Stentless porcine valves in the right ventricular outflow tract: improved durability?

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Received 1 September 2008; received in revised form 10 December 2008; accepted 15 December 2008; Available online 10 February 2009

Abstract

Objective: Stentless porcine valves are commonly used for aortic valve replacement in adults, yet their long-term performance in the right ventricular (RV) outflow tract is unknown. We evaluated intermediate-term performance of stentless porcine valves in the RV outflow tract in 150 children and adults over a 10-year period. Methods: We retrospectively reviewed data on all patients undergoing placement of a pulmonary valve or RV-PA conduit with a stentless porcine prosthesis (≥ 19 mm) from 1998 to 2008. Valvar function was assessed with echocardiography. Freedom from reintervention (explantation or catheter-based intervention) was determined by actuarial methods. Results: A stentless porcine prosthesis was placed in the pulmonary position in 150 patients with a median weight and age of 50.1 kg (range 9.8—127) and 15.8 years (range 1.4—55), respectively. There were three early deaths (2%) and no late deaths. Actuarial freedom from reintervention was 100% at 1 year and 95.5% at 5 years. Peak transvalvar gradient at 1 and 5 years was 13 ± 12 mmHg and 25 ± 11 mmHg, respectively. At last follow-up no patient had severe insufficiency (PI), five patients had moderate PI and the remainder mild or no PI. Conclusions: Stentless porcine valves function well in the pulmonary position over the intermediate-term and are associated with low rates of reintervention in patients requiring a >19 mm valve or valved conduit. Longer-term follow-up and comparison with other alternatives will be necessary to determine if these valves are superior to commonly used allograft or bovine jugular venous valved conduits.

Keywords: Conduit; Pulmonary valve replacement; Stentless porcine valve

1. Introduction

The implantation of a right ventricle to pulmonary conduit or insertion of a pulmonary valve is commonly used in the repair of a variety of congenital heart defects in both children and adults. Valve choices vary from cryopreserved allografts, bovine jugular venous valved conduits, and stented or stentless bioprostheses. Stentless porcine valves have been utilized extensively in the left ventricular outflow tract in adults [1], but information on durability in the right ventricular outflow tract has been limited, particularly in children [2—8]. Since 1998 we have utilized stentless porcine valves for many children and young adults needing either replacement of a conduit or placement of a pulmonary valve in the right ventricular outflow tract. This report evaluates the durability and performance of these valves in the right ventricular outflow tract over the intermediate-term.

2. Patients and methods

2.1. Patients

This study was approved by the institutional review board at the University of Utah. Data on all consecutive patients undergoing placement of a stentless porcine aortic bioprosthesis in the right ventricular outflow tract at the University of Utah Medical Center or Primary Children’s Medical Center between January 1998 and December 2007 were reviewed. During this time period, stentless porcine valves were utilized selectively along with cryopreserved allografts and stented bioprostheses. Selection of valve type was determined by surgeon preference and anatomic situation. In general, the stentless valve was chosen over the pulmonary allograft when valve insufficiency was the primary indication, since it was felt that the porcine valve remains competent longer than allografts. Pulmonary allografts were often
preferentially used during this period for situations that involved extensive pulmonary artery reconstruction. Approximately half of all valves ≥19 mm placed in the right ventricular outflow tract during this time period were stentless porcine bioprostheses, and form the basis for this study. Patient records were reviewed to determine patient demographics, diagnosis, indication for operation, other coexisting cardiac anomalies, size and manufacturer of the implanted valve, valve position (orthotopic vs extracardiac conduit), operative techniques, bypass and cross-clamp times. End points for evaluation of the valve or valved conduit included, reintervention (catheter-based or re-operation), late valve function determined by echocardiography, and death.

3. Valves and sizing

All valves were sized according to calculated Z-scores and the patient’s weight and body surface area. In general, a Z-score between +1 and +3 was targeted and as large a valve as easily inserted was chosen. The smallest stentless porcine valve that is commercially available in the USA is a 19 mm. All 19 mm valves in this study were Medtronic Freestyle valves (Medtronic, Minneapolis, MN, USA). Valves sized 21 through 29 mm were Edwards Prima Plus valves (Edwards LifeSciences Corporation, Irvine, CA, USA).

4. Operative technique

All procedures were accomplished with cardiopulmonary bypass with vacuum assisted venous drainage and mild hypothermia to approximately 34 °C. We do not routinely cross-clamp unless there is a need to do an additional procedure such as closure of an intracardiac defect or intracardiac valve procedure. We use ventricular fibrillation during the conduit or valve placement to avoid any possible air entry, in the case of an unrecognized intracardiac shunt or inadvertent entry into the left side of the heart or left atrium during the valve or conduit implantation.

