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REVIEW ARTICLE

Percutaneous Pulmonary Valve Implantation: Current Status and Future Perspectives

Bart W. Driesen[1,2,*], Evangeline G. Warmerdam[1], Gert-Jan Sieswerda[1], Folkert J. Meijboom[1], Mirella M.C. Molenschot[1], Pieter A. Doevendans[1,3,4], Gregor J. Krings[1], Arie P.J. van Dijk[2] and Michiel Voskuil[1]

[1]*Department of Cardiology, University Medical Center Utrecht, Utrecht, The Netherlands;* [2]*Department of Cardiology, Radboudumc, Nijmegen, The Netherlands;* [3]*Netherlands Heart Institute, Utrecht, The Netherlands;* [4]*Central Military Hospital, Utrecht, The Netherlands*

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Abstract: Patients with congenital heart disease (CHD) with right ventricle outflow tract (RVOT) dysfunction need sequential pulmonary valve replacements throughout their life in the majority of cases. Since their introduction in 2000, the number of percutaneous pulmonary valve implantations (PPVI) has grown and reached over 10,000 procedures worldwide. Overall, PPVI has been proven safe and effective, but some anatomical variations can limit procedural success. This review discusses the current status and future perspectives of the procedure.

Keywords: Congenital heart disease, right ventricular outflow tract dysfunction, percutaneous pulmonary valve implantation, transcatheter pulmonary valve replacement, melody, sapien.

1. INTRODUCTION

Congenital heart disease (CHD) is the most common of all congenital defects. Almost 1% of live births are affected [1]. Around 20% of these patients have right ventricular outflow tract (RVOT) or pulmonary valve anomalies. These include Fallot's tetralogy (ToF), pulmonary atresia with a ventricular septal defect (PA-VSD), double outlet right ventricle (DORV), isolated pulmonary valve stenosis (PS), and truncus arteriosus communis, which are usually corrected surgically early in life. Additionally, RVOT abnormalities are introduced after both the Ross Procedure, used for the correction of congenital aortic valve disease, as well as after surgical correction of complex transposition of the great arteries.

Improvement in surgical techniques has substantially enhanced short- and long-term outcomes in this patient cohort over the last decades. Nowadays, over 90% of affected children will reach adulthood [2, 3].

Historically, two treatment options for initial (early childhood) surgical repair have been used. First, up to the nineties, excision of the dysplastic PV and implantation of a non-valved trans-annular patch were preferentially used, leading to free regurgitation and right ventricular volume overload. Thereafter, surgeons mainly implanted valved conduits such as homografts (human tissue) or grafts with the use of porcine or bovine material (*e.g.* Contegra, Freestyle, Shelhigh, Sorin, Hancock). Implantation of a valved conduit in early childhood will eventually lead to degeneration, resulting primarily in stenosis and subsequent right ventricular (RV) pressure overload within 15 years after implantation [4]. Concomitant pulmonary branch stenoses may be present and may need either surgical or transcatheter intervention.

Thus, pulmonary regurgitation (PR) and PS are common problems in patients with congenital heart disease such as ToF, PA-VSD, and DORV, but also in patients post-Ross or post-Rastelli surgery. Most of these patients need multiple RVOT interventions throughout life.

Percutaneous pulmonary valve implantation (PPVI) has been developed as a nonsurgical, less invasive alternative for the treatment of RVOT dysfunction. Bonhoeffer *et al.* performed transcatheter PV implantation for the first time in 2000 [5]. Hereafter, various percutaneous pulmonary valves have been developed. Since then, experience with percutaneous pulmonary valve implantation has grown rapidly and it has become widely accepted for the treatment of RVOT dysfunction. In this review, we will discuss the indications for percutaneous valve replacement, the available devices and

*Address correspondence to this author at the Department of Cardiology, Division Heart and Lungs, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands;
E-mail: b.w.driesen@umcutrecht.nl

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techniques, outcomes and complications of the procedure, as well as current developments and future perspectives.

2. INDICATIONS FOR PULMONARY VALVE REPLACEMENT

In clinical practice, the indication for intervention in the case of stenosis is generally reasonably straightforward, since it is mainly based on the Doppler gradient; a peak instantaneous gradient >64 mmHg regardless of symptoms, or a peak instantaneous gradient <64 mmHg with symptoms or decreased RV function is considered an indication for valve replacement in the ESC guideline [6]. In many centers, a mean gradient of 35 mmHg is also used. In the 2018 ACC/AHA guideline, valve replacement in isolated PR is indicated in symptomatic patients with moderate or greater PR with RV dilatation or dysfunction. Valve replacement is appropriate for the preservation of ventricular size and function in asymptomatic patients with repaired TOF and ventricular enlargement or dysfunction and moderate or greater PR [7].

In combined stenosis and regurgitation, the debate remains. As the main goal for intervention in the volume overloaded RV is reverse remodelling, research is concentrated on finding thresholds for valve replacement after which reverse remodelling should still take place. Over the years, various thresholds have been suggested for optimal timing of intervention.

Previously, the end-diastolic volume was considered the most important parameter, though no threshold is reported after which RV volumes do not decrease [8]. RVEDV thresholds of >150ml/m2 to 170ml/m^2 were used as cut-off points because normalization of RVEDV was reported by several authors [9, 10] when valve replacement was performed before these cut-off points. Currently, end-systolic volume and RV ejection fraction are used more often as both are markers of RV function. End-systolic volumes (RVESV) of <82ml/m^2 to < 90ml/m^2 are used [10-14]. An RV ejection fraction <30% is associated with major adverse clinical outcomes [15].

Furthermore, tricuspid regurgitation (TR) has to be taken into account. In moderate or severe TR, combined PPVI with tricuspid valve repair should be considered because PPVI probably will not reduce TR sufficiently [16, 17]. Therefore, in case of significant TR, there might be an indication for surgical pulmonary valve replacement, instead of PPVI, as it can be combined with tricuspid valve plasty.

Electrocardiography parameters like a broadened QRS width of 140ms to180ms, or progression of QRS duration have been used in decision-making [10, 12, 18-24].

An early intervention strategy will have the most favorable effect on the preservation of RV function. However, such a strategy has to be weighed against the procedural risks of intervention, the risk of endocarditis and the need for repeat interventions. Currently, patients with dilated RVs survive into their '60s. It is unknown if prognosis will improve with earlier intervention and a goal of RV normalization.

3. TRANSCATHETER PULMONARY VALVES

Currently, two types of percutaneous implantable pulmonary valves are CE and FDA approved; the Melody transcatheter pulmonary valve (Medtronic, Minneapolis, Minn, USA) for implantation in valved conduits (Fig. **1**) and the Sapien Edwards XT (Edwards Lifesciences, Irvine, Ca, USA) for implantation in valved conduits and non-conduit (native) RVOT (Fig. **2**).

Fig. (1). The Melody transcatheter pulmonary valve (Medtronic, Minneapolis, Minn, USA).

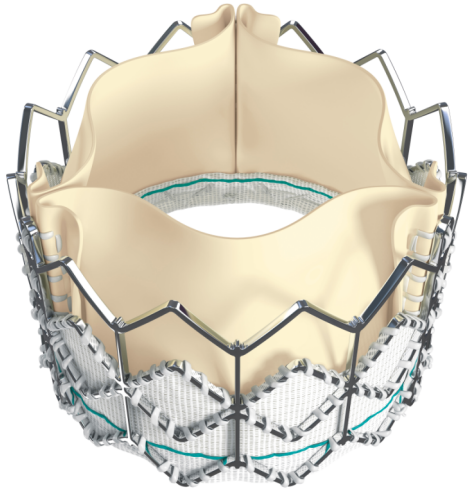

Fig. (2). The Edwards SApien XT (Edwards Lifesciences, Irvine, Ca, USA) for implantation in valved conduits and non-conduit (native) RVOT.

The valvular component of the Melody valve is similar to that of the surgical Contegra (Medtronic) valved conduit and consists of a bovine jugular vein (BJV) valve. The BJV is sutured within a balloon-expandable Cheatham Platinum stent (CP; NuMED, Hopkinton, NY, USA). The valve comes into two sizes: 16mm (up to 20mm deployment) and 18mm (up to 24mm deployment). The Melody Ensemble transcatheter delivery system comes in three sizes; 18, 20 and 22mm. The valve is crimped on the balloon-in-balloon (BiB) catheter of the Ensemble delivery system. Covered by a flexible 16 Fr shaft, with a true 22 Fr outer diameter profile, the valve/balloon combination is advanced to the landing zone over a stiff exchange guidewire. The maximal outside diameter of the Melody valve with fully inflated balloon reaches about 20mm, 22mm or 24mm, respectively (for the

Ensemble sizes 18, 20 or 22mm). The 34mm stent length will shorten to about 26mm, 24mm or 23mm after delivery using the Ensemble 18mm, 20mm or 22mm, respectively.

