm (Lurz et al 2009a). During the implantation procedure, the valve is crimped onto a balloon-in-balloon front-loading delivery system (Ensemble™);
Medtronic Inc., Minneapolis, MN, United States). The sheath is constructed from Teflon and the guidewire lumen is braided while a retractable sheath prevents displacement of the valve during delivery (Lurz and Bonhoeffer 2008).

2010 Clinical Need and Burden of Disease
The Australian Institute of Health and Welfare database indicates that there were a total of 161 pulmonary valve repair or replacement procedures performed from 2006 to 2007. In Australia, the incidence of tetralogy of Fallot is relatively low, with 82 new cases being identified in 2003 (Australian Institute of Health and Welfare 2009).

2010 Diffusion
The Melody TPV received the CE mark of approval in October 2006. The United States Food and Drug Administration recommended conditional approval for use of the Melody TPV under a Humanitarian Device Exemption application (H080092) in July 2009 (Medtronic 2009). Devices approved under this exemption are intended for use in fewer than 4000 patients per year in the United States. Currently, the Melody TPV is not approved for use in Australia.

Over 500 PPVIs have been performed worldwide, with over 230 of these being performed in the United Kingdom (Lurz et al 2009a). The Melody TPV post-market surveillance study is currently ongoing and has an enrolment of 63 patients with dysfunctional RVOT conduits. This prospective, multi-centre observational study will assess the long-term clinical performance of the Medtronic Melody TPV over a 5-year period. The expected completion date is August 2014 (ClinicalTrials.gov identifier: NCT00688571). Another study, the Melody TPV feasibility study, was initiated in January 2007 to assess the safety, procedural success, and short-term effectiveness of the TPV in patients with dysfunctional RVOT conduits. The trial is currently recruiting, with a target enrolment of 120 patients. The estimated completion date is January 2014 (ClinicalTrials.gov identifier: NCT00740870) (Clinicaltrials.gov 2009).

2010 Comparators
The comparator to PPVI is percutaneous dilation with BMS. BMS has been shown to decrease right ventricular pressures and potentially prolong the lifespan of conduits, but at the expense of inducing pulmonary regurgitation.

2010 Safety and Effectiveness Issues
Study description
One prospective, non-randomised comparative study on PPVI was identified for inclusion (Lurz et al 2009b), which examined the acute physiological effects of BMS in comparison to PPVI in the perioperative period using an X-ray/magnetic resonance hybrid laboratory. A total of 14 consecutive children (median age 12.9 years, range 9.9 to 17.8) were studied between September 2007 and June 2008. Patients were included if they had a clinical indication for PPVI in the context of significant RVOT obstruction and fulfilled the morphology requirements for PPVI. The majority of patients had tetralogy of Fallot (64%, 9/14) or a similar variant morphology. Patients underwent BMS followed by PPVI, which essentially confounds the results for PPVI due to the presence of BMS. Nevertheless, this study will be discussed due to the paucity of evidence available on PPVI. Magnetic resonance imaging was utilised before and after both procedures to assess acute physiological changes (Lurz et al 2009b).

Seven prospective case series studies were identified from the literature. All of these publications focused on a group of patients treated with PPVI by a single surgeon at various sites in France and the United Kingdom. The latest and most comprehensive paper on this patient cohort was included (Lurz et al 2008). Between September 2000 and February 2007, a total of 155 patients (median age 21.1 years, range 7 to 71) with RVOT dysfunction underwent PPVI. The majority of these patients had tetralogy of Fallot or one of its variants (61%). Pressure measurements and angiography were performed before and after PPVI. Echocardiographic follow-up was performed at 1, 6, 12, 36 and 70 months post-treatment. The median length of follow up was 28.4 months. The investigators also examined the impact of the learning curve by comparing the results for the first 50 patients with those of the subsequent 105 patients. The rationale for this was that after the 50th patient, the device design was finalised and the investigators believed that the learning curve had plateaued in terms of technical experience and patient selection (Lurz et al 2008).

2010 Safety

The comparative study by Lurz et al (2009b) reported no major complications for BMS or PPVI in the perioperative period. In one patient, a guidewire injury resulted in minor lung bleeding. There were no additional details on the incidence of minor complications or the incidence of device related complications during the study.

The case series study by Lurz et al (2008) reported a complication rate of 9% (14/155) over the median 28.4 month follow-up period. Seven of these were considered major complications: device instability in five patients, which included dislodgement of the device (n=2) and homograft rupture (n=3); compression of the
left main coronary artery (n=1); and obstruction of the origin of the right pulmonary artery (n=1). Five of the patients with major complications required surgical RVOT revision. During the follow-up period, five patients were diagnosed with endocarditis a median 4.9 months after PPVI, which led to valve removal in three patients. Another patient also required valve removal after developing haemolysis, despite a technically successful valve implantation. The investigators attributed this to a significant residual pressure gradient of 60 mmHg in a small homograft in addition to external compression of the RVOT. A stent fracture led to stent embolisation in the right pulmonary valve in one patient, requiring surgical removal of the Melody valve (Lurz et al 2008).

