

Right ventricular outflow tract revalvulation using the Melody Valve: The next frontier

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INTRODUCTION

Various congenital heart lesions with anatomical abnormalities involving the right ventricular outflow tract (RVOT) will require surgical repair early in childhood. Classical lesions include tetralogy of Fallot, pulmonary atresia and truncus arteriosus. A significant number of these will, over time, develop additional problems of the RVOT which will need to be addressed in order to prevent right ventricular dysfunction.

SURGICAL REVALVULATION

Surgery has been the preferred method of establishing RVOT revalvulation. It has traditionally been reserved for children older than 3 years. Surgical revalvulation consists of the implantation of allo- or xenografts. Pulmonary homografts are generally preferred, but other valves e.g. Contegra® or prosthetic conduits are also being used. Due to improvements in surgical techniques, mortality for re-operation has declined and is now in the region of 3.7%.

However, failure of the conduit eventually occurs because of limited longevity. Conduit degeneration is observed in more than 75% of homografts over time. Lifespan of conduits are measured

ABSTRACT

Congenital heart lesions with abnormal right ventricular outflow tract anatomy will require early surgical intervention. Re-intervention rates in these patients are high due to homograft degeneration. Until recently, surgery was the only treatment option for right ventricular outflow tract dysfunction. Percutaneous pulmonary valve implantation has been introduced as a new therapeutic alternative to prolong conduit life span and to reduce surgical re-intervention rates. Short- and mid-term results have been favourable and showed that it is a safe and effective therapy. These are reviewed with emphasis on the Melody valve.

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in terms of years of freedom from re-operation. Freedom from re-operation varies (see Table I) with rates of 97% at one year to, on average, 70% and 31% after 10 and 15 years respectively.⁽¹⁻³⁾ Low body weight, younger age at insertion, small size grafts and longer cross-clamping times are factors associated with early graft failure.^(1,4) It has been estimated that these patients may require up to 5 conduit revisions over a lifetime.

Multiple conduit revisions in these patients often result in prolonged hospital stays, increased morbidity and mortality due to the fact that difficulty of surgery increases with every re-operation. This may result in a considerable increase in medical costs and a negative impact on quality of life. Nevertheless, surgery has good long term survival and should be considered as the gold standard of treatment.

PERCUTANEOUS RVOT REVALVULATION

Until recently, surgery was the only option for managing RVOT dysfunction. The first percutaneous pulmonary valve was implanted

TABLE I: Freedom from surgical re-intervention

Series	Number(n)	Published	Freedom from re-intervention (%)			
			1y	5y	10y	15y
Kim ⁽¹⁾	112	2011	97	77	35	
Dearani ⁽³⁾	1095	2003			55	32
Stark ⁽²⁾	656	1998		84	58	31

TABLE 2: Melody® valve: Indications and contraindications

Inclusion criteria	Exclusion criteria
Weight ≥30kg	Unfavorable coronary artery anatomy
Conduit size ≥16mm	Central vein obstruction
Dysfunctional RVOT conduits with clinical indication for reintervention, and either: Regurgitation: ≥ moderate regurgitation or Stenosis: mean RVOT gradient ≥35mmHg	Venous anatomy cannot accommodate a 22-Fr size introducer Pregnancy Active infection

in the year 2000 by Professor Philippe Bonhoeffer.⁽⁵⁾ This work resulted in the development of the Melody® valve (Medtronic, Minneapolis, MN, USA), which is a dedicated percutaneous pulmonary valve which is now commercially available. The Edwards SAPIEN transcatheter heart valve (Edwards Lifesciences, Inc., Irvine, California) was initially developed for patients with severe aortic stenosis. This valve has since been used and adapted for RVOT dysfunction in the pulmonary position.⁽⁶⁾ The current Melody® valve is available in 18 - 22mm diameters and the Edwards SAPIEN valve in 23 and 26mm sizes.

CURRENT INDICATIONS FOR PERCUTANEOUS PULMONARY VALVE IMPLANTATION

Only patients meeting indications for surgical re-intervention qualify for consideration of valve implantation. Clinical and morphological indications and contraindications for Melody® valve implantation can be viewed in Table 2.

