PEDIATRIC AND CONGENITAL HEART DISEASE

Core Curriculum

Nonsurgical Pulmonary Valve Replacement: Why, When, and How?

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Percutaneous transcatheter interventions for valve replacement or implantation is one of the most exciting developments in the field of interventional cardiology. Valvular stenosis has been treated by balloon dilatation with early and late results; however, treatment for valvular regurgitation has remained surgical until now. Most new designs have been investigated for implantation of valves in the left or right ventricular outflow tracts. Patients with surgery on the right ventricular outflow tract for congenital heart disease constitute the most common group for reoperations during late follow-up. Surgical pulmonary valve replacement can be performed with low mortality; however, it sets up a substrate for future operations. Also, the risk of cardiopulmonary bypass, infection, bleeding, and ventricular dysfunction remains. A transcatheter technique is likely to have more acceptance and may expand the indications for early intervention for right ventricular outflow tract dysfunction. Catheter Cardiovasc Interv 2004;62:401–408.

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INTRODUCTION

Nonsurgical cardiac valve replacement is one of the most exciting developments in the field of interventional cardiology [1–4]. Despite transcatheter treatment of valvular stenosis being well established [5–7], treatment of valvular regurgitation remains entirely surgical. The prospect of nonsurgical transcatheter treatment of valvular regurgitation holds great promise in view of the inherent advantages to patients and the medical community alike. There have been various developments in the designs of implantable valves and systems to deploy them through percutaneous route with variable success [4,8,9]. Most of these developments are designs for treatment of semilunar valve regurgitation. The basic principle consists of use of a valve that can be mounted on a balloon-expandable stent using standard catheter techniques. However, the underlying morphological differences between the left and right ventricular outflow tracts provide major challenges to these designs. The right ventricular outflow tract commonly requires intervention during correction of congenital heart disease. While relief of stenosis was considered the main strategy during the early repair of conditions such as tetralogy of Fallot, only recently has the importance of maintaining a competent pulmonary valve been emphasized [10–12]. Despite the fact that surgical pulmonary valve replacement can be performed with low mortality, there still exists the morbidity of reoperations and the need to replace these valves surgically, particularly when they are implanted at a young age.

We describe our approach in embarking on treatment of pulmonary regurgitation secondary to surgical or transcatheter intervention on the pulmonary valve in congenital heart disease.
WHY?

Despite acceptance of early postoperative pulmonary regurgitation as a benign lesion in the early era of congenital heart surgery, long-term follow-up has revealed the detrimental hemodynamic effects on the right and left ventricular function [11–13]. Chronic volume overload of the right ventricle leads to ventricular dilatation and impairment of systolic and diastolic function [14,15]. The tricuspid annulus dilates and may lead to onset of new or worsening of preexistent tricuspid regurgitation. The combination of these two valvular lesions is responsible for right heart dilatation. In the long term, this causes atrial and ventricular arrhythmia, heart failure, and increases the risk of sudden death. Prolongation of QRS duration, risk of malignant ventricular arrhythmia, and sudden death are all linked to pulmonary regurgitation during late follow-up after tetralogy of Fallot repair [16].

Impaired exercise capacity after repair of tetralogy of Fallot has been shown to be related to pulmonary regurgitation [17]. Right ventricular diastolic dysfunction due to restrictive physiology, however, protects the ventricle from dilatation and maintains better exercise performance compared to patients without restrictive physiology [10]. Preservation or restoration of pulmonary valve competence at an appropriate time has resulted in improvement in right ventricular function, incidence of arrhythmias, and effort tolerance [13,18–20].

WHEN?

The optimal timing of establishing pulmonary competence before irreversible dysfunction of right ventricle has not yet been determined. The conventional indications of surgery for pulmonary regurgitation have been onset of symptoms, effort intolerance, arrhythmias, progressive dilatation of right ventricle, worsening right ventricular function, or associated lesions that exacerbate pressure or volume overload to the right ventricle (residual ventricular septal defect, outflow obstruction, severe tricuspid regurgitation) [19,21,22]. However, there are concerns that this may be too late and irreversible changes in the right ventricle may already set in. Therrien et al. [20] reported no improvement in right ventricular volumes, right ventricular (RV) function, and exercise performance after late pulmonary valve replacement performed more than 20 years after the initial repair. They concluded that late intervention for pulmonary regurgitation might compromise the recovery of right ventricular function. Also, other investigators have clearly shown that pulmonary valve replacement can improve right ventricular function, control arrhythmias, and improve exercise performance if performed at an appropriate time [18,23,24]. However, there is no single investigation that gives a reliable indication from the currently available data. Onset of right ventricular dysfunction, tricuspid regurgitation, and worsening symptoms may all be markers of diminished reversibility and probably are not justified as indicators for appropriate time of intervention.

