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Original Article

Transcatheter pulmonary valve insertion, expanded use and future directions*

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Abstract Transcatheter pulmonary valve replacement with the Melody® valve is an accepted alternative to surgical replacement of the pulmonary valve for some patients and therefore a complementary strategy in the long-term management of several groups of patients with congenital heart disease. It allows at least extending the time between sternotomies and possibly improving late outcomes. With a combined surgical and percutaneous approach, late morbidity for some of these patients will likely be diminished. This manuscript will review the current expanded applications for this technology, demonstrate several examples of its use and discuss future directions for this evolving equipment.

Keywords: Right ventricular outflow tract dysfunction; right ventricle to pulmonary artery conduit; surgical pulmonary valve replacement; pulmonary artery stenting; transcatheter pulmonary valve replacement

The development, approval and clinical success of transcatheter pulmonary valve replacement technologies has resulted in a paradigm shift for many diverse groups of patients with congenital heart disease.[1,2] It has changed the surgical approach in most centres in ways both narrow – upsizing conduits in smaller patients when feasible – and broad – reconsidering and expanding the use of the Ross autograft operation for aortic valve replacement.[3] It has changed the way we counsel the expectant family of a foetus likely to need surgical reconstruction of the right ventricular outflow tract – fewer lifetime operations.[4] The ability to less invasively provide improved function of the right ventricular outflow may allow us to better ask and hopefully answer questions such as how much chronic dysfunction of the pulmonary valve is acceptable in the long term for good late function of the right ventricle and minimised lifetime arrhythmia risk. Most immediately important, however, is the new possibility of giving good pulmonary valve function to poor surgical candidates who do not have circumferential conduits, especially those with multiple comorbidities.[5–7] This could potentially make the inoperable patient back into an operable one.

The initial and medium-term success of the Melody® has also led to its expanded use in patients with dysfunction of the right ventricular outflow tract but without a circumferential conduit,[5–7] and to its use in the tricuspid, mitral and aortic positions in selected cases all with encouraging early results.[8,9]

Previously, we discussed the basics regarding insertion of the Melody® valve.[10] In this paper, we intend, through multiple case presentations, to demonstrate expanded applications and discuss future directions for this evolving technology.

Methods

This is a retrospective review of procedures and outcomes for patients who have undergone transcatheter pulmonary valve replacement in a single centre. All procedures are performed following informed consent granted by the patient and/or the patient's legal guardian and in accordance with local institutional review board approval and oversight.

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Indications and contraindications

Although with future experience this may expand, the indications for transcatheter pulmonary valve replacement remain the same as those for surgical replacement of the pulmonary valve and include significant stenosis and/or regurgitation with resultant secondary dilation and/or dysfunction of cardiac chambers.[11] In the presence of significant systolic or diastolic dysfunction of the right ventricle; symptoms of fatigue or dypsnoea; arrhythmias; or worsening function of the tricuspid valve, we are less rigid in the application of these guidelines.

Contraindications to current transcatheter pulmonary valve replacement include lack of an adequate landing zone and extrinsic coronary compression with balloon dilation of the anticipated valve insertion area. An adequate landing zone is a location in the right ventricular outflow tract or main pulmonary artery that has a segment that is or can be dilated to no smaller than 17–18 and no larger than 22 mm. Generally speaking, for patients with a surgical history of a near adult-sized circumferential conduit and significant dysfunction of the pulmonary valve, there almost always winds up being a landing zone small enough and large enough for the valve.

In a non-circumferential conduit patient, this translates to a significant degree of narrowing somewhere in the main pulmonary artery or right ventricular outflow tract. Sometimes this can be rather challenging to sort out without invasive testing and balloon sizing. Similar to conduit patients, however, a landing zone 17–22 mm with balloon sizing is necessary to ensure stable valve seating.

Coronary compression, dynamically assessed, must also be excluded before hardware insertion in the outflow tract of the right ventricle. This is performed with balloon enlargement of the outflow tract to the diameter at which valve will be implanted. This is the most important safety concern to conclusively understand before stent implantation in the outflow tract, as inadvertent coronary compression has on a few occasions led to life-threatening consequences.[12] Both left and right coronary artery compression are possible, and sometimes a combination of ascending aortic angiography and selective coronary angiography are necessary to convince yourself that the coronaries are indeed remote enough from the expanded area of the outflow tract. In our limited experience, this appears to be less of an issue in patients with native outflow tracts.

