Transcatheter Pulmonary Valve Replacement: Impact on Management

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Abstract

Transcatheter valve therapeutics has revolutionized interventional cardiology in the twenty-first century. When Bonhoeffer and colleagues performed the first-in-man percutaneous pulmonary valve implantation (PPVI) in 2000, it changed the treatment paradigm of what we can offer patients with congenital heart disease (CHD). In the span of this chapter, we will discuss the underlying burden of pulmonary valve disease in the CHD population and the current indications for surgical pulmonary valve replacement. We will outline the PPVI procedure from procedural and technologic perspective and then review the state of the evidence regarding clinical outcomes, risks & benefits, and potential future perspectives.

Keywords

Transcatheter pulmonary valve replacement • Surgical pulmonary valve replacement • Percutaneous pulmonary valve replacement • Valve systems

Introduction

Transcatheter valve therapeutics has revolutionized interventional cardiology in the twenty-first century. When Bonhoeffer and colleagues performed the first-in-man percutaneous pulmonary valve implantation (PPVI) in 2000, it changed the treatment paradigm of what we can offer patients with congenital heart disease (CHD). In the span of this chapter, we will discuss the underlying burden of pulmonary valve disease in the CHD population and the current indications for surgical pulmonary valve replacement. We will out-

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M.K. Friedberg, A.N. Redington (eds.), *Right Ventricular Physiology, Adaptation and Failure in Congenital and Acquired Heart Disease*, https://doi.org/10.1007/978-3-319-67096-6_17

line the PPVI procedure from procedural and technologic perspective and then review the state of the evidence regarding clinical outcomes, risks & benefits, and potential future perspectives.

Pulmonary Valve Disease Burden

The majority of pulmonary valve pathology is either congenital or a consequence of surgery or intervention. Native pulmonary valve stenosis or right ventricular outflow tract (RVOT) obstruction occurs in ~25% of patients with CHD, in isolation or in association with other congenital syndromes such as Tetralogy of Fallot (TOF). The majority of isolated congenital pulmonary stenosis (PS) is valvular; while patients with TOF or Williams syndrome can present with PS at the subvalvular, valvular, and supravalvular anatomic levels. Depending on the patient's age and the degree of obstruction to pulmonary blood flow, PS can lead to variable clinical presentations. In the case of severe fetal PS or pulmonary atresia, a neonate may present with ductal-dependent physiology requiring emergent intervention. Children with mild or moderate valvular PS may be asymptomatic; but symptoms can develop or progress in severity later in life. Worsening PS can lead to secondary RV hypertrophy, decreased compliance, and elevated diastolic filling pressures. Patients may seek medical attention with exertional dyspnea, dysrhythmias, or rarely congestive heart failure.

Pulmonary regurgitation (PR) is a common finding in CHD patients especially in those with repaired conotruncal abnormalities. While significant PR may be present as an isolated congenital condition, it is typically iatrogenic from cardiac surgery or intervention. PR can develop after surgical valvotomy or balloon valvuloplasty performed for valvular pulmonary stenosis. After surgical TOF repair, PR is a near universal finding especially when a transannular patch is inserted. It can develop as a consequence of valve dysplasia, bilateral pulmonary artery (PA) stenosis, or with significant pulmonary hypertension. Adding to disease prevalence, with the passage of time, nearly all surgical implanted homografts, monocusps or bioprosthetic valves in the pulmonary position will develop some combination of PS and/or PR.

Historically severe PR was considered benign as it can be tolerated for many years. However, by the third or fourth decade, many patients will notice changes in exertional capacity or other symptoms. Chronic RV volume loading will lead to RV dilation, secondary decrease in LV filling volumes, and reduction in biventricular efficiency and cardiac output. Changes in RV compliance and dimensions can further lead to fibrosis, reduced ejection fraction in both ventricles, secondary tricuspid regurgitation, an increased preponderance for dysrhythmias and electrical instability. In addition to dyspnea/fatigue with exertion, patients may present with palpitations, syncope, edema, hepatic congestion, and sudden cardiac death.