The Edwards SAPIEN XT transcatheter heart valve (Edwards Lifesciences, Irvine, Ca, USA) consists of a trileaflet bovine pericardial tissue valve hand-sutured in a balloon expandable cobalt-chromium stent. It is available in sizes 20, 23, 26, and 29mm, allowing for deployment in RVOTs up to 29-30mm. Similar to the Melody valve, the Sapien XT stent shortens after deployment. For example, the cobalt-chromium stent of 26mm valve shortens 2.9mm from 20.1 to 17.2mm after implantation. Accordingly, the stent length after deployment is 13.5, 14.3, 17.2 and 19.1mm for the 20, 23, 26, and 29mm valve, respectively.

The delivery system that is used for the Edwards SAPIEN XT transcatheter heart valve is the NovaFlex+ system (usable length 105 cm) which consists of a 20Fr split sheath. This delivery system includes a flex wheel for articulation of the flex catheter, a tapered tip at the distal end of the delivery system to facilitate crossing the valve, and a balloon catheter for deployment of the valve. The handle also contains a flex indicator depicting articulation of the flex catheter and a valve alignment wheel for fine adjustment of the valve during valve alignment. The balloon catheter has radiopaque markers defining the valve alignment position and the working length of the balloon. A radiopaque double marker proximal to the balloon indicates flex catheter position during deployment.

The Edwards Sapien S3 transcatheter heart valve (Edwards Lifesciences, Irvine, Ca, USA) is FDA approved for use in the aortic position. Many centers use the S3 valve also for PPVI. The S3 differs from the XT by an outer skirt at the distal part of the valve which was designed to reduce paravalvular leak. The frame is longer than that of the XT and the delivery catheters (Commander) allow for more precise valve positioning. The delivery system uses 14 or 16 French sheaths designed to reduce access site complications. The S3 valve is available in four sizes: 20mm, 23mm, 26mm and 29mm.

4. PROCEDURE

4.1. Pre-procedure

It is common to perform PPVI under conscious sedation or general anaesthesia allowing adequate pain control, the use of rapid pacing and ventilation control. Pre-treatment with antibiotics (cefazolin 2gram in our center) and acetylsalicylic acid (500mg iv, hereafter 80-100mg daily), and periprocedural heparin (unfractionated heparin 100IE/kg) is standard care. In case of an extended procedure (>4hours), an extra dose of cefazolin can be administered. One extra dose of antibiotics is given 8hours after the procedure. Vascular access site for both devices is commonly the femoral vein, but jugular or subclavian access is also possible.

Pre-procedural magnetic resonance angiography (MRA), computed tomography angiography (CTA) or echocardiography can be used as an overlay for roadmapping the procedure, which makes anatomic orientation easier for the operator and enhances safety of the procedure.

4.2. Assessment Pre-valve Implantation

The first step in PPVI after non-invasive pre-procedural imaging is confirming the indication for PPVI by cardiac catheterization for angiography and pressure measurements. The relationships between the main pulmonary artery (MPA), left and right pulmonary arteries, aorta, and coronary arteries should be assessed. It has been shown that approximately 5% of PPVI candidates are at risk for CC [25]. Hereby, also special attention should be made to the presence of pulmonary artery branch stenoses, the RVOT landing zone (diameter and support for stenting), and thus the potential for coronary compression (CC). The latter can be avoided by performing balloon interrogation with simultaneous selective coronary angiography.

Multiple biplane angiography acquisitions or alternatively, a three-dimensional angiography (3DRA) are needed to acquire a reliable assessment. 3DRA allows for views in every angle while radiation and contrast doses are equal to 2-5 biplane acquisitions [26].

4.3. PPVI in Valved Conduits

PPVI in conduits follows a different approach than PPVI in native or patched RVOT's. In conduits often multiple balloon dilatations and covered stents are necessary before implanting the valve. After careful assessment, especially for CC, one can proceed by pre-stenting the conduit. For Melody valves, pre-stenting is required to reduce stent fractures [27]. Although in Sapien valves, stent fractures have not been reported, pre-stenting is generally advised to create a landing zone.

4.4. PPVI in Native or Patched RVOT's

In RVOTs >25 mm, sizing can be performed by occluding the RVOT with a large (eg 30mm) balloon and infusing contrast in the RV while executing a push-and-pull manoeuvre to ensure a stable position before stent implantation. In patients with native RVOTs, PPVI can be attempted in RVOT diameters <28 mm measured with balloon testing [28], but pre-stenting may be particularly challenging in these cases. Initially, valve implantation was delayed up to several months after pre-stenting ensuring good stent ingrowth and stable position. Subsequently a combined approach with immediate valve implantation became common practice. Nowadays, more often direct implantation of a Sapien 29mm is performed without pre-stenting [29].

4.5. Post-procedure

The access site vessel can be closed with manual compression or with the Perclose ProGlide (Abbott, Illinois, U.S.A) suture-mediated closure system. Alternatively, a subcutaneous suture using the 'figure-of-eight' results in quick hemostasis. Post-interventional observation commonly takes place in telemetry wards and lasts until late afternoon the day after the procedure. An electrocardiogram, chest x-ray and echocardiography are performed to check for valve function and potential complications.

It is of importance to instruct the patient and other health workers to use antibiotic prophylaxis. The use of low-dose

acetylsalicylic acid varies among institutions and ranges from no use at all, to a 6 or 12 month period to life-long use. Though evidence is scarce, life-long acetylsalicylic acid use might be warranted. In a prospective study with 86 patients, discontinuation of acetylsalicylic acid was found to be a risk factor for the development of infective endocarditis [30].

4.6. Clinical Outcomes

PPVI has proven to be safe over the years. Excellent early and short-term outcomes have been reported [31-33], which are equal or better than surgical PVR [27]. After PPVI, right ventricular parameters, pulmonary regurgitation [34, 35], left ventricular filling properties [36], and exercise capacity [31, 37-40] improve and electrical remodelling can be seen [41]. PPVI has lower morbidity than PVR [42]. There are few re-operations directly after the procedure [43]. A recent systematic review showed a pooled peri-procedural mortality of 1.4% in 12 studies with 677 patients [44]. Freedom from re-intervention was 76±4% at 5 years in 148 patients studied post-Melody implantation by Cheatham *et al*. [45]. The presence of a pre-stented conduit and a lower post-interventional RVOT pressure gradient was associated with longer freedom from re-intervention.

A small conduit diameter (<16mm) seems to be associated with early valve failure [46], although the acute hemodynamic results of the Melody implantation were good in these patients.

Besides obvious benefits of percutaneous treatment, such as faster patient recovery and less invasive procedure, cost-benefits have been described as well. Vergales *et al*. reported a significant cost advantage of PPVI over PVR. In their model, PPVI would only lose its cost-effectiveness with an annual PPVI failure rate of 17% [47]. Currently, in-hospital costs are higher for PPVI mainly due to the high costs of the stent and valve. If device costs would be reduced in the future, PPVI would be cost-saving even with a device cost of five times that of a surgical valve [48].

4.7. Complications

In the most recent systematic review, procedural complications were limited [44]. Coronary compression was present in 1.2%, valve embolization in 2.4%, conduit rupture in 2.6% and pulmonary artery obstruction in 1.2%. Earlier studies reported a CC risk of around 5% [25, 49]. Probably the rate of CC is lower in the review by Virk *et al.*, because of improved pre-procedural risk assessment [44].

4.8. Coronary Compression

Coronary compression is the most important complication to avoid. In case of CC, urgent surgery or percutaneous coronary intervention may be necessary [50-52]. Fatal cases have been described [35]. Abnormal coronary anatomy is common in CHD. These patients are at high risk for CC because the coronaries may be close to the RVOT/stent area.