Transcatheter pulmonary valve replacement: case examples

Case 1

This patient is a 10-year-old girl with an initial diagnosis of atresia of the aortic valve, tiny ascending aorta, large ventricular septal defect and balanced ventricles. Her prior surgical history included neonatal Yasui operation followed by upsizing of her right ventricle to pulmonary artery conduit 1 year later with a 19 mm Contegra® bovine jugular vein valved conduit (Medtronic). She developed marked dysfunction of the conduit with both stenosis and insufficiency, marked enlargement of the right atrium and ventricle, dysfunction of the right ventricle, hypertension of the right ventricle and moderate to severe regurgitation of the tricuspid valve. She underwent transcatheter pulmonary valve replacement as a two-step process. At the first procedure, candidacy was assessed with balloon compliance testing of her conduit and coronary evaluation. At the first procedure, she underwent balloon dilation of her stenotic right pulmonary artery and stenting of her dysfunctional conduit. Stenting of the conduit was very difficult because of this patient's marked right heart enlargement. This was finally accomplished after several attempts, delivering a 26 mm IntraStent™ LD Max™ stent (EV3, Plymouth, MN, United States of America) on a 16 mm diameter, 2-cm-long Atlas balloon (Bard Peripheral Vascular, Tempe, AZ, United States of America). Several months later, she was brought back to the catheterisation laboratory. At this procedure, a second stent was delivered in the conduit because of recoil of the first stent. This was a P3110 Palmaz® XL stent (Johnson & Johnson, Miami, FL, United States of America) delivered on a 16 mm diameter by 2-cm-long Atlas balloon. This was followed by the Melody® delivered on an 18 mm Ensemble® delivery system (Medtronic, Minneapolis, MN, United States of America). Delivery of both the second stent and the valve were also very challenging because of this patient's marked right heart dilation. It took a long time and a lot of finesse to get both the stent and valve to the conduit for deployment. Despite this, the procedure was a success. The final haemodynamic assessment showed a final right ventricle to pulmonary artery pressure gradient of 11 mm of mercury and trivial insufficiency of the valve. At 2 years' follow-up she is asymptomatic and there has been impressive improvement in right heart chamber sizes, which are now mildly enlarged, her Doppler outflow tract gradient is 19 mm of mercury, insufficiency of the pulmonary valve is trivial and regurgitation of the tricuspid valve is now mild. See Figure 1 for selected angiograms of this valve implantation.

Case 2

The next patient is a 27-year-old man with an initial diagnosis of Tetralogy of Fallot with absent pulmonary valve syndrome. He had a few early

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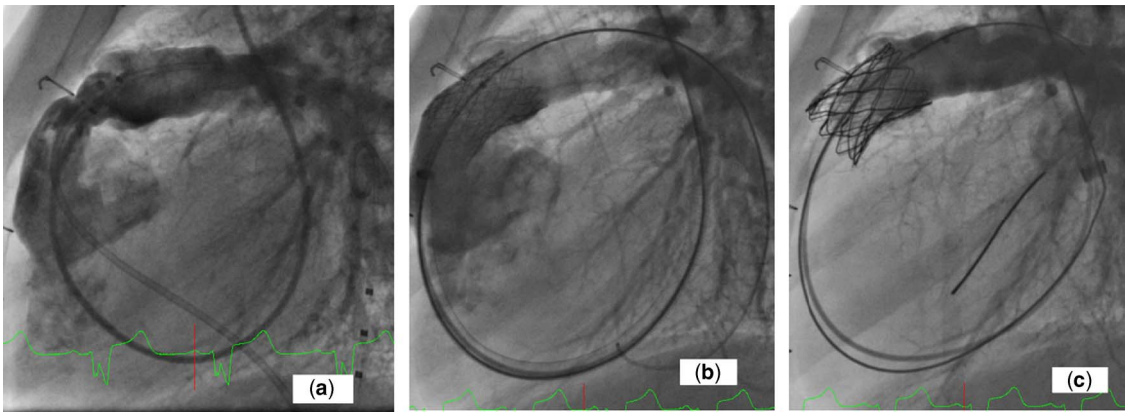

Figure 1.
*(**a**) A lateral view of the conduit before intervention; note the marked calcification and narrowing of the valve and severe regurgitation. (**b**) Marked enlargement of the conduit with stenting. (**c**) The competent new valve.*