Surgical Pulmonary Valve Replacement

Up until the start of this century, the only definitive therapy available for pulmonary valve disease was surgical replacement. Surgical PVR has been the gold standard in the treatment of severe PR, mixed native PS or PR, or failure of a prior surgical bioprosthetic valve, homograft, monocusp or conduit implants. In patients who develop symptomatic PV disease, including changes in functional status, the decision to offer surgery is relatively straightforward (Table 17.1). The more controversial question has been when to offer surgical PVR to the "asymptomatic patient" with severe PR—given the inherent procedural risks associated with open heart surgery and the limited durability of most valve prosthesis. Several observation studies have suggested cut offs of RV-end diastolic volume index (RVEDVI) of >150 to >170 ml/m^2 to offer asymptomatic patients surgical PVR [1–4] in addition to objective findings on formal exercise testing and Holter monitoring. Most adult congenital heart disease (ACHD) specialists use a holistic, individualized approach combining RV

Table 17.1 Suggested Indications for Pulmonary Valve Replacement

Figiola et al. [1]
• Significant PR (PR fraction ≥35% on MRI) with progressive RV dilation and dysfunction. RV/LV end-diastolic ratio ≥ 1.5 in symptomatic patients
• RV/LV end-diastolic ratio ≥ 2 in asymptomatic patients
• Reduced exercise capacity with or without documented arrhythmias
Geva et al. [2]
• Moderate or severe PR (PR fraction ≥25% on MRI) and 2 or more of the following:
• RV end-diastolic volume index ≥150 ml/m^2 (z score >4)
• RV end-systolic volume index ≥80 ml/m^2
• LV end-diastolic volume index ≥65 ml/m^2
• RV ejection fraction ≤47%
• RV outflow tract aneurysm
Clinical criteria: exercise intolerance, symptoms and signs of heart failure, cardiac medications, syncope, sustained ventricular tachycardia
• Presence of other hemodynamically significant lesions
• Patients who underwent TOF repair at age ≥ 3 years, PVR may be indicated sooner and in the presence of less severe RV dilation and dysfunction due to higher risk of adverse clinical outcomes

PVR pulmonary valve replacement, *PR* pulmonary regurgitation, *MRI* magnetic resonance imaging, *RV* right ventricular, *LV* left ventricular, *TOF* tetralogy of Fallot

size and function, LV function, functional status and disease burden in deciding when to offer surgical PVR.

Isolated surgical PVR is an effective therapy with low perioperative mortality (~1–2%) and relatively little perioperative morbidity [5]. There remain a variety of surgical approaches in performing PVR that depend on the choice of prosthesis, reduction of prior RVOT surgical patch, and the need for any additional repairs (e.g. tricuspid valve repair, RA MAZE procedure, pulmonary arterioplasty). The majority of PVR operations are performed with cardiopulmonary bypass, though off-bypass PVR has been described. The choice of prosthesis should take into account the patient's age, potential for growth and the need for future reoperations or interventions. In general, mechanical valves have not been implanted in the pulmonary position due largely to theoretical concerns of valve thrombosis in a low pressure system [6–8]. Homografts are commonly used in the children with complex RVOT obstruction because of the availability of smaller diameters [9]. Bioprosthetic implants are xenograft based valves (porcine, bovine, or equine) either animal valves or reconstructed pericardium encased in a metallic ring/stent or using a "stentless" design. Finally monocusp valves are constructed individually by the surgeon to fit the patient's anatomy using pericardial tissue or polytetrafluoroethylene (PTFE) [10].

Prospective comparisons between these surgical options are limited. Most retrospective series suggest ~50–80% 10-year freedom from redo-PVR, regardless of chosen valve type [5, 11–14]. Valve degradation over time is conjectured to occur from exaggerated fibrosis and calcification of valve leaflets related to the chemical cryopreservative used for the valves and possibly exacerbated by an autoimmune response. In general, it appears that most patients after surgical PVR will require a repeat operation ~5–15 years after implantation.

Percutaneous Pulmonary Valve Replacement

While surgical PVR remains a success story in congenital cardiac disease, there are many clinical scenarios in which surgery is high risk or contraindicated. Young patients undergoing RVOT reconstruction will likely require multiple sternotomies throughout their lives. Each subsequent surgery adds surgical risk and higher perioperative mortality from adhesions, scar tissue, and anatomic disruption [15]. Each subsequent ventriculotomy theoretically increases the possibility of scar related VT from the healed incision. Some patients are poor surgical candidates due to comorbidities including physical or mental challenges that can complicate post-op recovery. The desire to find alternatives to open heart surgery also stems from the drive to minimize risk. Our patients demand the least invasive means of

accomplishing the medical task—in order to minimize procedural risk. Patients intuitively seek out approaches that will minimize discomfort and recovery times. Likewise, cosmetic concerns related to sternotomies, wound healing, complications related to cardiopulmonary bypass all come into play.