Patients after Ross procedures are of special concern because the coronaries are re-implanted in a more cranial part of the aorta during their initial treatment. The risk of CC might be as high as 22% in abnormal coronaries, versus 1.8% in normal anatomies [25]. Pre-procedural MRA or CTA do not allow for reliable risk assessment of this phenomenon because they are both off-line, CTA is static and MRA has a low spatial resolution. Another aspect that cannot be anticipated using CTA or MRA alone is the behaviour of the mass between MPA and coronaries. Even if the distance between MPA and coronaries seems enough (>5 mm), the risk of CC exists because this mass might not be compressible, especially if it consists of calcified tissue or residues of stents and conduits. So, real-time assessment in the catheterization laboratory as previously described is warranted.

4.9. Aortic Compression

Similar to CC, compression of the aortic root can occur with or without consequent aortic insufficiency (AI) [53, 54]. In a majority of cases, aortic root compression will occur in native or TAP RVOTs [55], but its clinical significance is unclear. A study by Torres *et al.* showed no progression of AI during follow-up after PPVI [53]. However, attention should be paid for this potential phenomenon during balloon interrogation because it may constitute an important contra-indication for PPVI.

4.10. Stent Fracture

Stent fracture (SF) used to be one of the most common complications encountered in the earlier era of Melody valve implantation. Since the use of pre-stenting, the incidence of stent fractures has been significantly reduced [45, 56]. SF is only reported for Melody valves. Commonly SF involves the rupture of only one or more stent struts without the loss of stent integrity and therefore usually has no clinical consequences [56]. However, SF may lead to dysfunction of the valve as well and may necessitate repeat intervention. If SF leads to loss of stent integrity or embolization of stent fragments, re-stenting or surgical intervention might be indicated.

4.11. Conduit Rupture

The overall incidence of conduit rupture was reported to be 6% in a retrospective analysis by Bishnoi and coworkers, with no significant differences between homografts or other type of conduits. The only identifiable risk factor was a highly elevated RVOT gradient [57]. Mostly, bleeding is contained by the surrounding scar tissue and only monitoring is necessary, but major bleeding with procedural death can occur. Urgent stenting with covered stents is then indicated [27]. Implantation of the NuMED Covered Cheatham-Platinum Stent can be performed without a negative impact on the TPV function [57]. Urgent surgery might be an option too but will often take far more critical time. Pre-stenting severe calcified homografts over the entire length with a covered stent is probably the only way to prevent conduit rupture or cardiac tamponade.

4.12. Valve Embolization

Embolization or migration of stents and valves is very rare, but cases have been described [34, 58]. Often surgical intervention will be necessary to explant the device, but tran-

scatheter retrieval has also been reported [59]. It may be necessary to implant the device in a pulmonary artery branch or vena cava (valve leaflets can be stented to flatten them out) [60].

4.13. Tricuspid Valve Damage

In PPVI with Sapien XT or S3 valves, there is a risk of tricuspid valve (TV) damage with subsequent tricuspid regurgitation. The valve passes the TV while it is uncovered on the sheath with the risk of entrapment in the TV apparatus.

4.14. Infective endocarditis

Infective endocarditis (IE) is a serious concern in PPVI. For Melody valves, high rates of IE are described, whereas, for Sapien valves, the incidence of IE seems low. However, the later introduction of Sapien valves for the pulmonary position has to be taken into account (less valves implanted and shorter follow-up).

Several reports concerning endocarditis in post-PPVI patients treated with Melody valves have been published [30, 31, 49, 61, 62]. Van Dijck *et al*. report 7.5% incidence of IE in 107 patients with a mean follow-up of 2 years and an annual event rate of 3%. The 5 years IE free survival was 84,9%. Interestingly, they compared Melody endocarditis to IE in Contegra conduits and homografts, the latter having an annual event rate of only 0.8% [61]. In New-Zealand, higher numbers of IE are reported by O'Donnell. After 2.9 years follow-up, the incidence of Melody IE was 16% in their cohort [63]. The study with the longest follow-up after Melody implantation (7 years) reports a 5-year freedom from IE of 89 ± 3% [45]. The same (89%) 5-year freedom from IE was confirmed in the most recent, and large publication on IE in Melody valves [64].

Recently the longest Sapien follow-up to date (mean 3,5 years), showed no endocarditis [65]. In the prospective multi-institutional COMPASSION trial, freedom from endocarditis at three years was 97,1% with an annualized PPVI related IE of 0,5% per patient per year [66]. Several other publications with relatively short follow-up periods reported a low incidence of IE in Sapien valves in the pulmonary position [67-69]. The study of Hascoët *et al*. [70] showed no cases of IE after 40 months in 47 patients treated with the Sapien valve and a cumulative incidence of IE of 24% in 32 patients treated with the Melody. In a recent publication of Haas *et al*. [71] the risk of bacterial endocarditis was 5-8-times higher for Melody valves compared to other valves in a group of 246 patients with all types of pulmonary valves. There was no bacterial endocarditis in the patients treated with Sapien valves during follow-up.

Etiology of IE post-PPVI is unknown; it is suggested, that the type of material might play a role in the risk of developing IE. Melody valves and Contegra conduits compared to pulmonary homografts, demonstrate different flow patterns with high shear stress and turbulence, jet lesions or local stress, whilst blood stasis in and around the conduits might contribute to this increased risk. Both systems are composed of bovine material, and the tissue characteristics might contribute to the IE risk as well [61, 72]. This concept is supported by a small in vitro study by Jalal and coworkers that showed an increased bacterial adhesion of S. Aureus and S. Sanguis on healthy Melody valve tissue, which increased after procedural preparation. The authors hypothesized that miniature fractures resulting from procedural preparation provide a bacterial trap and form the preferred location for bacterial adhesion [73, 74].

Sharma *et al*. recently reported a higher incidence of endocarditis with BJV valves than other types of right ventricle–to–pulmonary artery conduits. There was no difference in the incidence of endocarditis between catheter-based bovine valves and surgically implanted bovine valves, suggesting that the substrate for future infection is related to the tissue rather than the method of implantation [75]. These results are strengthened by the results of Veloso *et al*.

Adhesion of *Staphylococcus aureus, Staphylococcus epidermidis,* and *Streptococcus sanguinis* to bovine pericardium patch, bovine jugular vein, and cryopreserved homograft tissues under static and shear stress conditions indicated similar bacterial adhesion to all tissues. These data provide evidence that the surface composition of BJV and cryopreserved homograft tissues themselves, bacterial surface proteins, and shear forces per se may not be the prime determinant.

One of the major risk factors for IE has been shown to be the post-interventional RVOT gradient [31, 76]. The higher flow velocity might cause endothelial damage with non-bacterial thrombus formation, which might get infected later. This observation might explain the higher rates of IE reported in patients who discontinued acetylic salicylic acid [30, 49, 67]. Buber *et al*. reported male sex, longer procedure time and multiple RVOT stents as risk factors [76]. Additionally, traditional IE risk factors like previous IE, unprotected dental procedures, skin wounds and personal hygiene (like nail biting), all contribute to IE risk.

When patients present with IE, urgent intervention seems warranted, because of a 50% mortality rate as reported by Fraisse *et al*. Two of their patients died before urgent (next-day) surgery could be performed [49].

So far, it seems that the risk of IE is lower in the Sapien valve as compared to the Melody valve, although no head-to-head comparison has been made up till now. A different patient selection for the 26 to 29 mm Sapien valve, *i.e*. larger sized conduits and valve implantation in native RVOT's might explain the reported differences in the incidence of IE. Future studies, preferably a randomized trial comparing the Melody and the Sapien valves, are needed to definitely answer the IE issue.

5. FUTURE PERSPECTIVES

5.1. Patient Selection and Timing

In the last decades, knowledge concerning RV volumes and function, and changes in electrocardiographic parameters and exercise parameters has grown. A wide range of thresholds for valve replacement has been proposed, after which reverse remodelling can still take place and right ventricular function recovers (RVEDV, RVESV, QRS width, EKG parameters and others). However, little is known about the RV

histopathology and the long-term functional outcomes of pulmonary valve implantation. More research is needed to better define the ideal timing for (re-)intervention in RVOT dysfunction.

Currently, the team is performing a study with magnetic resonance imaging of irreversible RV fibrosis using T1 and T1rho mapping (The RV-REPAIR study, NL53771.041.15). Strain measurements using speckle-tracking echocardiography and feature tracking cardiac MR, combined with the investigation of novel biomarkers of RV function will probably aid in a better patient selection, earlier intervention and possibly even improved long-term outcomes. The fact that earlier intervention can lead to improved outcomes has been shown in a recent study of Pagourelias and co-workers. They reported a more pronounced biventricular remodelling reaching near normal values in patients with PPVI <7 years after the last RVOT operation [77]. Ideally, large cohorts with very long (life-long) follow-up will be created and timing might shift to earlier intervention in the future.