DIAGNOSTIC EVALUATION

Patients with right ventricle to pulmonary artery (RV-PA) conduit dysfunction need to be evaluated for possible percutaneous pulmonary valve implantation (PPVI). ECG holter is performed to identify possible arrhythmias and for calculation of QRS intervals. Objective functional assessment to determine exercise capacity can be done by measuring the peak oxygen uptake (VO2max) and anaerobic threshold derived from respiratory gas analysis during maximal exercise testing.⁽⁷⁻⁹⁾ Transthoracic echocardiography is used to determine right ventricular pressure load, size and categorical assessment of pulmonary regurgitation. However, echocardiographic right ventricular functional assessment does not correlate well with cardiac magnetic resonance imaging (MRI).^(10,11)

Pulmonary regurgitation severity should be assessed and classified. RVOT anatomy, RV-PA mean gradients, mitral- and tricuspid regurgitant jets can yield valuable information.⁽⁸⁻¹¹⁾

High resolution computed tomography (CT) angiography of the RVOT gives important information regarding RVOT anatomy and the spatial relationship to the coronary arteries.⁽⁸⁾ CT angiography does, however, have added radiation exposure compared to MRI. Cardiac MRI gathers valuable information regarding ventricle mass, function and volumes and is currently the preferred investigation.^(7,8,13)

TECHNICAL ASPECTS OF RVOT REVALVULATION BY MEANS OF THE MELODY® VALVE

The Melody® valve consists of a segment of modified-bovine jugular vein sutured into a platinum iridium stent of 34mm in length. The valve can be crimped down to 6mm and re-expanded from a minimum of 18mm to a maximum of 22mm (Figure 1A).

Delivery system

The Ensemble transcatheter delivery system was designed for percutaneous Melody® valve implantation and consists of a balloon-in-balloon structure with a retractable sheath for valve covering post crimping. The system is 100cm in length and has an outer diameter of 22Fr size (Figure 1B).

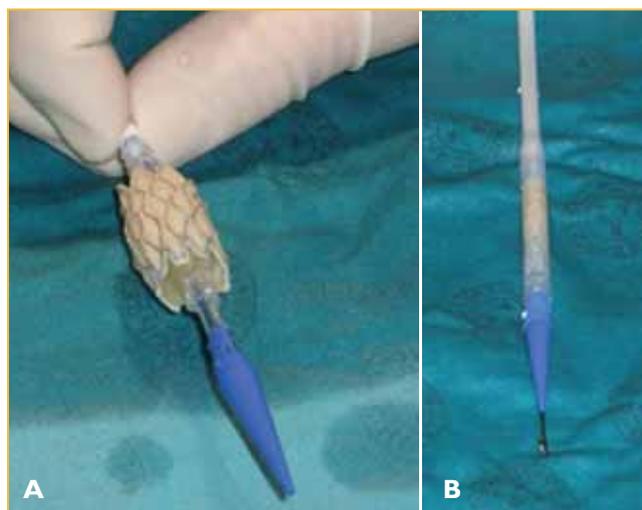


FIGURE 1: Melody® valve and Ensemble delivery catheter
(A) The valve is partially crimped over the balloon portion of the catheter. (B) The valve can be seen fully crimped and covered with the outer sheath.