After overcoming multiple technologic hurdles of developing compressible valves that can be delivered through catheter-based systems, the first-in-man percutaneous PVR was performed by Dr. Philipp Bonhoeffer in 2000 [16]. Since then, thousands of pulmonary valves have been implanted worldwide using primarily the Medtronic Melody® valve (Minneapolis, MN) and Edwards SAPIEN®, Sapien XT® and Sapien 3® valves (Edwards Life Sciences, Irvine, CA).

Indications

PPVI has become an alternative to surgical pulmonary valve replacement (PVR) in patients with dysfunctional bioprosthetic pulmonary valves, homografts, or conduits with intermediate-to-long-term follow-up [17, 18]. Severe PR, progressive symptoms, exercise intolerance, arrhythmias, RV dilation and dysfunction are all (in various combinations) considered criteria for replacement or implantation of a pulmonary valve (see Table 17.1) [19]. Patient selection is important and as in all congenital heart disease should be performed using a multidisciplinary construct using echo and MRI assessment of outflow tract morphology and PR severity, cardiopulmonary exercise testing (as a measure of exercise capacity), serial assessment of change in symptoms, and cardiac catheterization to confirm findings, assess PA pressures, and examine the coronary arteries. One must ensure that there is no subvalvular or supravalvular (including PA) obstruction that requires treatment with stents prior to PPVI. In patients for whom additional repairs are needed such as atrial arrhythmia treatment (MAZE) or with significant tricuspid valve regurgitation and requires direct repair, surgery remains a preferred strategy over PPVI.

The Valve Systems

The two valve systems with greatest worldwide experience for percutaneous PVI are the Melody® valve and Ensemble® delivery system (Medtronic Inc) and the Edwards Sapien® Pulmonic Transcatheter valve (Edwards Lifesciences) and the Edwards RetroFlex III® transfemoral delivery system. Newer generation valves from Edwards (Sapien XT® and Sapien 3®) and newer delivery systems (Novoflex® and Commander®) have also been used in the pulmonic position.

The Melody® valve and corresponding Medtronic Ensemble® delivery system (Fig. 17.1) were approved in Canada and Europe in 2006 and by the U.S. Federal Drug Administration (FDA) in 2010. The Melody® valve consists of a harvested valve bovine jugular vein that is sutured into a 28 mm long, 18 mm in diameter platinum/iridium stent frame. The valve is preserved in a proprietary mixture of glutaraldehyde and alcohol and must be manually crimped onto a 22 Fr. balloon-in-balloon catheter (BIB, NuMED Inc., Hopkinton, New York) with available balloon diameters of 18, 20 and 22 mm (stent-valve outer diameter up to 24 mm on the 22 mm balloon). The Ensemble® delivery system allows the valve to remain sheathed until positioned in the landing zone, achieving the correct position at the pulmonary annulus.

The original Sapien® valve consisted of bovine pericardial leaflets with a proprietary Thermafix® treatment to prevent calcification, sewn into a balloon expandable stainless steel platform. The Sapien XT® and Sapien 3® use a cobalt chromium alloy in place of stainless steel and the Sapien 3® adds a polyethylene terephthalate outer skirt to minimize paravalvar leak. The Sapien 3® is available in 20 mm, 23 mm, 26 mm, and 29 mm sizes—and given its lower profile with improved stent design is expected to supplant prior valve generations. The Commander® delivery system requires an Edwards eSheath® that is 14 Fr. for smaller valve sizes and 16 Fr. for the 29 mm valve (that expands to 18 and 20 Fr. outer diameter—allowing delivery in vasculature $\geq$5.5 mm and $\geq$6 mm in diameter respectively).