Based on the current knowledge, it is arguable that the most appropriate time of intervention would be before the onset of symptoms, or significant right ventricular dilatation in patients with severe pulmonary regurgitation where serial cardiopulmonary exercise testing indicates diminishing effort tolerance.

HOW?

Surgical pulmonary valve replacement can be performed with very low mortality [25,26]. Despite this, adolescents and adults are reluctant to have reoperations where the longevity of the new valved conduit does not guarantee freedom from further operations [27].

We have developed a new percutaneous technique for pulmonary valve implantation with a bovine jugular venous valve sutured inside a stent and implanted using a delivery system designed to track a front-loaded device without difficulty. After initial animal studies, we have implanted this valved stent in humans [8].

The most common indications for surgical pulmonary valve replacement are pulmonary regurgitation with or without stenosis, right ventricular dilatation, malignant arrhythmias, and residual hemodynamic lesions [28]. The majority of patients referred for surgical pulmonary valve replacement have diagnosis of tetralogy of Fallot with pulmonary stenosis or pulmonary atresia or have surgical treatment for critical pulmonary valve stenosis [24,29]. Other diagnostic groups included transposition of great arteries with ventricular septal defect and pulmonary stenosis who had Rastelli operation and placement of a right ventricle to pulmonary artery conduit, as well as patients with Ross operation with dysfunction of the pulmonary homograft [30]. The conventionally accepted intervention has been surgical with use of homografts (aortic or pulmonary) [31], monocusp valves (pericardial or Gore-Tex) inside Gore-Tex tubes [32–34], and conduits with xenograft valves [35,36] and mechanical valves [37]. Recently, bovine jugular venous valved conduits [38,39] have been used for reconstruction of the right ventricular outflow tract. Despite major advances in terms of durability, the life span of the prosthetic conduits is limited. Calcification, stenosis, intimal proliferation, and graft degeneration cause progressive stenosis or regurgitation. Indeed, these patients are committed to multiple reoperations for life. Though these procedures can be carried out with reasonably low risks, one still had to consider risks of reoperations in these patients, includ-
ing bleeding, infection, and the risk of graft failure or prosthetic valve dysfunction. The graft failure always sets up need for reoperations and the risk increases with the number of previous conduit implantations [40]. Also, right ventriculotomy could lead to right ventricular dysfunction and form a substrate for malignant ventricular arrhythmias [41].

A transcatheter intervention for pulmonary valve replacement would be less invasive, avoid the risks of ventriculotomy and cardiopulmonary bypass, and avoid the risks of bleeding and infection associated with reoperation and reduce the costs by avoiding postoperative intensive care. The procedure would have to provide a comparable safety and efficacy to established surgical procedures.

Transcatheter implantation of cardiac valves is evolving as one of the most exciting developments in the field of interventional cardiology. Hufnagel et al. [42] first reported the use of a ball valve prosthesis designed for rapid insertion into descending aortal for treatment of aortic regurgitation. Andersen et al. [43] described a valve mounted inside a stent, which could be implanted with percutaneous transluminal techniques in the ascending aorta and the aortic root. Bonhoeffer et al. [1,44] described a similar model with a bovine jugular venous valve sutured inside a stent, which was deployed using a custom-made delivery system into the right ventricular outflow tract. After a series of successful animal experiments to show the feasibility, safety, and efficacy of this technique and device, human implantation was performed in patients with pulmonary valve dysfunction for regurgitation and stenosis (Fig. 1).