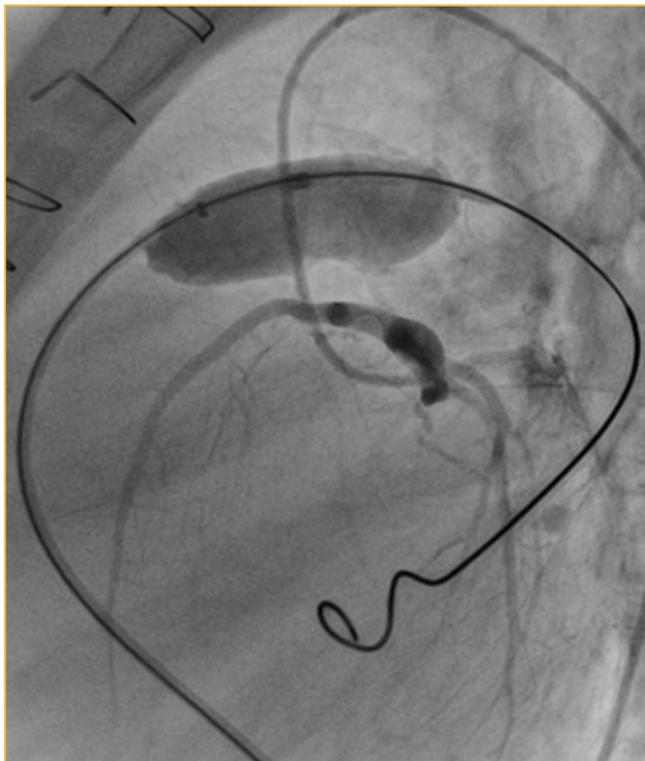


FIGURE 2: Demonstration of coronary artery proximity
 Simultaneous coronary angiogram with inflation of a low pressure balloon in the RVOT demonstrates that the coronary arteries are not in danger of occlusion.

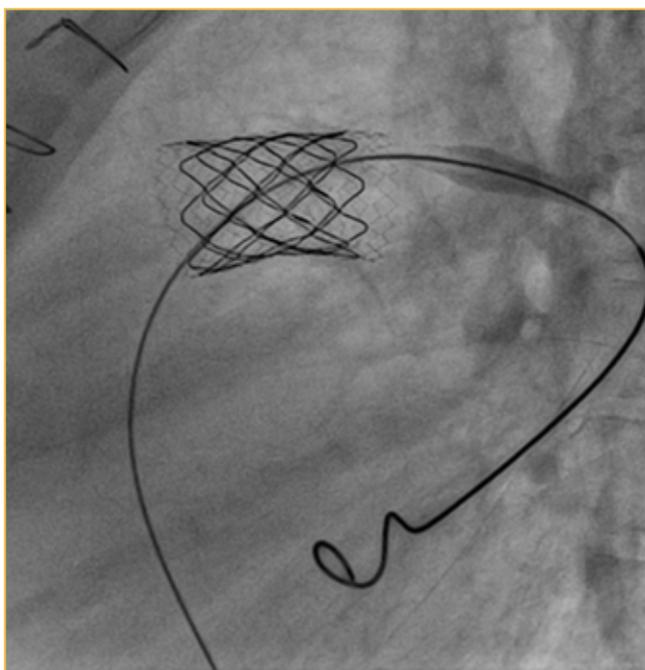


FIGURE 3: Melody® valve expanded
 The Melody® valve delivered into the pre-presented RVOT. Note the distal tip of Ensemble delivery system.

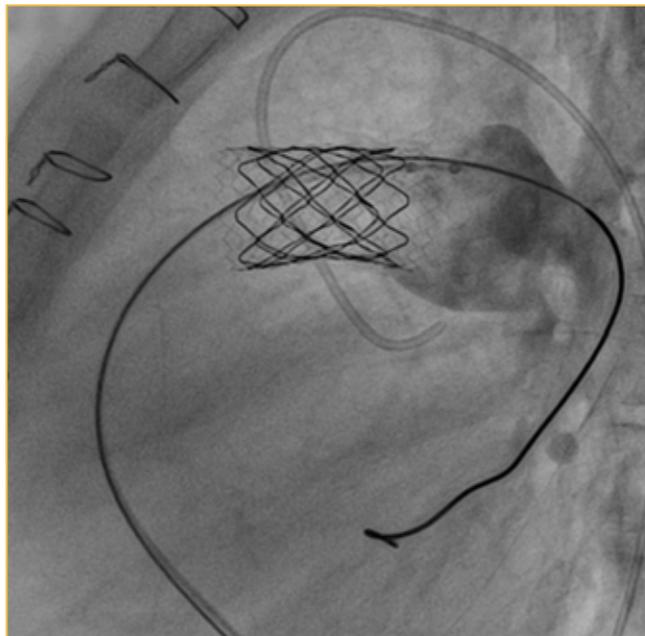


FIGURE 4: Post valve implantation angiogram
 Angiogram in pulmonary artery distal to newly implanted valve demonstrates no pulmonary regurgitation.