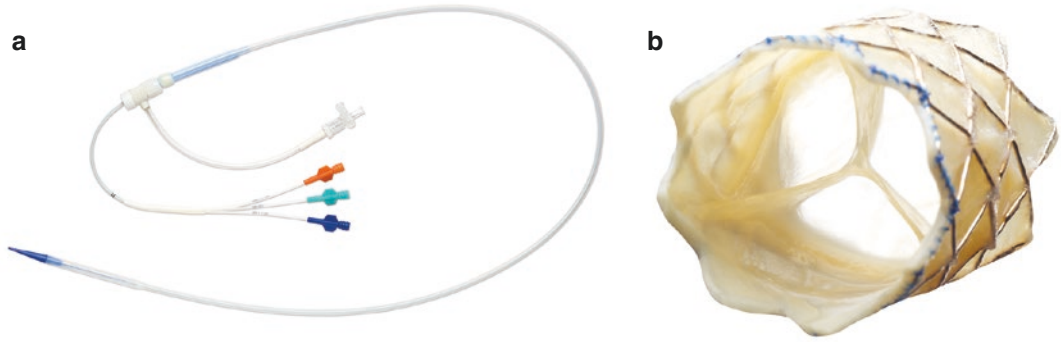

Fig. 17.1 The Medtronic Melody® Transcatheter Pulmonary Valve and Ensemble® Delivery System. *Panel A*. The Medtronic Melody® Valve which is a harvested bovine jugular vein valve that is sewn onto a 28 mm long platinum/iridium stent. *Panel B*. Medtronic Ensemble® delivery system is 22 Fr. delivery system with an integrated sheath designed for Melody® valve via the femoral or internal jugular veins. The Ensemble® delivery system comes with expandable balloon sizes of 18, 20, and 22 mm. Images published with permission—Melody® and Ensemble® systems are trademarks of Medtronic

Table 17.2 Approved valves in North America used for PPVI

	Medtronic melody® valve	Edwards SAPIEN XT® valve
Valve sizes	*Initial diameter:* 18 mm	16, 17, 20, 22 mm
	Crimped diameter: 6 mm	*Specialized crimper*
	Final diameter: 16–22 mm	20, 23, 26, 29 mm[a]
Valve type	Bovine jugular	Bovine pericardial
Balloon	BiB – 18, 20, 22 mm	Semi-compliant 23 or 26 mm
Stent platform	Platinum/iridium	Cobalt chromium
Sheath size	22 Fr.	22 or 24 Fr. (outer diameter 25 or 28 Fr.)
Delivery catheter	Ensemble® delivery system	Retroflex 3® system
	Nose cone sheath	Deflectable nose cone

PPVI percutaneous pulmonary valve implantation, *BIB* balloon in balloon
[a]The final diameters for the Melody® valve is the inner diameter, for the Sapien® it is the outer diameter, depending on balloon size for the Melody® vale. The Sapien XT® valve comes in four different sizes

Procedural Summary

PPVI should be conducted under general anesthesia to minimize movement and patient discomfort during valve delivery. Biplane or multi-angle single plane angiography will delineate the anatomy and confirm measurements made with non-invasive imaging. The lateral projection or a shallow RAO projection will usually provide optimal views of the conduit. Both the Melody® and Sapien 3® valves use balloon expandable delivery systems. Occasionally, rapid right ventricular pacing may be used to assure valve stabilization at the target zone. In the pulmonary (or tricuspid valve-in-valve) position, access is usually from the femoral or internal jugular vein—which should be of adequate size to accommodate the delivery sheath. In addition, periventricular valve delivery has been described using hybrid approach with direct surgical RV ventriculotomy [20]. The Edwards 26 and 29 mm valves allow for implantation in larger RVOTs than the Melody® valve (Table 17.2; Fig. 17.2). Beyond considerations of annulus size, there are several differences between these two valve platforms that should be considered when choosing one over the other. It is optimal for an ACHD cath lab to have access to both valve choices if performing PPVI.

Table 17.3 summarizes a procedural guide for performing a PPVI. A stiff exchange length

Fig. 17.2 Edwards SAPIEN® transcatheter heart valve and transfemoral delivery A. Edwards SAPIEN® Valve—Consists of bovine pericardial leaflets sewn into a balloon expandable cobalt chromium platform. Currently available in 23 mm and 26 mm sizes B. RetroFlex 3® delivery system—transfemoral delivery catheter used for the Edwards SAPIEN® valve. Images published with permission—Edwards, Edwards SAPIEN, Edwards SAPIEN XT, RetroFlex®, RetroFlex 2®, RetroFlex 3®, and SAPIEN® are trademarks of Edwards Lifesciences Corporation)

wire should be positioned in the pulmonary artery, preferably the left PA when coming from a femoral approach. PA position should initially be achieved via a balloon tipped catheter to avoid catheter entanglement at later stages with the tricuspid valve apparatus. Prior to valve implantation, compression coronary angiography must be performed to assess for coronary impingement. Using simultaneous non-compliant balloon inflation in RVOT to similar sizes as expected with the pulmonary valve implant, coronary angiography of the left and right coronary arteries should be performed obtained for evidence of coronary compression (see Fig. 17.3). This phenomenon can occur in 1–4% of patients and is more common in ToF with anomalous coronary origins, pulmonary homografts and valves after the Ross procedure [21].