The patient selection for percutaneous transcatheter pulmonary valve implantation was crucial to the success of this technique in human subjects. The animal studies confirmed that the valve stent assembly could be safely anchored in the native right ventricular outflow tracts of lambs. When considering the patient groups referred for percutaneous pulmonary valve implantation, we had to identify first the diagnostic groups and then the nature of the right ventricular outflow tracts within these groups. Tetralogy of Fallot and its variants remains the most common diagnostic group in clinical practice requiring pulmonary valve implantation for pulmonary regurgitation during late follow-up. When associated with pulmonary atresia, a valved conduit is used to establish continuity between the right ventricle and the pulmonary artery. Homografts and porcine bioprosthetic valves are the commonly used means of establishing this continuity. The right ventricular outflow tract dysfunction during late follow-up results from degeneration of the valve leaflets with or without stenosis related to fibrous or fibromuscular proliferation at the anastomotic site at the proximal end involving the ventriculotomy or at the distal end involving the pulmonary artery or its branches. Calcification of the homograft also contributes to the reduction of the luminal diameter. For relief of right ventricular hypertension due to stenotic lesions, balloon dilatation and stent implantation have been successfully used in the conduits [45,46]. However, this does not provide relief from regurgitation and may in fact result in the exacerbation of the regurgitant component of right ventricular outflow tract dysfunction [47,48].

Fig. 1. Angiograms in lateral projection showing complete abolition of pulmonary regurgitation.
We believe that the homograft provides an excellent bed for implantation of our device. In most cases, the homograft degeneration provides a combination of stenosis and regurgitation. The stenotic component is helpful for creating an implantation point for the valve, which leads to successful anchoring. Most conduit stenosis have been shown to respond favorably to balloon dilatation and stenting despite heavy calcification, and there is no reason to believe that this would not be the case with our device [45]. The limiting factor in these patients would then be the size of the conduit. A large conduit, which is larger than the fully expanded dimension of the valve stent assembly, would clearly be unsuitable for this technique. So would a small conduit (< 16 mm), which cannot be diluted to the diameter of the device and lead to an incompletely expanded valve-stent assembly with a large profile.

In contrast, patients with a native outflow tract with repair of tetralogy of Fallot involving only a valvotomy or valvectomy may not provide a very discrete implantation point at the site of the pulmonary valve annulus. If there is augmentation of the right ventricular outflow with an outflow tract patch or transannular patch, the outflow tracts tend to be dilated and may not have any secure implantation point at all (Fig. 2). The outflow tract in such cases appears dilated and may in fact form a part of the right ventricular outflow tract aneurysm [48]. The patch, being a noncontractile part of the outflow tract, moves paradoxically to the rest of the ventricle and increases in dimension in systole. These are the most unfavorable outflow tracts for transcatheter techniques with currently available devices. The dimensions of the outflow do not provide any secure anchorage to the valve-stent assembly. Also, the paradoxical motion of a noncontractile patch leads to further increase in dimension during systole. The right ventricle is usually dilated in these patients and they may have additional patch or extension of the transannular patch on the right ventricular wall.

The valve-stent assembly and their dimension also limit their use in the dilated outflow tracts. The bovine jugular venous valve are usually not more than 18 mm in diameter. However, the leaflets have a much larger area than in homografts and tend to have a larger coaptation surface. Because of this, the valve leaflets still remain competent despite the dilatation of the venous wall. This has been shown by in vitro dilatation of the bovine venous valved conduit [1]. Similar phenomenon is seen in patients who have surgical implantation of the bovine jugular venous wall for the reconstruction of the right ventricular outflow tract and there is dilatation of the conduit. This is commonly associated with distal stenosis of the branch pulmonary arteries or due to stenosis of the distal anastomosis. Nevertheless, severe dilatation would lead to disruption of the valvular mechanism and dysfunction of the conduit. The stent also limits the overdi-
lation of the venous valve up to a certain limit beyond its natural diameter due to the inherent external constraint provided by the size of the stent. Due to these reasons, we believe that the currently available device would not be suitable for use in patients with outflow tract dimensions beyond 22 mm.

Homografts and other bioprosthetic conduits placed in an extra-anatomic position after surgical correction of transposition of great arteries with ventricular septal defect and pulmonary stenosis, common arterial trunk or pulmonary atresia with ventricular septal defect and major aortopulmonary collaterals requiring unifocalization provide a different challenge for surgical or transcatheter intervention. The position of the valved conduit is determined by the variations in the morphology of the primary lesion. The conduits could sometime lie behind the sternum and pose problems during reexploration. The position behind the sternum would also lead to external compression by the sternum and adhesions to the anterior chest wall (Fig. 3). Surgical exploration in these situations is fraught with risks of fatal hemorrhage due to transection of the conduit during sternotomy and many surgeons prefer to use femoral bypass during resternotomy.