The valves are rigorously prepared according to the washing instructions of the manufacturer and left in saline until implantation. The valves are then prepared for implantation by oversewing of the coronary arteries utilizing a double suture line of 5—0 polypropylene sutures. All attempts are made to avoid kinking or bending of the graft and to prevent turbulence within the valve or conduit. The usual orientation of the valve for both orthotopic and conduit applications resulted in the oversewn porcine right coronary nearly directly anterior and the left coronary posterior and leftward. This allowed the slight curvature of the porcine graft to adapt to the natural curvature of the patient’s right ventricular outflow tract. The distal end of the valve is beveled posteriorly to within approximately 1—2 mm of the sinotubular junction so that the conduit or valve is short posterior. Existing hoods of allograft or prosthetic material are utilized proximally. In some cases, the valve is sewn to the native outflow tract or ventriculotomy posteriorly and a small hood of prosthetic material such as expanded polytetrafluoroethylene or bovine pericardium anteriorly. Typically, the valve is sewn to the pulmonary artery bifurcation distally by direct suture. In cases of distal pulmonary artery stenoses, the distal narrowing is reconstructed utilizing cryopreserved pulmonary allograft tissue and the stentless porcine valve implanted into the reconstructed bifurcation.

5. Echocardiography

Complete two-dimensional, Doppler and M-mode trans-thoracic echocardiograms were performed postoperatively to evaluate prosthetic valved conduit or valve function. Valvar stenosis was evaluated by measuring the peak instantaneous transvalvar pressure gradient utilizing both directed pulse wave and continuous wave Doppler interrogation from all available views. Valvar regurgitation was graded as none to trace, mild, moderate, or severe utilizing previously described semi-quantitative methods including the ratio of the diameter of the color Doppler regurgitant jet to the diameter of the valve or conduit valve annulus from the parasternal short-axis view, and the presence or absence of holodiastolic flow reversal in the branch pulmonary arteries [9]. All available postoperative echocardiograms were analyzed as above.

6. Follow-up

All operative survivors underwent follow-up by their individual cardiologist and accrual of reintervention and survival information was obtained between June and August 2008. Valve-related or conduit-related reintervention was defined as any re-operation or catheter-based reintervention for either valve or conduit insufficiency or stenosis. In general, the indication for reintervention included peak instantaneous Doppler gradient of >50 mmHg and conduit valve insufficiency of moderate or greater in combination with symptoms, right ventricular enlargement, or diminished right ventricular function.

7. Statistical methods

Normally distributed data are presented as mean ± SD. Non-normally distributed data are described as median and range. Survival and event-free survival were calculated and presented in Kaplan–Meier format [10].

8. Results

From January 1998 until March 2008, a total of 150 patients underwent placement of a stentless porcine valve in the right ventricular outflow tract, either in the native position or within an RV-PA conduit. Patient diagnoses are as shown in Table 1. Median patient age was 15.6 years (range 1.4—55 years). Median weight was 49 kg and ranged from 9.8 to 127 kg. The indication for pulmonary valve or valved conduit insertion was insufficiency in 76 patients (50.7%), stenosis in 24 patients (16%), mixed stenosis and insufficiency in 49 (32.7%) and endocarditis in 1 patient (0.7%). The
output and multisystem organ failure on ECMO following the
a 31-year-old patient on postoperative day 3 of low cardiac
mortality of 2% (3/150). One of these early deaths occurred in

stentless valve insertion was the first valve or conduit
placement in the pulmonary position in 65 patients (43.3%),
the second in 48 (32%), the third in 30 (20%), and the fourth or
greater in 7 (4.7%) patients. The stentless valve was
implanted in an orthotopic position in 108 patients and as
an extracardiac conduit in 42 patients. For all patients, the
stentless valve procedure involved a redo sternotomy with the
stentless pulmonary valve insertion occurring with the
first redo sternotomy (second sternotomy) in 80 patients, the
second redo sternotomy (third sternotomy) in 48, the third
redo sternotomy (fourth sternotomy) in 14, the fourth redo
sterntomy (fifth sternotomy) in 7 and the fifth redo
sterntomy (sixth sternotomy) in 1 patient. Valve sizes
implanted included 19 mm in 5 patients, 21 mm in 11
patients, 23 mm in 14 patients, 25 mm in 17 patients, 27 mm
in 36 patients and 29 mm in 66 patients. Concomitant
procedures are shown in Table 2.

Table 1
Diagnosis in 150 patients undergoing placement of stentless porcine valve.