Pre-stenting is generally recommended in all implants using the Melody valve to reduce the incidence of stent fracture [22] and in most implant situation with the Edwards valve other than valve-in-valve into bioprosthetic rings. Where available we recommend using a covered stent, i.e., the Cheatham-Platinum (CP) covered stents® (NuMED Inc., Hopkinton, New York) for homograft or conduit preparation. This accounts for any possible dissection or rupture that calcified homografts and conduits can be

Table 17.3 Basic procedural steps leading up to valve implantation

• Time-out—check list of equipment, personnel, and patient
• General anesthesia—patient is sedated and intubated for the procedure
– valve implantation can be painful and relies on precise placement
• Large caliber venous access (22–24 Fr.)
– consider preclose technique using a suture mediated closure device
– Prostar XL® (Abbott Vascular, Santa Clara, CA) and Perclose ProGlide® (Abbott Vascular)
• Bail out equipment for femoral, iliac, or inferior vena cava stenting
– e.g. Bard Fluency stent
• 5–6 Fr. arterial access for pressure monitoring and coronary injections
– frequent catheter flushing, heparin 100 U/kg to goal ACT ~250; perioperative antibiotic dose 1 h prior to procedure
• Diagnostic evaluation:
– right heart catheterization—use balloon tipped catheter to enter PA (avoid tricuspid apparatus), confirm no associated branch or peripheral PA stenosis that must be addressed
– Use stiff exchange wire (e.g. Amplatz Ultrastiff® or Lunderquist®) with shaped end for positioning
– L-PA preferable to R-PA for easier valve delivery
• RVOT angiographic assessment via 6 or 7 Fr. Multi-track® catheter
– keep distal wire position while allowing for both pull back pressure measurements and angiography
– Balloon predilation—use non-compliant balloon sized to valve (~22 mm) with full inflation and simultaneous coronary injections.
– ensure that coronaries are distant from implant site—otherwise an abrupt coronary occlusion can be a lethal (and avoidable) complication
• Pre-stenting—choose stent size, type, and number
– availability of covered stents; number of stents planned
– sequential angiographic and hemodynamic assessment
• Placement of percutaneous pulmonary valve
– Melody® or SAPIEN® valve and their corresponding delivery systems
– final angiograms and pressure measurements

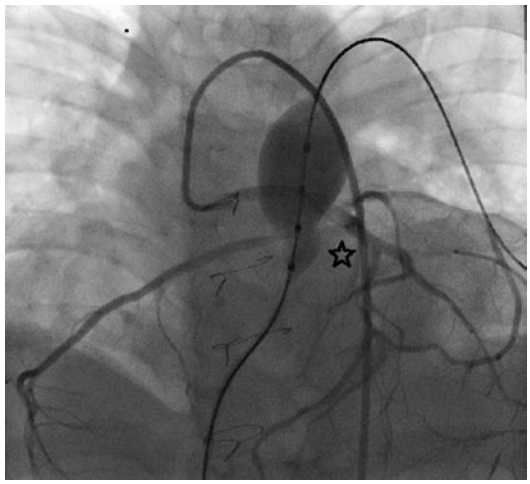

Fig. 17.3 Selective angiogram in a child with a single coronary artery during balloon occlusion of a right ventricular to pulmonary artery conduit. Note (*star*) area of obstructed flow in the coronary during balloon inflation

prone to [23]. In addition, Palmaz XL® series (J&J Interventional Systems Co., Warren, NJ) stents and Andrastent XL® or XLL® series (Andramed, Reutlingen, Germany) are bare metal stent options when placing a covered stent is unfavorable. It is important to receive full stent expansion at this stage without residual gradient.

For both Melody® and SAPIEN® valves, positioning and catheter stability are the crucial tenets during implantation. Once the Melody® valve is in position, the sheath is pulled back unveiling the valve. The Edwards valve is brought directly up to position. Slow inflation with either the BiB® or Edwards balloon allows time to make micro-adjustments in the event of device slippage. Once the valve is in place, post-inflation is occasionally needed to achieve full stent-valve expansion.