Transcatheter course through an extra-anatomic conduit can be difficult, especially in the presence of severe stenosis and calcification. However, with better catheters, guidewires, and low-profile balloons with good tracking capability, interventions on these conduits have become less complicated. Despite this, positioning of large sheaths and delivering stents could require long procedures with difficult manipulations. The current design of the valve-stent assembly requires a specially designed front-loading delivery sheath to deliver the valve-stent assembly. The delivery sheath has a profile up to 22 Fr, which requires dilatation of the femoral vein and may pose difficulties in tracking it through a complex intracardiac course. Maintaining distal guidewire position can be difficult during the tracking of the device to achieve an appropriate position to deploy the valved stent. This could increase the procedure times and screening times and may require expert manipulation.

The conventional techniques to image the right ventricular outflow tract include echocardiography, angiography, and magnetic resonance imaging (MRI). Echocardiography provides hemodynamic information with estimation of right ventricular systolic pressure from the tricuspid regurgitation jet, assessment of right ventricular
outflow tract (RVOT) gradient with continuous-wave Doppler, and assessment of pulmonary regurgitation using color flow mapping and spectral Doppler analysis of the pulmonary regurgitation (PR) jet for pressure halftime, half-time index, and deceleration slope [49,50]. Despite this, there are limitations in obtaining good morphological information due to the limited windows in older patients. Angiography has been the traditional technique and has been replaced for diagnostic purposes by MRI.

We believe that MRI is an excellent technique for investigating the form and function of the right ventricular outflow tract and the consequences of its dysfunction on the right ventricle [48,51]. Not only does it provide excellent images to delineate the structure of the outflow tract, it can provide hemodynamic information from the tricuspid regurgitation (TR) jet velocity and RVOT velocity. In addition, assessment of RV volumes and systolic and diastolic function and regurgitant volume and fractions helps in assessing the effects of intervention short- and long-term follow-up [52–54]. Three-dimensional reconstruction of the right ventricular outflow adds a completely different level of information that cannot be obtained by echocardiography or angiography. The homografts and conduits have two sites of anastomosis that are influenced by the morphology of structures at both ends. The surgeons have to suture the conduits in optimum position to keep it away from external constraints such as the sternum and to conform to anastomosis at the distal pulmonary artery bifurcation. This can introduce folds and twists in the conduit, which could lead to stenosis and cause regurgitation by distortion of the valve leaflets. The twists or folds can be underestimated by angiography, as the decrease in caliber looks quite minimal (Fig. 4). Three-dimensional reconstruction of the outflow tract by volume-rendered gadolinium images delineates these types of stenosis extremely well.

We believe that with the currently available device, homografts between 16 and 22 mm would form most suitable outflow tracts for percutaneous pulmonary valve implantation. The length of stenosis should not be greater than 5 cm. Any additional stenosis close to the site of implantation should be dealt with before the valve deployment. However, there would be concerns about rupturing the balloon of the delivery system for the valve, if there are stents adjacent to the site of deployment. Proximity of the implantation point to the pulmonary artery bifurcation with origin stenosis in the branches can provide a difficult combination for intervention on the outflow tract. Undilatable stenosis still remains a problem with severely calcified homografts with extrinsic constraints due to retrosternal position.

Transcatheter implantation of pulmonary valves has been the first clinical experience for nonsurgical management of valvular regurgitation. Our group has shown the feasibility, safety, and efficacy of pulmonary valve implantation in humans. There are still various unanswered questions about the durability of this valve in the long term. However, recourse to surgery still remains a viable option for patients with valvular dysfunction. There are limitations to the application of this technique in young and small patients and patients with either too small or too large outflow tracts. We are in the process of developing devices for providing anchoring for the valved stent in patients with outflow tract aneurysms. With more experience and the results of long-term follow-up, nonsurgical pulmonary valve implantation may expand the boundaries of pulmonary valve replacement in patients with pulmonary regurgitation and reduce the long-term deleterious effects on the right ventricle.

REFERENCES