<table>
<thead>
<tr>
<th>Original diagnosis</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetralogy of Fallot</td>
<td>66</td>
</tr>
<tr>
<td>Tetralogy of Fallot with pulmonary atresia</td>
<td>19</td>
</tr>
<tr>
<td>Tetralogy of Fallot/absent pulmonary valve</td>
<td>7</td>
</tr>
<tr>
<td>Tetralogy of Fallot/AVSD</td>
<td>4</td>
</tr>
<tr>
<td>Truncus arteriosus</td>
<td>6</td>
</tr>
<tr>
<td>TGA/VSD/PS</td>
<td>8</td>
</tr>
<tr>
<td>PS or PA/IVS</td>
<td>20</td>
</tr>
<tr>
<td>Aortic atresia with VSD</td>
<td>2</td>
</tr>
<tr>
<td>DORV with PS/PA</td>
<td>8</td>
</tr>
<tr>
<td>AS (Ross procedure)</td>
<td>9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>150</strong></td>
</tr>
</tbody>
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AS: aortic stenosis; TGA, transposition of the great arteries; DORV, double outlet right ventricle; VSD, ventricular septal defect; PA, pulmonary atresia; IVS, intact ventricular septum; AVSD, atrio-ventricular septal defect.

Follow-up was complete for 94% of the 147 operative survivors (138 patients). Reintervention for valve-related reasons has occurred in four (4/150, 2.6%) patients, all due to stenosis. To date there have been no reinterventions for branch pulmonary artery stenosis distal to the valve and there have been no instances of valve endocarditis. Successful reintervention by balloon valvuloplasty was performed in three patients at 18 months, 30 months and 42 months following implantation. All of these three valves showed signs of stenosis at the valve annulus and proximal suture line and occurred in 27 mm valves that were implanted orthotopically. To date, no valves sized 19 mm, 21 mm, 23 mm, or 29 mm at implantation have required reintervention. The only valve explanted to date, occurred 41 months following orthotopic implantation of a 25 mm valve in a child 9.8 years old and weighing 25 kg. The actuarial freedom from reintervention is 95.5% at 5 years and the actuarial freedom from valve replacement is 98.7% at 5 years.

Valve function is depicted in Figs. 1 and 2 and is generated by 220 routine postoperative echocardiograms obtained after valve implantation at roughly yearly intervals. Valve function with regards to development of valve stenosis as measured by peak instantaneous Doppler gradient from echocardiography is depicted in Fig. 1. The peak instantaneous gradient does increase slightly over time from an average of 13 ± 12 mmHg

**Fig. 1.** Mean ± SD peak instantaneous Doppler derived gradients on post-operative echocardiograms in 147 survivors of stentless aortic porcine valves implanted into the right ventricular outflow tract. The numbers in parentheses represent the numbers of patients used to derive each follow-up point.
immediately postoperatively to 25 ± 11 mmHg at 5 years (p > 0.05). Valve function with regards to valvar regurgitation is shown in Fig. 2. Most patients have mild or none to trace regurgitation, even at 5 years. Only five patients have evidence of moderate valve regurgitation and no patient has severe valve regurgitation.

9. Discussion

Placement of a pulmonary valve or a right ventricle to pulmonary conduit has become one of the most common procedures affecting children with congenital heart disease. Pulmonary valves are required for repair or re-operation in a wide variety of anomalies including tetralogy of Fallot, pulmonary atresia, truncus arteriosus, and others. Failure of cryopreserved allografts in the pulmonary position, as well as limited availability has led some to consider alternative choices such as bovine venous valved grafts or bioprosthetic valves of bovine or porcine origin. Recent experiences with stentless porcine valves in the aortic position in adults have emphasized their advantage with regards to low profile and transvalvar gradient, as well as improved valve durability due to low pressure fixation techniques [1]. Early experience with the stentless porcine valves in the right ventricular outflow tract [2] has been encouraging, but more extensive and longer-term experience is lacking. Our study demonstrates that this valve has excellent durability in the intermediate-term with an acceptable progression of stenosis in the valve and minimal insufficiency. Our report represents one of the largest and longest-term evaluations of stentless porcine valves in the right ventricular outflow tract in the literature.

Previous reports of stentless porcine valves in the right ventricular outflow tract position have been relatively few and have demonstrated mixed results, particularly with the development of stenosis and need for re-operation [2–8]. Erek and associates reported a relatively high incidence of re-operation in children receiving a stentless bioprosthesis, with a freedom from re-operation of only 28% at 7 years [7,11]. Of note, these patients were younger and, as such, had smaller valves implanted [7]. Others too, have reported late problems with constricting fibrous reaction of the valve requiring re-operation, leading them to abandon use of these valves in the right ventricular outflow tract [12]. Of note, our series was comprised of stentless porcine valves of aortic origin only and were almost exclusively of the Edwards Prima Plus valve type. The long-term success of this specific valve in the pulmonary position has, until now, not been assessed with data on only three patients previously reported [7].