6. ADVANCED IMAGING

6.1. Advanced Imaging in the Assessment of RV Function

Pressure-volume loops would be ideal (load-independent) for the assessment of the RV in RVOT dysfunction. But PV-loops are not routinely used because of several disadvantages including the invasiveness of the procedure. Therefore, non-invasive methods are used to determine the RV function. In clinical practice, echocardiography and MRI are the routine diagnostics for follow-up of RVOT dysfunction. Their measurements are load-dependent. Strain and strain-rate are less load dependent than other parameters and therefore increasingly used for assessment of intrinsic function. Different strain and strain rate parameters are associated with volume overloading, RV dys-synchrony and RVEF [78, 79]. Other authors report a significant correlation between RV contractility (RV peak longitudinal systolic strain) and TAPSE [80]. TAPSE, in general, is not reliable in post-operative hearts but can be used for follow-up of the longitudinal function when the RV declines. Real-time 3D echocardiographic assessment of RVEF in congenital heart disease has proven to be reliable and feasible in small studies but as to be examined further [81].

In CMR, T1 mapping is increasingly used to quantify the extracellular volume (ECV). ECV is a validated surrogate marker of diffuse fibrosis. When excess collagen appears in the interstitium native T1 and ECV increase and post-contrast T1 decreases [82]. ECV has a good correlation with histological global fibrosis [83] and is correlated with arrhythmia in TOF patients with volume overloading due to PR [82]. With the evolving ability for non-invasive assessment of RV fibrosis, preservation of RV myocardium might take the lead over volumes and pressures in determining the timing of PV replacement [82, 84]. However, it is unclear how to translate ECV to function and prognosis. Moreover, it is still not possible to reliably measure T1 in the RV free wall [84, 85] since the spatial resolution approaches the thickness of the myocardium [82]. It is questionable if septal ECV represents fibrosis of the RV since there is a regional difference in RV wall stress due to its complex geometry. Chen *et al*. did measure ECV of the RV and reported elevated ECV values in rTOF patients, these were associated with RV volume overload and arrhythmia [86].

Another advance in CMR is four-dimensional flow cardiac magnetic resonance (4D flow CMR). This technique can be used to derive advanced hemodynamic measures such as wall shear stress, pressure difference maps, pulse wave velocity, energy loss, turbulent kinetic energy and others [87] without radiation burden. The use of 4D flow in RVOT dysfunction in the future might result in an improved understanding of RV physiology and remodelling [88, 89].

6.2. Advanced Imaging in Performing PPVI

Computational fluid dynamics (CFD) is a tool to derive the same hemodynamic measurements as 4D flow CMR. This tool calculates flow patterns and pressure changes within a virtual model of the cardiovascular system [90]. It can predict physiological responses to intervention and compute hemodynamic parameters [91]. CFD tools may support the assessment of pulmonary valve dysfunction and treatment decisions, especially by predicting the post-treatment changes [92, 93]. Recently the use of finite element modelling was described to predict RVOT intervention outcomes and periprocedural risks [54].

Three-dimensional rotational angiography (3DRA) is used in an increasing number of clinics. Superior imaging quality has been reported [94] and may facilitate higher procedural success and decreased the risk of serious adverse events by assessment of coronary compression and vessel-airway interactions (Fig. **3**) [95, 96]. It has been shown that the use of 3DRA does not result in increased radiation or contrast dose [26, 97], on the contrary, lower radiation dose can be achieved [98]. Furthermore, adequate and safe balloon interrogation in large (native) RVOTs is possible, potentially resulting in more PPVI's in patients with native RVOT's and wide conduits.

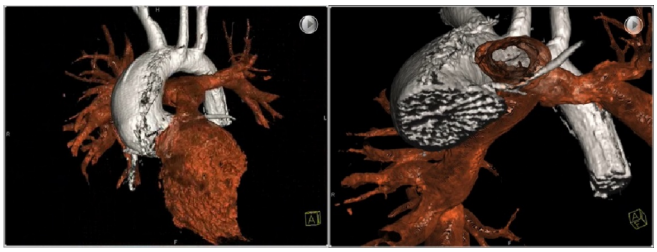

Fig. (3). 3DRA showing critical proximity of LCA to posterior MPA, not suitable for PPVI.

6.3. 3D-models

Three-dimensional printed models may aid in patient education [99]. *In vitro* simulation with 3D models might help planning PPVI in native RVOTs [100].

6.4. New Device Technology

Several devices for the reduction of large diameter (native) RVOT's are being developed and tested to broaden the treatment scope for PPVI. The first-in-man use of the Alterra Adaptive Prestent (Edwards Lifesciences, Irvine, CA, USA)

was reported recently (Fig. **4**) [101]. Devices under development are; the Harmony Transcatheter Pulmonary valve (Medtronic, Minneapolis, MN, USA) (Fig. **5**), which was formerly known as Native Outflow Tract Device [102]. Alternative new devices include the Venus P-valve (MedTech, Shanghai, China) [103], the Pulsta valve by TaeWoong Medical Company (Gyeonggi-do, Republic of Korea) [104, 105], the RVOT reducer (Fig. **6**) [106], and the Downsize stent [107].

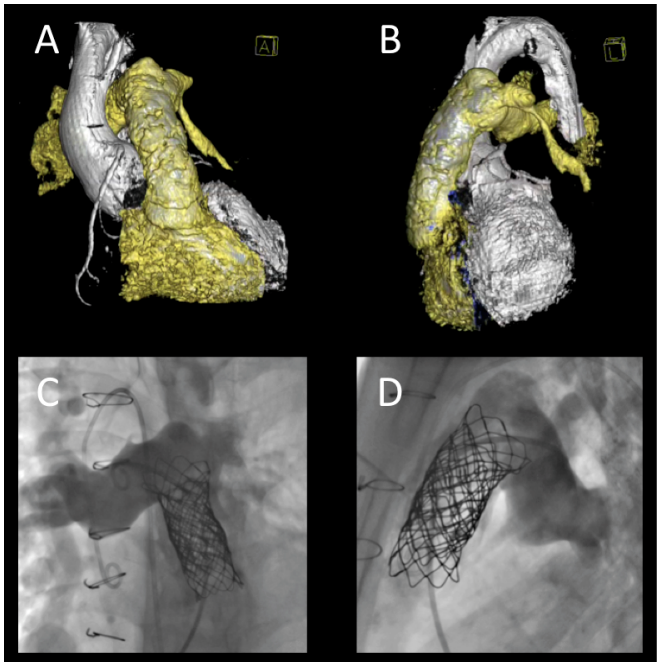

Fig. (4). A and **B**; 3D rotational angiography in patient with severe homograft stenosis. **C** and **D**; angiographic images after implantation of 3 covered CP stents and Sapien 20mm..tiff.

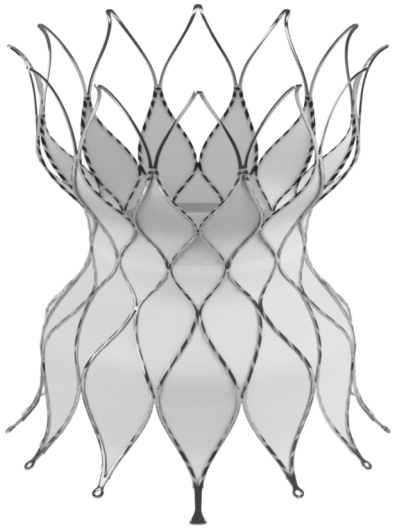

Fig. (5). The Alterra Adaptive Prestent (Edwards Lifesciences, Irvine, CA, USA).

Fig. (6). The Harmony Transcatheter Pulmonary valve (Medtronic, Minneapolis, MN, USA).

The Harmony valve has an hourglass geometry with the smaller central diameter holding the (porcine pericardium) valve. The system uses a self-expanding nitinol stent with a polymeric graft, which aims to improve the stability of the device in various RVOT anatomies [106]. Recently the results of the first FDA approved early feasibility study were presented, which revealed high procedural success and favorable acute hemodynamics [65].

The Venus p-valve (MedTech, Shanghai, China) is a self-expanding percutaneous heart valve designed to be implanted in a native patched right ventricle outflow tract. This valve is currently available up to a maximum diameter of 34 mm for use in an RVOT diameter up to 30–32 mm. Three in-man studies have been published so far in tetralogy of Fallot patients with trans-annular patch repair. Results are encouraging and the use of the Venus p-valve in large (native) RVOTs seems possible [103, 108].