Evidence and Outcomes of PPVI

With nearly two decades of experience, PPVI implantation can be achieved with high procedural success and overall good procedural safety. PPVI achieves clinical results similar to surgical PVR. In the treatment of PR, there is reverse remodeling with a reduction in RV size and improvement in RV function over time. PPVI achieves increases in LV end diastolic volumes with subsequent improvement in early diastolic filling, decreased RV wall stress, and more balanced intraventicular septal interaction [24, 25]. When treatment is performed for PS, PPVI leads to reduction in RV systolic pressure and improved hemodynamics that is sustained in intermediate and long-term follow-up [26].

Periprocedural Outcomes

The largest published evidence pool in the pulmonary position rests with the Melody® valve. The U.S. Melody Transcatheter Pulmonary Valve study is a prospective, nonrandomized trial designed to assess safety, procedural success, and short-term efficacy of the Melody® valve in patients with dysfunctional RVOT conduits, following patients up to 7 years after their procedure [17]. This US Investigational Device Exemption trial enrolled 171 pediatric and adult patients at a median age of 19 years. Of the 148 patients who received a valve and were discharged were followed for a median of 4.5 years (range, 0.4–7 years). Thirty-two patients underwent right ventricular outflow tract re-intervention for obstruction ($n = 27$, with stent fracture in 22), endocarditis ($n = 3$, 2 with stenosis and 1 with pulmonary regurgitation), or right ventricular dysfunction ($n = 2$). Eleven patients had the Melody® valve explanted as an initial or second re-intervention. Five-year freedom from re-intervention and explantation was 76 ± 4% and 92 ± 3%, respectively. Conduits that were prestented and those with a lower right ventricular outflow tract gradient at hospital discharge had longer freedoms from re-intervention. Of 113 patients who were alive and re-intervention free, the follow-up gradient (median, 4.5 years after implantation) was unchanged from early after valve implantation, and all but 1 patient had mild or less pulmonary regurgitation. Almost all patients were in New York Heart Association class I or II. More severely impaired baseline spirometry was associated with a lower likelihood of improvement in exercise function after TPV replacement. In a similar study of consecutive patients from both a pediatric and adult congenital heart disease program, cardiac MRI, echocardiography, metabolic exercise testing, chest radiography, and hemodynamics before intervention were compared with repeated follow-up measurements to assess changes over time. Fifty-one patients (including 23 patients <16 years old) were followed for a mean 4.5 ± 1.9 (0.9–6.9) years after Melody® valve implantation. Freedom from any re-intervention was 87% and 68% at 3 and 5 years, and freedom from surgery was 90% at 5 years. For every decade younger at implantation, there was an increase of 3.9% ± 1.0% in cardiac MRI left ventricular ejection fraction ($p < 0.001$) and 2.4 ± 0.9 ml/kg/min in maxVO_2 ($P = 0.005$) and a decrease of 0.7 ± 0.2 cm in RV end-diastolic dimension ($p < 0.001$) after intervention. Younger patients displayed an additional decline in the RV/left ventricular end-diastolic volume ratio ($p = 0.05$) and trended toward improved RV ejection fraction in late follow-up (50% ± 7% versus 41% ± 12%, $p = 0.07$) [27].

With regards to the Edwards SAPIEN® and Sapien XT® valves, these valves have been in clinical use for RVOT lesions since 2011. The COMPASSION trial (COngenital Multicenter trial of Pulmonic vAlve regurgitation Studying the SAPIEN interventIONal) is a prospective, nonrandomized multicenter study that uses the SAPIEN® valve in the treatment of dysfunctional RV-to-PA conduits with moderate to severe PR or with PS. The FDA Phase I results were reported on 36 patients with the SAPIEN® valve resulting in an acute reduction in RV pressure to a median of 42 mm Hg and a reduction in peak gradients across the RVOT to a median of 12 mm Hg. There was trace or no PR in 31 of 33 patients on post-procedure angiography [18]. In a similar single centre 'real world' study from Toronto [28], 25 patients (70% male, mean age 34 ± 8.9 years) with an