In contrast to these reports of poor long-term longevity, others have demonstrated a favorable outcome with the use of stentless porcine valves in the right ventricular outflow tract. Kanter and associates have reported 56 children that had a Freestyle stentless aortic root porcine valve inserted in the right ventricular outflow tract, with only 1 requiring re-operation with 30 months of follow-up [5]. The progression of peak gradient and valve competency in Kanter’s study was very similar to what we have seen in our series, with a late peak echocardiographic gradient of 18—25 mmHg and over 90% with less than moderate insufficiency [5]. Likewise, Black and associates have reported good results using a Toronto SPV valve in the right ventricular outflow tract in 21 children with tetralogy of Fallot noting no explants at a mean post-operative follow-up of 38 months [13]. The progression of peak systolic gradient in Black’s series was similar to ours and showed a 15—20 mmHg peak systolic gradient at the 3—5-year mark [13]. It is known that the peak systolic Doppler derived gradient can overestimate the actual gradient determined by catheterization and that mean Doppler gradient more accurately correlates with catheter derived gradients [14]. More experience and longer-term follow-up will be needed to determine the importance of this echocardiographic pressure gradient and whether it continues to increase significantly over time.

Implantation of this valve is relatively simple and similar to that of a standard cryopreserved pulmonary allograft in patients with a relatively normal right ventricular outflow tract. Differences between the stentless aortic porcine root and standard cryopreserved pulmonary allograft have to do with the relative rigidity of the stentless porcine valve root. In addition, since the stentless graft itself is relatively short and the distance between the right ventricle and pulmonary arteries can be longer than the graft, an extension either proximally, in the form of an anterior hood [5] or distally with an allograft or pericardial patch can be necessary [3]. Also, proximal or distal extensions may be necessary to get the relatively straight porcine graft to ‘curve’ into the natural shape of a right ventricular outflow and pulmonary artery course. In those patients that have orthotopic placement, this can usually be accomplished without additional material by beveling the graft distally, trimming the distal native pulmonary artery short posteriorly, and ‘telescoping’ the proximal posterior sewing ring into the right ventricular outflow tract. We feel it is important to get the valve into a position that maintains its normal, straight orientation to allow the graft to function appropriately without compression or distortion of the valve and sinus of Valsalva mechanism. We feel that a normal sinus of Valsalva mechanism inherent in these grafts may improve durability and cusp function. Ultimately we have utilized these extension techniques liberally thinking that a normal shape of the graft will allow proper function and, hopefully, longevity and durability of the graft.

Direct comparisons of these stentless porcine valves with stented heterografts, cryopreserved allografts or bovine...
jugular venous valved conduits is lacking and beyond the scope of our study. Freedom from re-operation or explants of the valves in our series was greater than 95% at 5 years and compare very favorably to large scale studies looking at cryopreserved valved allografts [15], bovine jugular venous valved conduits [16,17] or stented porcine or pericardial valves [18,19] where an 80–85% freedom from explantation or reintervention at 5 years can be expected. These valves also rarely showed evidence of even mild insufficiency and compare favorably with cryopreserved allografts, where some insufficiency is common and moderate insufficiency occurs about 15–25% of the time in the intermediate-term [20,21]. Because of this excellent intermediate-term ability to remain competent (Fig. 2), we feel these valves are particularly advantageous over cryopreserved pulmonary allografts when the primary indication for valve or conduit replacement is valve insufficiency.

The main limitation of this study is a rather short follow-up period. Much more time will be needed to determine if these valves are truly comparable to stented porcine, stented pericardial, bovine jugular venous valved conduits or the standard cryopreserved allografts over the long-term. These valves are not available in sizes less than 19 mm, so utilization of these in the most demanding infant and neonatal group is not possible at the current time. In addition to a bias toward the older patient, our series was also comprised of a majority of patients in whom the valve was implanted in the orthotopic position, rather than in the more demanding extracardiac position for long term function [20]. Only a direct comparison between similar patients or a randomized trial will be able to determine if stentless porcine valves truly are more durable than other valve or conduit choices at the current time.

References

But you have to keep in mind that all of these valves are 19 mm or larger, so these are being placed in larger patients. We know that particular group of patients, even the homografts fail at a much lower rate than in smaller patients, so I really can’t answer that first question.