Four patients died during follow-up, resulting in a survival rate of 96.6% at 83 months post-treatment. PPVI was performed as a palliative procedure in two of these patients who had cardiogenic shock and multiorgan failure at the start of the study. The other two patients died suddenly at 8 and 35 months after the PPVI procedure, presumably due to arrhythmia. Both patients had good valvular competence at their last echocardiographic follow up (Lurz et al 2008).

2010 Efficacy

Lurz et al (2009b) reported that the total procedure, catheterisation and fluoroscopy times were 209 ± 14, 92 ± 14 and 21 ± 12 minutes (mean ± standard deviation), respectively. The BMS and PPVI procedures were successful in all patients. BMS achieved significant reduction in mean right ventricular systolic pressure (63 vs. 37 mmHg; p<0.001), mean pulmonary artery to right ventricular pullback gradient (43 mmHg vs. 13 mmHg; p<0.001) and the mean ratio of right ventricular to systemic pressure (0.75% vs. 0.41%; p<0.001). However, PPVI did not produce any statistically significant changes in these measurements. In contrast, the mean pulmonary artery diastolic pressure increased significantly after PPVI compared to BMS, indicating that pulmonary valvular competence was restored (9 mmHg before BMS vs. 11 mmHg after PPVI; p = 0.048). There were no statistically significant changes in systemic pressures after BMS, although there was a slight but not statistically significant increase after PPVI. Magnetic resonance readings indicated that there was a significant increase in pulmonary regurgitant factor after BMS (21.3% vs. 41.4%; p<0.001) compared to before BMS. In addition, there was a decrease in right ventricular end-systolic volume (53.1 mL/m² vs. 41.7 mL/m²; p<0.001) and an increase in total right ventricular stroke volume (44.2 mL/m² vs. 56.6 mL/m²; p=0.002) and right ventricular ejection fraction (48.7% vs. 60.7%; p<0.002) as a result of a reduction in ventricular afterload after BMS compared to pre-BMS measurements. Despite these improvements, the lack of overall gain in effective
right ventricular stroke volume (33.8 mL/m² vs. 32.6 mL/m²) after BMS indicated that these changes did not compensate for the pulmonary regurgitation induced by BMS (Lurz et al 2009b). In contrast, pulmonary regurgitation was virtually eliminated following PPVI as indicated by measurements of pulmonary regurgitation fraction (41.4% after BMS vs. 3.6% after PPVI; p<0.001). Right ventricular end diastolic volume was also significantly lower (98.3 mL/m² vs. 85.3 mL/m², p=0.021) and there was a significant improvement in effective right ventricular stroke volume after PPVI compared with the post-BMS state (32.6 mL/m² vs. 41.0 mL/m²; p=0.004). However, there were no significant changes in right ventricular end systolic volume or right ventricular ejection fraction after PPVI, compared with post-BMS measurements (Lurz et al 2009b).

The results of this study indicated that both BMS and PPVI had an effect on left ventricular volumes and function (Lurz et al 2009b). Left ventricular end diastolic volume decreased slightly after BMS but significantly increased after PPVI (65.9 mL/m² after BMS vs. 75.4 mL/m² after PPVI; p<0.001). Similarly, effective left ventricular stroke volume did not change after BMS, but increased significantly after PPVI (33.1 mL/m² vs. 32.5 mL/m²; p=0.013). The significant increase in effective right and left ventricular stroke volume following PPVI was accompanied by a significant reduction in heart rate (75.5 beats per minute vs. 69.0 beats per minute; p=0.006) relative to post-BMS measurements. As a result, there was no significant change in cardiac output after PPVI. During cardiopulmonary exercise testing, the authors noted that peak oxygen uptake increased significantly from 67.6% to 75.7% (p=0.048) (Lurz et al 2009b). However, the relevance of these results is severely limited since PPVI results were confounded by the presence of the BMS.