A feasibility study of the Pulsta valve (by TaeWoong Medical Company, Korea) was recently reported. The Pulsta self-expandable valve consists of a knitted nitinol wire stent mounted with a treated trileaflet α-Gal–free porcine pericardial valve. Implantation of this valve was feasible and showed short-term effectiveness without serious adverse events [104].

Besides these innovations, existing valves with a bigger diameter will become available and will be increasingly used. Although the SAPIEN 3 valve (Edwards Lifesciences, Irvine, CA), available in 23, 26, and 29 mm sizes, was designed and FDA approved for the aortic position, this valve is also used in the pulmonary position [109]. Direct implantation (without pre-stenting) of the S3 valve, which has a strong stent frame, is being performed in native RVOT's. With sizes up to 29 mm, clearly, the spectrum of patients that can be treated with a percutaneous procedure grows.

As an alternative to percutaneous device techniques, a hybrid plication technique has been reported by Sosnowski *et al*. [110]. After full median sternotomy and minimal dissection of the heart and great vessels, RVOT angiography was performed to measure the main RVOT and pulmonary artery diameter and to determine the extent of plication. A sizing balloon was used for procedural guidance and plica-

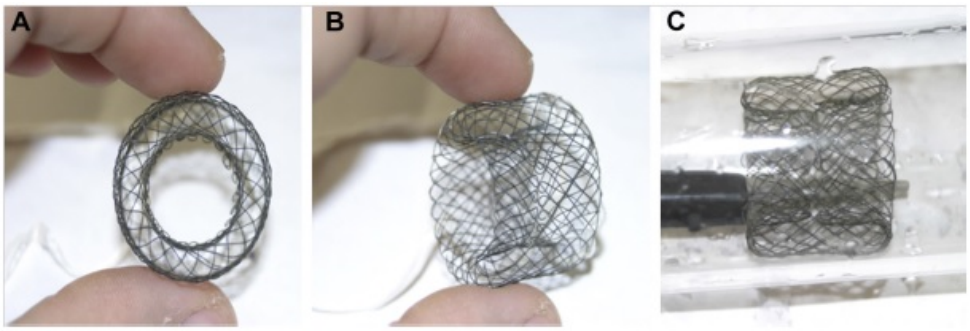

Fig. (7). The RVOT reducer device. Courtesy of Y. Boudjemline, permission to re-use granted.

tion was performed with a pledged longitudinal running suture to provide a more elongated reduction of the RVOT. In case of calcification of a pre-existing RVOT patch, a mattress suture was used to provide a focal narrowing of the RVOT size to approximately 22-24 mm. After this plication, a PPVI was performed [110].

7. DECELLURARIZED HUMAN VALVES

Small studies, with conflicting results, have described the use of decellularized human valves [111-113]. High immunogenic competence in children and young adults contributes to allo- and xeno-graft (*i.e.* cryopreserved homografts and bovine jugular vein grafts) degeneration. With heart valve tissue engineering it is possible to eliminate immunogenic cells from the valvular matrix, hereby creating viable, non-immunogenic, and biologically active grafts. Elimination of immunogenic cells from the valvular matrix seems to significantly decrease immunologic response in valve recipients. Extensive remodelling *in vivo* by repopulation with autologous cells and reduced re-operation rates compared to crypreserved homografts and BJV's were reported in preclinical and mid-term outcomes of clinical studies [111, 112]. Another publication reported disappointing results of the use of decellularized valves; abnormal immunologic response leading to significant and long-standing xenograft inflammation appeared to be the reason for graft stenosis and failure early after surgery. Moreover, the asserted endothelialization of the valve leaflets could not be confirmed by histology [114].

Other innovations are tissue-engineered valves (feasibility in sheep) [115], new wire and sheath techniques [116], and promising results on the valve in valve replacements [117]. A double stent technique was reported by Valverde *et al*. [99]. A 3D print was used to test double stent implantation in a 36 mm RVOT. Subsequently, two stents were implanted adjacent to each other, after which one stent was used as a landing zone for PPVI and the other stent was occluded with a vascular plug.

8. INFECTIVE ENDOCARDITIS

Further research and long-term outcome results are required to address the risk for endocarditis. Results of the Sapien valves have scarcely been available till now. Results of the currently running COMPASSION trial will give further insight into the infection risk in Sapien valves. The association between IE and bovine material (Contegra and Melody) has to be examined further [73]. In addition, randomized clinical trials have to be conducted to investigate whether the life-long use of acetylicsalicylic acid prevents IE. Patient instructions concern dealing with unexplained fever, aspirin use, dental procedures and personal hygiene (including tattoos and piercings) remain of utmost importance.

SUMMARY

PPVI has become an accepted and widely used technique for treating RVOT dysfunction in several congenital heart disease states, particularly after initial surgical repair. In short- and medium-term follow-up reports, outcomes are excellent. Coronary compression, with possibly dramatic consequences, is the most important complication to avoid. Post-PPVI, infective endocarditis is a concern. In this, a possible predisposition of the Melody valve should be elucidated. In the near future, RVOT reducer devices will become available that make PPVI in large (native) RVOTs feasible (Fig. **7**). Advances in imaging techniques such as 3DRA, 4D flow CMR and CFD will improve understanding of RV (reverse) remodelling and perhaps (possibly ?) influence the timing of intervention. Larger sizes studies with long-term follow-up will also contribute to improved timing of pulmonary valve replacement.

AUTHORS CONTRIBUTIONS

Bart. W. Driesen conceptualized this study, assisted with design, led data analysis/interpretation and drafted and edited the manuscript.

Evangeline. G. Warmerdam: Assisted with drafting the manuscript.

Gert-Jan Sieswerda: Assisted with data collection and critical revision of the manuscript.

Folkert. J. Meijboom: Assisted with data collection and critical revision of the manuscript.

Mirella. M.C. Molenschot: Assisted with data collection.

Pieter. A. Doevendans: Assisted with critical revision of the manuscript.

Gregor. J. Krings: Assisted with design, data analysis/interpretation and drafting and critical revision of the manuscript.

Arie. P.J. van Dijk: Assisted with critical revision of the manuscript.

Michiel Voskuil: Assisted with design, data analysis/interpretation and drafting and critical revision of the manuscript.

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES

[1] Krasuski RA, Bashore TM. Congenital heart disease epidemiology in the United States: Blindly feeling for the charging elephant. Circulation 2016; 134(2): 110-3.

[2] Moons P, Bovijn L, Budts W, Belmans A, Gewillig M. Temporal trends in survival to adulthood among patients born with congenital heart disease from 1970 to 1992 in Belgium. Circulation 2010; 122(22): 2264-72.

[3] van der Bom T, Bouma BJ, Meijboom FJ, Zwinderman AH, Mulder BJ. The prevalence of adult congenital heart disease, results from a systematic review and evidence based calculation. Am Heart J 2012; 164(4): 568-75.

[4] Davlouros PA, Karatza AA, Gatzoulis MA, Shore DF. Timing and type of surgery for severe pulmonary regurgitation after repair of tetralogy of Fallot. Int J Cardiol 2004; 97(Suppl 1): 91-101.

[5] Bonhoeffer P, Boudjemline Y, Saliba Z, *et al.* Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. Lancet 2000; 356(9239): 1403-5.

[6] Baumgartner H, Bonhoeffer P, De Groot NM, *et al.* ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). Eur Heart J 2010; 31(23): 2915-57.

[7] Stout KK, Daniels CJ, Aboulhosn JA, *et al.* 2018 AHA/ACC guideline for the management of adults with congenital heart disease: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019; 139(14): e637-97.

[8] Ferraz Cavalcanti PE, Sa MP, Santos CA, *et al.* Pulmonary valve replacement after operative repair of tetralogy of Fallot: Meta-analysis and meta-regression of 3,118 patients from 48 studies. J Am Coll Cardiol 2013; 62(23): 2227-43.

[9] Quail MA, Frigiola A, Giardini A, *et al.* Impact of pulmonary valve replacement in tetralogy of Fallot with pulmonary regurgitation: A comparison of intervention and nonintervention. Ann Thorac Surg 2012; 94(5): 1619-26.

[10] Oosterhof T, van Straten A, Vliegen HW, *et al.* Preoperative thresholds for pulmonary valve replacement in patients with corrected tetralogy of Fallot using cardiovascular magnetic resonance. Circulation 2007; 116(5): 545-51.