underlying diagnosis of Fallot's tetralogy in 15, after a Ross procedure in 5, and 5 miscellaneous RVOT surgeries underwent either a Sapien® or Sapien XT® valve implant. The RV outflow tract characteristics included: 16 biological valve and 9 homografts. Technical success was 96%. One patient required an elective surgical pulmonary valve replacement for a high residual gradient. Pre-stenting was performed in all cases (half with covered stents). Valve sizes were 23 mm in 8, 26 mm in 15), and 29 mm in 2 patients. Acute hemodynamics noted a decrease in the mean RV-to-systemic pressure ratio ($p < 0.001$) and RV-to-PA gradient ($p < 0.001$). No patient had clinically significant PR. At a mean follow-up of 3.5 ± 2.1 years (range 0.3–7.2 years), there were no deaths with 1 patient requiring re-intervention for severe PR at 1 year having a valve-in-valve procedure. There were no episodes of endocarditis and no stent fractures and there was preserved valve function during follow-up with no change in RV-to-PA gradient nor PR severity.

While percutaneous valve implantation in the pulmonary position has been a 'game changer' in the management of the patient with congenital heart disease, less than a quarter of patients with RVOT dysfunction have conduits. Rather, the majority of patients in need of a competent pulmonary valve have undergone surgical modification of the RVOT with some form of RVOT patch with or without crossing the annulus. As a result PR is the dominant lesion that must be addressed. As the Sapien® series has a 29 mm diameter valve, a number of investigators have implanted this valve into the RVOT of patients with transannular patch RVOT reconstructions in the 26 mm diameter range [29–36].

Long-term Outcomes

In long-term prospective studies, PPVI has been found to be an effective therapy to achieve a competent PV without significant regurgitation. There has been no direct randomized comparison with surgical PVR—however, studies examining equivalent populations have suggested similar clinical outcomes. Published follow-up after Melody® PPVI has been reported up to 7 years. Overall freedom from reintervention/reoperation are reported at 90–95% at 1 year, 85–90% at 2 years [37] and freedom from RVOT re-intervention 95% at 1 year and 88% at 2 years. A smaller Toronto series examined PPVI performed in an adolescent population and found freedom from transcatheter reintervention to be 91%, 80%, and 80%, at 12, 24, and 36 months, respectively [38]. Eicken et al. have published their 2-institution clinical experience 102 patients receiving PPVI between 2006 and 2010 [39]. Pre-stenting was routinely performed, and they report one procedural death secondary to coronary compression. At a median of 1 year clinical follow-up, 1 valve (1%) was removed secondary to endocarditis; 8 valves (8%) required repeat dilation for residual gradients from which 4 led to repeat valve-in-valve procedures.

With regards to stent fractures after PPVI, clinical series have reported 1-year rates ranging as low as 5% to as high as 40%, likely depending on case mix, incidence of pre-stenting, and the rigor of follow-up [37, 39–41]. At a mean of 13 months follow-up, Nordmeyer et al. reports a 21% rate of stent fracture with fracture free survival of 85.1% at 1 year, 74.5% at 2 years, and 69.2% at 3 years [40]. with most events occurring in the first 400 days. The Melody® Transcatheter Pulmonary Valve study has also reported stent fracture rates of 22% at 14 months follow-up. There are considerably fewer PPVI patients who have received a SAPIEN® compared to Melody® valves; however, there were no reported stent fractures at 6 months in the phase I of the COMPASSION trial [18]. Whether this finding will hold up over longer term and with increased patient numbers is unknown.

Published studies have consistently shown an improvement in New York Heart Association (NYHA) class after PPVI [42]. There are hemodynamic differences after PPVI seen between lesions treated for predominantly RVOT obstruction vs. significant PR [26, 43]. Reduction of RV afterload leads to improvement in RV functional parameters and functional capacity as seen on peak oxygen uptake during cardiopulmonary exercise testing, while this has not been found with resolution of pulmonary regurgitation alone [43]. The majority of the improvement in systolic RV function after PPVI for obstructive lesions

occurs early, and little additional improvement has been noted on sequential MRI evaluations beyond 1 year [25].

In the cohort treated for severe PR, Plymen et al. found a statistically significant decrease in QRS duration and in QT_c dispersion after PPVI, akin to observations after surgical PVR [44]. The decrease in QRS duration was not statistically significant for the PPVI cohort treated for RVOT obstruction. To date there is no evidence correlating improvement in ECG parameters after PPVI with any reduction in clinical arrhythmia burden; however, it is hypothesized that increased homogeneity in repolarization is a sign of favorable electrical remodeling.