In the case series study by Lurz et al 2008, the PPVI procedure was successful in 97% (150/155) of patients. The proportion of patients free from surgical revision (reoperation) was 93 ± 2%, 86 ± 3%, 84 ± 4% and 70 ± 13% at 10, 30, 50 and 70 months, respectively, whereas freedom from transcatheter interventions (balloon dilation or second valve implantation) was 95 ± 2%, 87 ± 3%, 73 ± 6% and 73 ± 6% at 10, 30, 50 and 70 months, respectively. Re-intervention was required in 7 patients because of conduit obstruction related to the “hammock” effect and in 9 patients owing to stent fractures. The total incidence of stent fractures was 21% in this study. Other reasons for a second valve implantation were restenosis of unknown origin (n=4) and residual RVOT gradient after the first PPVI (n=2). Echocardiography after PPVI showed that there was a significant reduction in mean right ventricular systolic pressure (63 mmHg vs. 45 mmHg; p<0.001) and RVOT gradient (37 mmHg vs. 17

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1 Refers to incidence where the venous wall of the valve stent hangs into the lumen, causing stenosis. This was observed in the first generation of the Melody TPV, which has been redesigned to address this issue.
mmHg; \( p<0.001 \) compared to baseline values. Post-procedural angiography demonstrated reduced pulmonary regurgitation, which was reflected in an increase in mean diastolic pulmonary artery pressure (10 mmHg vs. 14 mmHg; \( p<0.001 \)) compared to the baseline measurement. Valvular competence was maintained throughout the follow-up duration and of the 32 patients with data at 36 months after PPVI, 80% had little or no valve regurgitation.

The first 50 patients of this cohort required a reoperation earlier than the subsequent 105 patients (\( p<0.001 \)). Device removal was required in 32% of the first 50 patients, compared with 5% of 105 patients. Similarly, the incidence of a residual RVOT pressure gradient of >25 mmHg was higher in the first 50 patients (32%) compared with the subsequent patients (5%). Residual RVOT pressure gradients of >25 mmHg after PPVI were associated with higher rates of reoperation (\( p=0.01 \)) and transcatheter reintervention (\( p=0.008 \)) than gradients of <25 mmHg. The incidence of procedural complications also decreased from 6% (3/50) to 3% (3/105) as the learning curve plateaued. However, freedom from transcatheter reintervention did not decrease with experience as these were predominantly performed to rectify stent fractures, which are not related to the PPVI learning curve.

**2010 Cost Impact**

Nordmeyer et al (2006) examined the cost effectiveness of PPVI by comparing models over 25 years for PPVI based on data from 84 patients (with overlaps to Lurz et al 2008) against known costs and outcomes for pulmonary valve replacement in 94 contemporary patients. The model included costs for the initial procedure, complications and reoperations. The investigators noted that earlier studies of PPVI inferred shorter hospital stay, fewer complications and lower mortality. As a result of this, PPVI was more cost effective at all time points relative to surgery despite a higher re-intervention rate. Based on these models, Nordmeyer et al (2006) reported that the PPVI device would have to cost more than US$33,678 before it becomes more expensive than surgery, while mortality would need to be 25% at 25 years before PPVI lost incremental effectiveness. Assuming all late complications (>5 years) could be treated with a second PPVI, the authors noted that the repeat PPVI rate could reach 17% a year before the procedure became less cost effective relative to surgery. Therefore, the model states that the longevity of the percutaneous valve does not need to match that of surgically implanted valves to retain cost effectiveness (Nordmeyer et al 2006).

However, it is important to note that since the primary data utilised for the assumptions are limited (e.g. overlap with Lurz et al 2008 where results were
confounded by presence of BMS), the validity of these cost estimates may be impacted by future, better designed studies on PPVI.

2010 Ethical, Cultural or Religious Considerations
No issues were identified from the retrieved material.

2010 Other Issues
Both included studies were performed by the same core researchers. One of the authors is a consultant to Medtronic Inc., the manufacturer of the Melody TPV, and has received honoraria and royalties for this device. In addition to this, two other authors are consultants to and have received honoraria from Medtronic Inc.

2010 Summary of Findings
Perioperative haemodynamic outcomes from the comparative study (Lurz et al 2009) indicated that PPVI achieves similar improvement to BMS in haemodynamic variables without the problem of pulmonary regurgitation that is associated with BMS. However, the PPVI data was confounded by the presence of a BMS and it is not clear from this study how these improvements affect patient outcomes and reoperation rates.

The case series study (Lurz et al 2008) indicated that PPVI is a feasible procedure (in a select group of patients) and that most patients who underwent PPVI avoided surgical RVOT revision. Nevertheless, the proportion of patients who required re-do procedures (surgical or transcatheter) was quite substantial and increased over time. The results also indicated that patient outcomes improved substantially with operator experience.

2010 HealthPACT action
The limited evidence from a single case series study also suggests that PPVI is associated with low mortality rates and is relatively safe with encouraging short term results. There are no data on the longevity of the Melody valve.

The paucity of long-term data is unlikely to be addressed in the near future. However, there is limited evidence that PPVI is feasible despite the high revision rates. It is recommended that PPVI is monitored for 24 months with the view of retrieving some data on the longevity of these valves.

2010 Number of Studies Included
Total number of studies 2
Level III intervention evidence 1
Level IV intervention evidence 1
2010 REFERENCES


2010 SEARCH CRITERIA TO BE USED

Pulmonary valve AND ((Percutaneous replacement) OR (Percutaneous implantation))