[11] Alvarez-Fuente M, Garrido-Lestache E, Fernandez-Pineda L, *et al.* Timing of pulmonary valve replacement: How much can the right ventricle dilate before it looses its remodeling potential? Pediatr Cardiol 2016; 37(3): 601-5.

[12] Geva T. Repaired tetralogy of Fallot: The roles of cardiovascular magnetic resonance in evaluating pathophysiology and for pulmonary valve replacement decision support. J Cardiovasc Magn Reson 2011; 13: 9.

[13] Henkens IR, van Straten A, Hazekamp MG, *et al.* Preoperative determinants of recovery time in adult Fallot patients after late pulmonary valve replacement. Int J Cardiol 2007; 121(1): 123-4.

[14] Lee C, Kim YM, Lee CH, *et al.* Outcomes of pulmonary valve replacement in 170 patients with chronic pulmonary regurgitation after relief of right ventricular outflow tract obstruction: Implications for optimal timing of pulmonary valve replacement. J Am Coll Cardiol 2012; 60(11): 1005-14.

[15] Bokma JP, Geva T, Sleeper LA, *et al.* A propensity score-adjusted analysis of clinical outcomes after pulmonary valve replacement in tetralogy of Fallot. Heart 2018; 104(9): 738-44.

[16] Tanase D, Ewert P, Georgiev S, *et al.* Tricuspid regurgitation does not impact right ventricular remodeling after percutaneous pulmonary valve implantation. JACC Cardiovasc Interv 2017; 10(7): 701-8.

[17] Boudjemline Y. Percutaneous pulmonary valve implantation: What have we learned over the years? EuroIntervention 2017; 13(AA): AA60-7.

[18] Frigiola A, Tsang V, Bull C, *et al.* Biventricular response after pulmonary valve replacement for right ventricular outflow tract dysfunction: Is age a predictor of outcome? Circulation 2008; 118(14 Suppl): S182-90.

[19] Therrien J, Provost Y, Merchant N, Williams W, Colman J, Webb G. Optimal timing for pulmonary valve replacement in adults after tetralogy of Fallot repair. Am J Cardiol 2005; 95(6): 779-82.

[20] Buechel ER, Dave HH, Kellenberger CJ, *et al.* Remodelling of the right ventricle after early pulmonary valve replacement in children with repaired tetralogy of Fallot: Assessment by cardiovascular magnetic resonance. Eur Heart J 2005; 26(24): 2721-7.

[21] Henkens IR, van Straten A, Schalij MJ, *et al.* Predicting outcome of pulmonary valve replacement in adult tetralogy of Fallot patients. Ann Thorac Surg 2007; 83(3): 907-11.

[22] Frigiola A, Redington AN, Cullen S, Vogel M. Pulmonary regurgitation is an important determinant of right ventricular contractile dysfunction in patients with surgically repaired tetralogy of Fallot. Circulation 2004; 110(11 Suppl 1): II153-7.

[23] van Straten A, Vliegen HW, Lamb HJ, *et al.* Time course of diastolic and systolic function improvement after pulmonary valve replacement in adult patients with tetralogy of Fallot. J Am Coll Cardiol 2005; 46(8): 1559-64.

[24] Gengsakul A, Harris L, Bradley TJ, *et al.* The impact of pulmonary valve replacement after tetralogy of Fallot repair: A matched comparison. Eur J Cardiothorac Surg 2007; 32(3): 462-8.

[25] Morray BH, McElhinney DB, Cheatham JP, *et al.* Risk of coronary artery compression among patients referred for transcatheter pulmonary valve implantation: A multicenter experience. Circ Cardiovasc Interv 2013; 6(5): 535-42.

[26] Peters M, Krings G, Koster M, Molenschot M, Freund MW, Breur JM. Effective radiation dosage of three-dimensional rotational angiography in children. Europace 2015; 17(4): 611-6.

[27] Holzer RJ, Hijazi ZM. Transcatheter pulmonary valve replacement: State of the art. Catheter Cardiovasc Interv 2016; 87(1): 117-28.

[28] Georgiev S, Tanase D, Ewert P, *et al.* Percutaneous pulmonary valve implantation in patients with dysfunction of a "native" right ventricular outflow tract - Mid-term results. Int J Cardiol 2018; 258: 31-5.

[29] Morgan GJ, Sadeghi S, Salem MM, *et al.* SAPIEN valve for percutaneous transcatheter pulmonary valve replacement without "pre-stenting": A multi-institutional experience. Catheter Cardiovasc Interv 2018; [Epub ahead of print].

[30] Malekzadeh-Milani S, Ladouceur M, Patel M, *et al.* Incidence and predictors of Melody(R) valve endocarditis: A prospective study. Arch Cardiovasc Dis 2015; 108(2): 97-106.

[31] McElhinney DB, Hellenbrand WE, Zahn EM, *et al.* Short- and medium-term outcomes after transcatheter pulmonary valve placement in the expanded multicenter US melody valve trial. Circulation 2010; 122(5): 507-16.

[32] Lurz P, Nordmeyer J, Giardini A, *et al.* Early versus late functional outcome after successful percutaneous pulmonary valve implantation: Are the acute effects of altered right ventricular loading all we can expect? J Am Coll Cardiol 2011; 57(6): 724-31.

[33] Asoh K, Walsh M, Hickey E, *et al*. Percutaneous pulmonary valve implantation within bioprosthetic valves. Eur Heart J 2010; 31(11): 1404-9.

[34] Butera G, Milanesi O, Spadoni I, *et al*. Melody transcatheter pulmonary valve implantation. Results from the registry of the Italian Society of Pediatric Cardiology. Catheter Cardiovasc Interv 2013; 81(2): 310-6.

[35] Eicken A, Ewert P, Hager A, *et al*. Percutaneous pulmonary valve implantation: two-centre experience with more than 100 patients. Eur Heart J 2011; 32(10): 1260-5.

[36] Lurz P, Puranik R, Nordmeyer J, *et al*. Improvement in left ventricular filling properties after relief of right ventricle to pulmonary artery conduit obstruction: Contribution of septal motion and interventricular mechanical delay. Eur Heart J 2009; 30(18): 2266-74.

[37] Bonhoeffer P, Boudjemline Y, Qureshi SA, *et al*. Percutaneous insertion of the pulmonary valve. J Am Coll Cardiol 2002; 39(10): 1664-9.

[38] Khambadkone S, Coats L, Taylor A, *et al*. Percutaneous pulmonary valve implantation in humans: results in 59 consecutive patients. Circulation 2005; 112(8): 1189-97.

[39] Khambadkone S, Bonhoeffer P. Percutaneous pulmonary valve implantation. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2006: 23-8.

[40] Vezmar M, Chaturvedi R, Lee KJ, *et al*. Percutaneous pulmonary valve implantation in the young 2-year follow-up. JACC Cardiovasc Interv 2010; 3(4): 439-48.

[41] Plymen CM, Bolger AP, Lurz P, *et al*. Electrical remodeling following percutaneous pulmonary valve implantation. Am J Cardiol 2011; 107(2): 309-14.

[42] Nordmeyer J, Coats L, Bonhoeffer P. Current experience with percutaneous pulmonary valve implantation. Semin Thorac Cardiovasc Surg 2006; 18(2): 122-5.

[43] Lurz P, Gaudin R, Taylor AM, Bonhoeffer P. Percutaneous pulmonary valve implantation. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2009: 112-7.

[44] Virk SA, Liou K, Chandrakumar D, Gupta S, Cao C. Percutaneous pulmonary valve implantation: A systematic review of clinical outcomes. Int J Cardiol 2015; 201: 487-9.

[45] Cheatham JP, Hellenbrand WE, Zahn EM, *et al*. Clinical and hemodynamic outcomes up to 7 years after transcatheter pulmonary valve replacement in the US melody valve investigational device exemption trial. Circulation 2015; 131(22): 1960-70.

[46] Bensemlali M, Malekzadeh-Milani S, Mostefa-Kara M, Bonnet D, Boudjemline Y. Percutaneous pulmonary Melody(R) valve implantation in small conduits. Arch Cardiovasc Dis 2017; 110(10): 517-24.

[47] Vergales JE, Wanchek T, Novicoff W, Kron IL, Lim DS. Cost-analysis of percutaneous pulmonary valve implantation compared to surgical pulmonary valve replacement. Catheter Cardiovasc Interv 2013; 82(7): 1147-53.