Procedural aspects

Central venous accesses, preferably femoral access is obtained. Right and left heart catheterisation with a full set of hemodynamic calculations is performed. Patients meeting the inclusion criteria will then undergo simultaneous coronary angiography and inflation of a low pressure balloon in RVOT to exclude coronary artery compression (Figure 2).^(8,10) Absence of ischemic ECG changes in combination with normal coronary angiography information will be reassuring for continuation of the procedure.

Use of a stiff guidewire [Meier (Boston Scientific, Natick, MA, USA), Lunderquist™ Extra Stiff (COOK Medical, Bloomington, USA) and Amplatz Ultra Stiff (COOK Medical, Bloomington, USA)] in a safe and stable position is of critical importance and will prevent serious complications such as pulmonary artery perforations.

Preparing the “landing zone” for Melody® valve implantation is a crucial step in the procedure. This is done by predilating and pre-presenting the RVOT. High pressure balloons [Mullins-X Ultra high pressure (NuMED, Hopkinton, NY, USA) or Bard Atlas® PTA balloons (Bard Peripheral Vascular, Tempe, AZ, USA)] and stents with a high radial strength are preferred [Andra stent (Andramed GmbH, Reutlingen, Germany), Intrastent Max LD (ev3 Endovascular, Plymouth, USA)]. The decision to use a covered or bare

metal stent for pre-stenting will be influenced by the risks of homograft rupture. Most operators would nowadays prefer to use a long covered stent ($\geq 45\text{mm}$) in a homograft since calcified, crimped homografts fracture if dilated. In these patients flaring proximal and distal ends to appose tightly to the surrounding tissues at the proximal and distal anastomosis would be important. It is essential to create a stable Melody[®] landing site and any recoil during pre-stenting should lead to additional stenting. It is important to note that any residual RVOT gradient $> 15\text{mmHg}$ should not be accepted prior to valve deployment.

Once RVOT rehabilitation has been performed, the Melody[®] valve is delivered in an appropriate position (Figure 3). Repeat hemodynamic assessment and angiography are performed to evaluate the result (Figure 4). Residual gradients can be treated with high pressure balloon dilatation after valve implantation. Cardiothoracic backup is desirable during the procedure.

OUTCOMES OF PERCUTANEOUS PULMONARY VALVE IMPLANTATION

More than 3 000 valves have been implanted worldwide and overall mortality is very low (0% - 1%),^(7,10,12,14-17) Procedural success for attempted percutaneous valve implantation is excellent. The most common exclusion factor has been the risk of coronary compression. Significant reduction in outflow tract gradient and/or abolishment of pulmonary regurgitation was observed in all cases. Right ventricular volumes also improved markedly.

Major procedural complications included dislodgement of the valve, coronary compression, rupture of homograft and haemothorax due to pulmonary artery perforations.^(7,13-18) Dislodgement of the device occurred mostly during the initial development phase and could be related to operator inexperience as well as the early learning curve. It is now extremely rare, especially with pre-stenting. Coronary compression was responsible for virtually all deaths resulting from percutaneous revalvulation. Since this is a potentially avoidable complication, pre-selection with sophisticated imaging modalities as mentioned have become essential. Rupture of homograft conduits is a rare, but ever present risk. Therefore, making routine use of a covered stent or at least having one of these available during the procedure is essential. The pulmonary arteries may be perforated by the very stiff guidewires employed to deliver the valve. In the worldwide experience, some resolved spontaneously, could be treated by implanting a covered stent to seal off

the perforation or required a thoracotomy. Overall, early complications were rare during percutaneous procedures, occurring in less than 8.5% of implantations.^(8,16,17) This compares favorably to surgical series where early complications have been described in up to 9.6% of patients.⁽¹⁸⁾

Follow-up results for outcome are now short to mid-term. The most common complication has been stent fractures which occurred in 5% to 30% of cases.^(14,15,19) Although the vast majority of stent fractures remain asymptomatic, it may lead to the development of outflow tract gradients. However, this can easily be treated with the implantation of another percutaneous valve. This problem is likely to decrease due to the current practice of routine right ventricular outflow tract pre-stenting. Although extremely rare, endocarditis is a vexing problem and the most common reason for valve explantation.⁽²⁰⁾

Freedom from valve dysfunction or re-operation ranged from 95 - 100% at one year to 70% at seventy months during follow-up.^(8,14,15) These results provide evidence that the initial aim of prolonging the life-span of surgically placed right ventricular outflow tract conduits can be successfully achieved by the implantation of a percutaneous valve.