Recent studies have identified an increased risk of endocarditis in patients receiving bovine jugular vein implants to the RVOT compared to homograft implants [45–49]. Precise risk factors have yet to be determined, although the effect of a residual outflow gradient, turbulence in the valve sinuses, and the development of layered thrombus within the valve have been considered. Data are incomplete as to the endocarditis risk with a Sapien® valve, as the numbers of implants in the RVOT and length of follow up have been limited although endocarditis on the valve in the RVOT has been reported [50].

Up and Coming Pulmonary Valve Technologies

While PPVI has emerged as an alternative to surgical valve implantation, the diameters of the existing commercially available valves limits their application to surgically placed conduits, or those patients with small (26–27 mm) outflows as noted above. However, the majority (over three-quarters) of patients with congenital heart disease who undergo management of right ventricular outflow tract lesions have post operatively in longer-term follow up, large patulous outflows not amenable to existing transcatheter therapies [51]. As such, treatment of PR in this setting has traditionally been limited to surgical valve replacement. New techniques and technologies are being developed to facilitate valve insertion in such cases. Outflow tract reducers [52], valves placed in a hybrid manner (with simultaneous plication of the outflow) (Fig. 17.4) [53], and large diameter valve implants are currently under investigation (Fig. 17.5) [54–56]. Successful completion of these clinical trial will significantly alter the management options for the patient with CHD, the timing of interventions and ultimately indications.

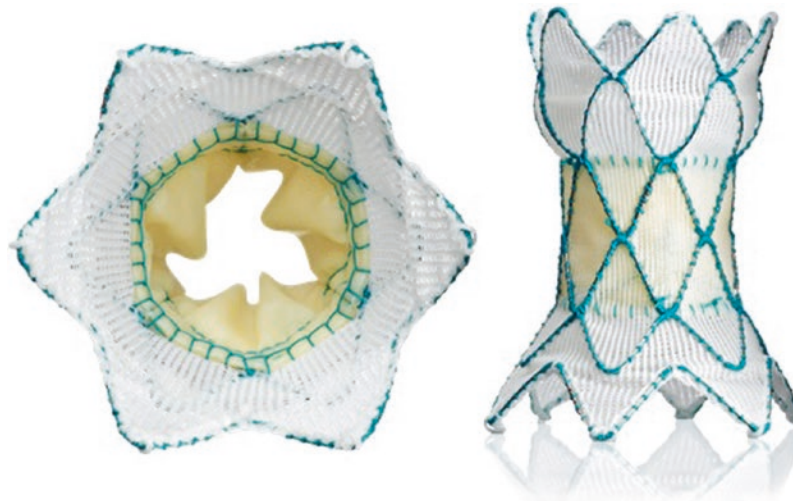

Fig. 17.4 The Harmony® self-expanding valve (Medtronic Inc. Minneapolis MN) is a 22 mm bovine pericardial valve (seen in the mid-portion of the *right panel*), shown into a Dacron® tube supported by a Nitinol® framework. *Left panel* shows the inflow portion of the implant. This implant has undergone an Early Feasibility FDA approved study and now in an early multicenter clinical trial

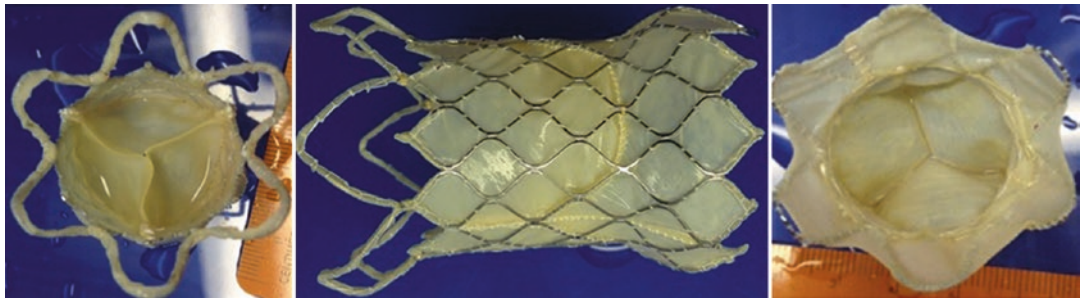

Fig. 17.5 The Venus P-valve® (Venus MedTech Inc., Hangzhou, China) is a Nitinol® self-expanding stent valve with leaflets made from porcine pericardium. *Left* and *right panels* show the outflow and inflow portions of the valve, the middle panel the Nitinol framework. Courtesy of Dr. S Qureshi

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