[48] Andresen B, Mishra V, Lewandowska M, *et al*. In-hospital cost comparison between percutaneous pulmonary valve implantation and surgery. Eur J Cardiothorac Surg 2017; 51(4): 747-53.

[49] Fraisse A, Aldebert P, Malekzadeh-Milani S, *et al*. Melody (R) transcatheter pulmonary valve implantation: Results from a French registry. Arch Cardiovasc Dis 2014; 107(11): 607-14.

[50] Mauri L, Frigiola A, Butera G. Emergency surgery for extrinsic coronary compression after percutaneous pulmonary valve implantation. Cardiol Young 2013; 23(3): 463-5.

[51] Kostolny M, Tsang V, Nordmeyer J, *et al*. Rescue surgery following percutaneous pulmonary valve implantation. Eur J Cardiothorac Surg 2008; 33(4): 607-12.

[52] Divekar AA, Lee JJ, Tymchak WJ, Rutledge JM. Percutaneous coronary intervention for extrinsic coronary compression after pulmonary valve replacement. Catheter Cardiovasc Interv 2006; 67(3): 482-4.

[53] Torres AJ, McElhinney DB, Anderson BR, *et al*. Aortic root distortion and aortic insufficiency during balloon angioplasty of the right ventricular outflow tract prior to transcatheter pulmonary valve replacement. J Interv Cardiol 2016; 29(2): 197-207.

[54] Caimi A, Sturla F, Pluchinotta FR, *et al*. Prediction of stenting related adverse events through patient-specific finite element modelling. J Biomech 2018; 79: 135-46.

[55] Lindsay I, Aboulhosn J, Salem M, Levi D. Aortic root compression during transcatheter pulmonary valve replacement. Catheter Cardiovasc Interv 2016; 88(5): 814-21.

[56] Nordmeyer J, Khambadkone S, Coats L, *et al*. Risk stratification, systematic classification, and anticipatory management strategies for stent fracture after percutaneous pulmonary valve implantation. Circulation 2007; 115(11): 1392-7.

[57] Bishnoi RN, Jones TK, Kreutzer J, Ringel RE. NuMED Covered Cheatham-Platinum Stent for the treatment or prevention of right ventricular outflow tract conduit disruption during transcatheter pulmonary valve replacement. Catheter Cardiovasc Interv 2015; 85(3): 421-7.

[58] Kenny D, Hijazi ZM, Kar S, *et al*. Percutaneous implantation of the Edwards SAPIEN transcatheter heart valve for conduit failure in the pulmonary position: early phase 1 results from an international multicenter clinical trial. J Am Coll Cardiol 2011; 58(21): 2248-56.

[59] Suradi HS, Hijazi ZM. Percutaneous pulmonary valve implantation. Glob Cardiol Sci Pract 2015; 2015(2): 23.

[60] Khambadkone S. Percutaneous pulmonary valve implantation. Ann Pediatr Cardiol 2012; 5(1): 53-60.

[61] Van Dijck I, Budts W, Cools B, *et al*. Infective endocarditis of a transcatheter pulmonary valve in comparison with surgical implants. Heart 2015; 101(10): 788-93.

[62] Malekzadeh-Milani S, Ladouceur M, Iserin L, Bonnet D, Boudjemline Y. Incidence and outcomes of right-sided endocarditis in patients with congenital heart disease after surgical or transcatheter pulmonary valve implantation. J Thorac Cardiovasc Surg 2014; 148(5): 2253-9.

[63] O'Donnell C, Holloway R, Tilton E, Stirling J, Finucane K, Wilson N. Infective endocarditis following Melody valve implantation: comparison with a surgical cohort. Cardiol Young 2017; 27(2): 294-301.

[64] McElhinney DB, Sondergaard L, Armstrong AK, *et al*. Endocarditis after transcatheter pulmonary valve replacement. J Am Coll Cardiol 2018; 72(22): 2717-28.

[65] Wilson WM, Benson LN, Osten MD, Shah A, Horlick EM. Transcatheter pulmonary valve replacement with the edwards sapien system: The Toronto experience. JACC Cardiovasc Interv 2015; 8(14): 1819-27.

[66] Kenny D, Rhodes JF, Fleming GA, *et al*. 3-year outcomes of the edwards SAPIEN transcatheter heart valve for conduit failure in the pulmonary position from the COMPASSION multicenter clinical trial. JACC Cardiovasc Interv 2018; 11(19): 1920-9.

[67] Patel M, Malekzadeh-Milani S, Ladouceur M, Iserin L, Boudjemline Y. Percutaneous pulmonary valve endocarditis: Incidence, prevention and management. Arch Cardiovasc Dis 2014; 107(11): 615-24.

[68] Hascoet S, Jalal Z, Baruteau A, *et al*. Stenting in paediatric and adult congenital heart diseases: A French multicentre study in the current era. Arch Cardiovasc Dis 2015; 108(12): 650-60.

[69] Vollroth M, Daehnert I, Kostelka M, Wagner R. First case of blood-culture proven Staphylococcus aureus endocarditis of a Sapien(R) XT valve after percutaneous pulmonary valve implantation. Eur J Cardiothorac Surg 2015; 48(6): e124-5.

[70] Hascoet S, Mauri L, Claude C, *et al*. Infective endocarditis risk after percutaneous pulmonary valve implantation with the melody and sapien valves. JACC Cardiovasc Interv 2017; 10(5): 510-7.

[71] Haas NA, Bach S, Vcasna R, *et al*. The risk of bacterial endocarditis after percutaneous and surgical biological pulmonary valve implantation. Int J Cardiol 2018; 268: 55-60.

[72] Uebing A, Rigby ML. The problem of infective endocarditis after transcatheter pulmonary valve implantation. Heart 2015; 101(10): 749-51.

[73] Jalal Z, Galmiche L, Lebeaux D, *et al*. Selective propensity of bovine jugular vein material to bacterial adhesions: An *in-vitro* study. Int J Cardiol 2015; 198: 201-5.

[74] Malekzadeh-Milani S, Houeijeh A, Jalal Z, *et al*. French national survey on infective endocarditis and the Melody valve in percutaneous pulmonary valve implantation. Arch Cardiovasc Dis 2018; 111(8-9): 497-506.

[75] Sharma A, Cote AT, Hosking MCK, Harris KC. A systematic review of infective endocarditis in patients with bovine jugular vein valves compared with other valve types. JACC Cardiovasc Interv 2017; 10(14): 1449-58.

[76] Buber J, Bergersen L, Lock JE, *et al*. Bloodstream infections occurring in patients with percutaneously implanted bioprosthetic pulmonary valve: A single-center experience. Circ Cardiovasc Interv 2013; 6(3): 301-10.

[77] Pagourelias ED, Daraban AM, Mada RO, *et al*. Right ventricular remodelling after transcatheter pulmonary valve implantation. Catheter Cardiovasc Interv 2017; 90(3): 407-17.

[78] Yu HK, Li SJ, Ip JJ, Lam WW, Wong SJ, Cheung YF. Right ventricular mechanics in adults after surgical repair of tetralogy of fallot: Insights from three-dimensional speckle-tracking echocardiography. J Am Soc Echocardiogr 2014; 27(4): 423-9.

[79] Focardi M, Cameli M, Carbone SF, *et al*. Traditional and innovative echocardiographic parameters for the analysis of right ventricular performance in comparison with cardiac magnetic resonance. Eur Heart J Cardiovasc Imaging 2015; 16(1): 47-52.

[80] Kempny A, Fernandez-Jimenez R, Orwat S, *et al*. Quantification of biventricular myocardial function using cardiac magnetic resonance feature tracking, endocardial border delineation and echocardiographic speckle tracking in patients with repaired tetralogy of Fallot and healthy controls. J Cardiovasc Magn Reson 2012; 14: 32.

[81] van der Zwaan HB, Helbing WA, McGhie JS, *et al*. Clinical value of real-time three-dimensional echocardiography for right ventricular quantification in congenital heart disease: Validation with cardiac magnetic resonance imaging. J Am Soc Echocardiogr 2010; 23(2): 134-40.

[82] Messroghli DR, Moon JC, Ferreira VM, *et al*. Clinical recommendations for cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume: A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI). J Cardiovasc Magn Reson 2017; 19(1): 75.

[83] Zile MR, Gregg D. Is biventricular fibrosis the mediator of late complications in tetralogy of fallot? JACC Cardiovasc Imaging 2016; 9(1): 11-3.