In terms of the orthotopic position, I would have to say, as you can see from the slide, in Utah most of my patients live at 1500 to 2000 meters elevation. And the effects of higher pulmonary vascular resistance on the incidence and the severity of pulmonary valve insufficiency I think is different than it is at sea level. So most of my patients, that is the most common patient that I see, is an old tetralogy who received a transannular patch, who comes in with wide-open PI, and they have a dilated right ventricle, frequently with arrhythmias, prolongation of the QRS, et cetera, et cetera. And that’s why I chose this valve in the beginning because homografts seem to fail in that situation rapidly. So I had to find something different that would remain competent, because I felt like if I was performing a valve replacement because of an indication of an incompetent valve, to give them another valve that’s going to be incompetent in 3 months, like a homograft might, is bad medicine. So that’s why we switched to these valves.

I think it’s very easy to get these into the orthotopic position, but you have to do that beveling of the distal, and you have to set the posterior annulus of this sewing ring, telescope it down into the ventricle, and then if you can’t reach it anteriorly, don’t pull it down, because that will distort the valve, but rather add in a little anterior hood. But I think that these are very good for the orthotopic position. In fact, like you mentioned, that’s where most of the patients came from. I have not used very many stented valves in the orthotopic position. I think they work okay.

My rationale, again, for this valve is that the stented valve is either man-made or human-mounted valve, and that if we can preserve the sinus mechanism in a valve that undergoes the latest and most advanced anticalcification and fixation techniques, if we can preserve that sinus mechanism and get it in right, that maybe that valve will last longer than a stented valve. But that may be false rationalization.

But as far as my colleagues and valve selection are concerned, the vast majority of these patients were second, third, fourth re-ops, and all of us believe these valves offer great pulmonary valve competence and the vast majority of the time my colleagues choose these valves over stented or homograft valves, for this reason.

Dr C. Schreiber (Munich, Germany): I would like to comment on something. Worldwide, more than 600 Melodies were implanted with great success. We have completely changed our strategy in Munich. We only try to order from the different sources homografts up to a size of 23 mm. We avoid placing, unlike you, valves of 25, 27 and 29 mm, because if the homograft or the biological valve fails, which we all know it will one day, the cardiologist may go ahead and put a Melody in. If you keep putting in these large valves no treatment option for catheter-based valves exist. Could you please comment on your strategy?

Dr Hawkins: Well, I have to admit that in the United States percutaneous catheter-based valves are not available. They’re only available at a few centers under investigational circumstances. So you’re asking me and I don’t have any exposure to that situation yet.

And I really can’t comment on your last question about the percutaneous valves. Really, it’s hard for me to imagine that a manufacturer can make a valve that can be compressed down into a little cylinder that works as well as one of these valves, but that’s a surgeon bias. My preference would then be to place as large a valve as possible to get the greatest longevity, disregarding percutaneous valve implantation needs.

Dr R. Pretre (Zurich, Switzerland): I have another question on the valve size.

You have a population of teenagers and young adults in your series, and you have put a lot of 27 and 29 mm valves. I don’t want to reiterate what was said regarding the subsequent transvenous insertion of a valve, but still those valves are extremely stiff and bulging. Are you not afraid to end up with a compression of the left coronary artery, especially when you close up the sternum?

Dr Hawkins: On one patient I got into the left main, but I have not seen any compression of the left coronary. It just takes a lot of work and I think you have to mobilize the distal pulmonary arteries and you have to add a patch so that you don’t have any tension on that left coronary artery area. But I just haven’t seen that problem.

Dr Pretre: I assume you also put the so-called noncoronary sinus of this graft on the posterior part of your insertion?

Dr Hawkins: It’s actually sort of posterior and —

Dr Pretre: You have two remnants of the coronary arteries, where are they when you put this stentless valve in the RVOT?

Dr Hawkins: One coronary is pointing straight anterior, the other one is sort of left and posterior, and then the none is sort of right and posterior. It’s almost an anatomic situation from the aorta.

Dr W. Ruschewski (Gottingen, Germany): I have often made the observation in the last 30 years with biological valves in pulmonary position which are too big that one of the leaflets doesn’t open or stays open. If you re-operate them, this leaflet stands rigid and calcified in closed position or stands open fixed to the wall of the pulmonary artery. This may be caused by the reduced flow velocity and indicates that it is not advantageous to implant oversize valves. Therefore I avoid to implant too big valves in patients.

Dr Hawkins: I think you’re right. I think it’s very important to try to get this in without distortion, because I have seen that in a couple of patients where one leaflet is held open or there is a little kink posteriorly and that turbulence probably leads to calcification.