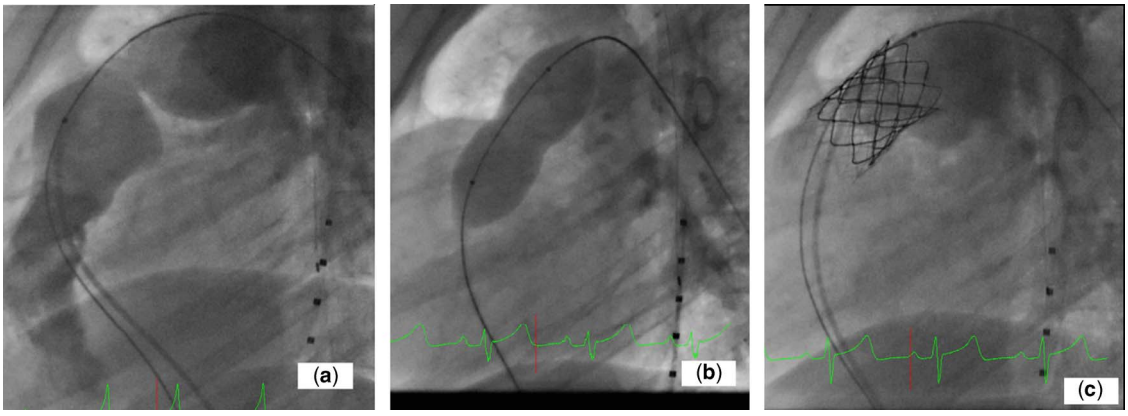

Figure 2.
*(**a**) A lateral view of the conduit before intervention; note the complete lack of calcification but significant narrowing at the prior valve annulus. (**b**) Marked compliance of the conduit with balloon sizing. (**c**) The competent new valve.*

respiratory issues and therefore underwent surgical repair consisting of patch closure of the ventricular septal defect, branch pulmonary artery plication and 15 mm aortic homograft right ventricle to pulmonary artery conduit in late infancy. Miraculously, he did well for over two and a half decades, but was referred for evaluation because of progressive combined stenosis and regurgitation of the conduit with secondary hypertension of the right ventricle. At cardiac catheterisation, he was found to have a uniquely non-calcified conduit with a minimal diameter of 13.3 mm by angiography. The conduit pressure gradient was 46 mm of mercury and the systolic pressure of the right ventricle was 84% systemic. Angiographically, insufficiency of the pulmonary valve was severe. Balloon sizing of the conduit was performed and it was found to be remarkably compliant and the coronaries were judged remote.

Two P3110 Palmax® XL stents were sequentially delivered in the conduit, the second delivered because of significant recoil of the first. Both were delivered on a 22 mm outer balloon diameter by 4-cm-long BIB® balloon (Numed, Hopkington, NY, United States of America). The Melody® valve was then delivered on a 22 mm Ensemble® delivery catheter. The valve and stents were post-dilated with a 20-mm-diameter Atlas balloon. The final result was excellent despite the initial conduit size with a final right ventricle to pulmonary artery pressure gradient of 13 mm of mercury and trivial angiographic insufficiency of the pulmonary valve (see Fig 2). At 1-year follow-up, he continues to do well with no symptoms, and trivial insufficiency and stenosis of the pulmonary valve.

Case 3

This patient is a 27-year-old man with Tetralogy of Fallot. He underwent initial repair at 1 year of age. Owing to marked insufficiency of the

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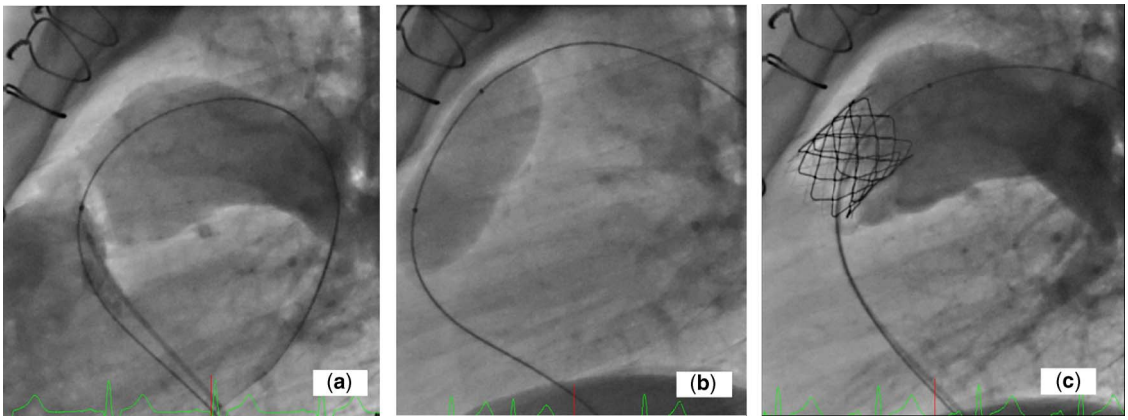