[84] Broberg CS, Chugh SS, Conklin C, Sahn DJ, Jerosch-Herold M. Quantification of diffuse myocardial fibrosis and its association with myocardial dysfunction in congenital heart disease. Circ Cardiovasc Imaging 2010; 3(6): 727-34.

[85] Plymen CM, Sado DM, Taylor AM, *et al*. Diffuse myocardial fibrosis in the systemic right ventricle of patients late after Mustard or Senning surgery: An equilibrium contrast cardiovascular magnetic resonance study. Eur Heart J Cardiovasc Imaging 2013; 14(10): 963-8.

[86] Chen CA, Dusenbery SM, Valente AM, Powell AJ, Geva T. Myocardial ECV fraction assessed by CMR is associated with type of hemodynamic load and arrhythmia in repaired tetralogy of fallot. JACC Cardiovasc Imaging 2016; 9(1): 1-10.

[87] Markl M, Schnell S, Barker AJ. 4D flow imaging: Current status to future clinical applications. Curr Cardiol Rep 2014; 16(5): 481.

[88] Kamphuis VP, Westenberg JJM, van der Palen RLF, *et al*. Unravelling cardiovascular disease using four dimensional flow cardiovascular magnetic resonance. Int J Cardiovasc Imaging 2017; 33(7): 1069-81.

[89] Dyverfeldt P, Bissell M, Barker AJ, *et al*. 4D flow cardiovascular magnetic resonance consensus statement. J Cardiovasc Magn Reson 2015; 17: 72.

[90] DeCampli WM, Argueta-Morales IR, Divo E, Kassab AJ. Computational fluid dynamics in congenital heart disease. Cardiol Young 2012; 22(6): 800-8.

[91] Morris PD, Narracott A, von Tengg-Kobligk H, *et al*. Computational fluid dynamics modelling in cardiovascular medicine. Heart 2016; 102(1): 18-28.

[92] Slesnick TC. Role of computational modelling in planning and executing interventional procedures for congenital heart disease. Can J Cardiol 2017; 33(9): 1159-70.

[93] Goubergrits L, Riesenkampff E, Yevtushenko P, *et al*. MRI-based computational fluid dynamics for diagnosis and treatment prediction: Clinical validation study in patients with coarctation of aorta. J Magn Reson Imaging 2015; 41(4): 909-16.

[94] Aldoss O, Fonseca BM, Truong UT, *et al*. Diagnostic utility of three-dimensional rotational angiography in congenital cardiac catheterization. Pediatr Cardiol 2016; 37(7): 1211-21.

[95] Truong UT, Fagan TE, Deterding R, Ing RJ, Fonseca BM. Use of rotational angiography in assessing relationship of the airway to vasculature during cardiac catheterization. Catheter Cardiovasc Interv 2015; 86(6): 1068-77.

[96] Pockett CR, Moore JW, El-Said HG. Three dimensional rotational angiography for assessment of coronary arteries during melody valve implantation: Introducing a technique that may improve outcomes. Neth Heart J 2017; 25(2): 82-90.

[97] Haddad L, Waller BR, Johnson J, *et al*. Radiation protocol for three-dimensional rotational angiography to limit procedural radiation exposure in the pediatric cardiac catheterization lab. Congenit Heart Dis 2016; 11(6): 637-46.

[98] Goreczny S, Moszura T, Dryzek P, *et al*. Three-dimensional image fusion guidance of percutaneous pulmonary valve implantation to reduce radiation exposure and contrast dose: A comparison with traditional two-dimensional and three-dimensional rotational angiographic guidance. Neth Heart J 2017; 25(2): 91-9.

[99] Valverde I, Sarnago F, Prieto R, Zunzunegui JL. Three-dimensional printing *in vitro* simulation of percutaneous pulmonary valve implantation in large right ventricular outflow tract. Eur Heart J 2017; 38(16): 1262-3.

[100] Poterucha JT, Foley TA, Taggart NW. Percutaneous pulmonary valve implantation in a native outflow tract: 3-dimensional DynaCT rotational angiographic reconstruction and 3-dimensional printed model. JACC Cardiovasc Interv 2014; 7(10): e151-2.

[101] Zahn EM, Chang JC, Armer D, Garg R. First human implant of the Alterra Adaptive Prestent(TM): A new self-expanding device designed to remodel the right ventricular outflow tract. Catheter Cardiovasc Interv 2018; 91(6): 1125-9.

[102] Bergersen L, Benson LN, Gillespie MJ, *et al*. Harmony feasibility trial: Acute and short-term outcomes with a self-expanding transcatheter pulmonary valve. JACC Cardiovasc Interv 2017; 10(17): 1763-73.

[103] Garay F, Pan X, Zhang YJ, Wang C, Springmuller D. Early experience with the Venus pvalve for percutaneous pulmonary valve implantation in native outflow tract. Neth Heart J 2017; 25(2): 76-81.

[104] Kim GB, Song MK, Bae EJ, *et al*. Successful feasibility human trial of a new self-expandable percutaneous pulmonary valve (pulsta valve) implantation using knitted nitinol wire backbone and trileaflet alpha-gal-free porcine pericardial valve in the native right ventricular outflow tract. Circ Cardiovasc Interv 2018; 11(6): e006494.

[105] Kim GB, Kwon BS, Lim HG. First in human experience of a new self-expandable percutaneous pulmonary valve implantation using knitted nitinol-wire and tri-leaflet porcine pericardial valve in the native right ventricular outflow tract. Catheter Cardiovasc Interv 2017; 89(5): 906-9.

[106] Jalal Z, Thambo JB, Boudjemline Y. The future of transcatheter pulmonary valvulation. Arch Cardiovasc Dis 2014; 107(11): 635-42.

[107] Boudjemline Y, Agnoletti G, Bonnet D, Sidi D, Bonhoeffer P. Percutaneous pulmonary valve replacement in a large right ventricular outflow tract: An experimental study. J Am Coll Cardiol 2004; 43(6): 1082-7.

[108] Promphan W, Prachasilchai P, Siripornpitak S, Qureshi SA, Layangool T. Percutaneous pulmonary valve implantation with the Venus P-valve: clinical experience and early results. Cardiol Young 2016; 26(4): 698-710.

[109] Rockefeller T, Shahanavaz S, Zajarias A, Balzer D. Transcatheter implantation of SAPIEN 3 valve in native right ventricular outflow tract for severe pulmonary regurgitation following tetralogy of fallot repair. Catheter Cardiovasc Interv 2016; 88(1): E28-33.

[110] Sosnowski C, Matella T, Fogg L, *et al*. Hybrid pulmonary artery plication followed by transcatheter pulmonary valve replacement: Comparison with surgical PVR. Catheter Cardiovasc Interv 2016; 88(5): 804-10.

[111] Cebotari S, Tudorache I, Ciubotaru A, *et al*. Use of fresh decellularized allografts for pulmonary valve replacement may reduce the reoperation rate in children and young adults: Early report. Circulation 2011; 124(11 Suppl): S115-23.

[112] Sarikouch S, Horke A, Tudorache I, *et al*. Decellularized fresh homografts for pulmonary valve replacement: A decade of clinical experience. Eur J Cardiothorac Surg 2016; 50(2): 281-90.

[113] d'Udekem Y. Decellularized homografts: In fashion or really superior? Eur J Cardiothorac Surg 2016; 50(2): 291-2.

[114] Voges I, Brasen JH, Entenmann A, *et al*. Adverse results of a decellularized tissue-engineered pulmonary valve in humans assessed with magnetic resonance imaging. Eur J Cardiothorac Surg 2013; 44(4): e272-9.

[115] Spriestersbach H, Prudlo A, Bartosch M, *et al*. First percutaneous implantation of a completely tissue-engineered self-expanding pulmonary heart valve prosthesis using a newly developed delivery system: A feasibility study in sheep. Cardiovasc Interv Ther 2017; 32(1): 36-47.

[116] Shah RR, Poommipanit P, Law MA, Amin Z. Anchor balloon, buddy wire, and wire and sheath techniques to deploy percutaneous pulmonary valves in tetralogy of fallot patients. Catheter Cardiovasc Interv 2018; 92(5): 915-20.

[117] Tarzia P, Conforti E, Giamberti A, *et al*. Percutaneous management of failed bioprosthetic pulmonary valves in patients with congenital heart defects. J Cardiovasc Med (Hagerstown) 2017; 18(6): 430-5