Cost analyses have been favourable. Although the valve itself is expensive, the low morbidity and short hospital stay makes total cost comparable to that of surgery.⁽²¹⁾ It should be pointed out that cost comparisons for South Africa are currently not available. The main benefits of percutaneous pulmonary valve implantations are the low risks, short hospital stays, delay in the need for surgery and improvement in quality of life.

TIMING OF RIGHT VENTRICLE OUTFLOW TRACT REVALVULATION: THE CONTROVERSY

Right ventricular outflow tract dysfunction is one of the most common killers in congenital heart diseases. Although the indications for intervention in stenosis are clearly defined, the same cannot be said for pulmonary valve regurgitation. As a matter of fact, it is a well-established fact that some patients with pulmonary regurgitation and dilated right ventricles show little improvement after right ventricular outflow tract revalvulation. Optimal timing of surgery in this subgroup of patients is not clear and remains controversial. The reason for this is that we currently do

not know how much overload a right ventricle can tolerate before irreversible damage sets in.

Patients with pulmonary regurgitation present with dilated right ventricles because of the increased volume loads on the ventricles. Studies in post-operative patients with tetralogy of Fallot and pulmonary regurgitation have shown abnormal right ventricular deformation indices despite normal global right ventricular function.⁽²²⁾ Right ventricular ejection fractions assessed by cardiac MRI were normal, signifying that right ventricle systolic function parameters only become abnormal late in RVOT dysfunction and long after dysfunction at cellular level was present. In another study in elite cyclists, a disproportionate incidence of ventricular tachycardia and sudden death was observed.⁽²³⁾ Dilation of their right ventricles was demonstrated and ascribed to the large volume loads on the heart during frequent peak exercise. This caused right heart injury resulting in electrical dysfunction as the presenting symptom. It is important to take note of the fact that the dysrhythmias in all the athletes occurred before measurable right ventricular dysfunction became apparent.

Compare this to patients with right ventricular outflow tract dysfunction – we know that it leads to right heart dilation and that a significant number die unexpectedly due to arrhythmias. Furthermore, these dilated right ventricles have normal or near normal function on MRI. All these findings suggest that electrical and cellular level dysfunction set in long before global mechanical dysfunction becomes apparent. If we allow too much time to pass before revalvulation, irreparable damage may occur to the right ventricle explaining the poor results of revalvulation in some patients. In the past, physicians tended to wait as long as possible before intervening due to the risks and morbidity associated with surgery. In this new era of percutaneous valves, one may thus consider revalvulation at an earlier age in order to preserve right ventricular mechanics. As a result, some physicians advocate intervention in these patients before they become symptomatic. However, at present we still do not have the ability to accurately measure when it is time to intervene in asymptomatic patients and the timing of intervention is bound to remain controversial until we can scientifically define measureable right ventricle parameters to guide the decision.

FUTURE DEVELOPMENTS

New developments consist of mounting valves on stronger stents and a new version of the Melody[®] valve will soon become available.

Also, valves are being developed for larger outflow tracts which cannot be treated with the current valve sizes available. This has been a limiting factor in some patients, especially patients with dilated outflow tracts. Recent studies have also shown that the valve can be implanted in selected cases in younger patients (<20kg) and has even been used during hybrid procedures to avoid cardiac bypass.⁽²⁴⁾ Surgeons are also adapting techniques at initial procedures to construct conduit angles amenable to transcatheter intervention and at a safe distance from the coronary arteries.

CONCLUSION

Percutaneous pulmonary valves are a safe and effective therapy for revalvulation of the right ventricular outflow tract. The stented valves can be implanted with a high success rate as well as low morbidity and mortality. Results have proven that percutaneous pulmonary valves extend the lifespan of conduits. It is important to realise that percutaneous revalvulation is complimentary to surgery and not in competition with surgical revalvulation. The availability of percutaneous valves may change the way in which we approach right ventricular revalvulation in the future, but remains controversial at present for certain indications.

Conflict of interest: none declared.

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