Figure 3.
*(**a**) A lateral view of the dysfunctional ePTFE bivalve during systole; note the marked calcification and thickening of the posterior leaflet stuck in a partially open position. (**b**) Balloon sizing with a slight waist, at the valve, corresponding to the calcified posterior leaflet. (**c**) The competent new valve.*

pulmonary valve and the resultant dilation of the right ventricle, he underwent surgical replacement of the pulmonary valve with a 0.6-mm-thick ePTFE (Gore, Flagstaff, AZ, United States of America) bi-valve prosthetic reconstruction of the right ventricular outflow tract at 16 years of age. The bi-valve was sized to a 24 mm dilator at surgery. The patient did well for many years, but developed recurrent dysfunction of the pulmonary valve at 27 years of age consisting of both stenosis and insufficiency. Owing to concurrent clinical arrhythmias, he underwent diagnostic cardiac catheterisation and intracardiac electrophysiologic study. He was found to have inducible atrial tachycardia that was successfully ablated but was also found to have easily inducible sustained ventricular fibrillation. Intracardiac pressures and angiography demonstrated 34 mm of mercury pressure gradient between the right ventricle and pulmonary artery, 57% systemic pressure of the right ventricle, good function of the right ventricle and moderate regurgitation of the pulmonary valve. At angiography, it appeared clear that the annulus of the ePTFE leaflets was intact, but the leaflets were calcified, thickened and poorly mobile. They appeared to be stuck in a partially open position.

The patient was brought for cardiac catheterisation and attempted transcatheter pulmonary valve replacement at a separate procedure. Real-time three-dimensional transoesophageal echocardiography was performed at that procedure, which very much agreed with the angiographic appearance of the bi-valve prosthesis. The valve annulus was intact but the leaflets had limited excursion and poor coaptation leading to the dysfunction of the pulmonary valve. Balloon sizing was performed and the coronary arteries were confirmed to be remote from the landing zone. The balloon size of the annulus of the pulmonary valve was found to be 22 mm in multiple fluoroscopic planes consistent with our ability to hold the leaflets open in a round manner and therefore effectively stent the valve open with 360° apposition of the stent within the ePTFE bi-valve leaflets. The landing zone was determined to be inside the ePTFE valve itself, which was densely calcified, aiding in stent positioning. To ensure landing zone stability for the Melody® valve, the ePTFE valve was stented with a P4010 Palmaz® XL stent delivered on a 24 mm outer balloon diameter by 4-cm-long BIB® balloon. The Melody® was then delivered on a 22 mm Ensemble® delivery catheter (see Fig 3). Post right ventricle to pulmonary artery gradient was 9 mm of mercury, and trivial regurgitation of the pulmonary valve was noted. This patient is now over a year out from the procedure, is asymptomatic, and by echocardiography has minimal stenosis and regurgitation of the pulmonary valve. On repeat intracardiac electrophysiologic study 1 year post valve implant, there are no inducible arrhythmias, thereby averting the need for an implantable cardiac defibrillator at this time.

Discussion/conclusions

Our cases demonstrate a use of the Melody® valve considered within the United States Food and Drug Administration Humanitarian Device Exemption approved applications of the valve (Case 1), and two which display extended use of the valve (Cases 2 and 3). In the United States of America, these clinical uses are considered "off-label", but the majority of implanting centres in the United States of America have sought and obtained additional

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institutional review board approval for extended use of the valve. This includes its use in dysfunctional bio-prosthetic valves in several anatomic positions (pulmonary, tricuspid, aortic), use in native outflow tracts of the right ventricle without a circumferential conduit and use in additional surgical conduits (right atrium to right ventricle, left ventricle to descending aorta). It appears likely that Melody® valve function will be just as good in some of these extended applications as in approved circumferential conduits, particularly bio-prosthetic valves.[8,9,13]

In the 13 years since the initial successful human implant of what we now know as the Melody® valve, there have been over 4200 implants worldwide, 2000 in the United States of America alone.[14] There are currently 172 implanting centres on five continents.[14] This experience is also clearly dwarfed by the worldwide transcatheter aortic valve implantation experience, currently estimated at over 50,000 implants worldwide.[15] Clearly, these new technologies have taken the medical community by storm and have changed the culture of paediatric cardiology, adult cardiology and cardiovascular surgery in ways that are still evolving. Virtually, all implanting centres for transcatheter valves have developed heart teams that review cases, work together and foster integration of two previously alien cultures. Earlier, operating rooms and catheterisation laboratories were seen as separate planets in most hospitals with their only intersection being due to an emergency in one sphere or the other, which led to an acute interaction. Now the integration of technologies is becoming the norm with all the attendant possibilities working together creates.

It is clear that the Melody® valve is not without its shortcomings with both early stent fracture and endocarditis noted as significant issues.[16,17] Its 22 Fr delivery system remains rather large and long for our smaller patients. It will also clearly not be the answer for the majority of our congenital heart disease patients with a surgical history of transannular patch enlargement. Despite this, it is also clear that with marked creativity among operators and existing equipment, some of these patients may indeed be found to be transcatheter pulmonary valve implantation candidates.[5–7] Evolution, experience and new equipment will likely offer less-invasive further answers to many of our patients.

Taken altogether, the Melody® has been an enormous leap forward in the care of patients with congenital heart disease. It has brought congenital cardiologists and surgeons together to better discuss lifetime strategy in patient care, offered less-invasive valve replacement options to thousands of patients, and its shortcomings have shown the direction for future product development.

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