Institutional report - Valves

Outcomes with Toronto stentless porcine aortic valve: the Australian experience

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Abstract

The purpose of this study is to describe the Australian experience with TSPV in the aortic position in 543 patients followed for up to 8 years. Prospectively collected data were reviewed. The average age was 73.5 years, with 74.4% older than 70 years. Eighty-five percent of valves were calcified and 79.5% stenotic. Most valves implanted (79.3%) were sizes 25, 27, or 29 mm. Concomitant coronary bypass was performed in 45.3% of patients. Total cumulative follow-up for the 543 patients was 2131 patient years. At 6 years, 82.1% and at 8 years, 76.3% were in New York Heart Association class I, 55% had no aortic insufficiency. The average mean systolic gradient for all valves at 6 years was 7.4 mmHg. The effective orifice area varied from 1.7 cm$^2$ (23-mm valve) to 1.96 cm$^2$ (29-mm valve). Actuarial survival at 8 years was 79.3%. Freedom from valve-related deaths was 93.2%. There was one instance of primary tissue valve failure during follow-up, with 93.3% freedom from explant. The early hemodynamic benefits of the TSPV are well maintained during more than 8 years of follow-up, without evident significant valvular dysfunction. Longer follow-up time is required to validate durability.

Keywords: Heart valves; Stentless; Aortic valve replacement; Xenograft

1. Introduction

Over the past decade, the use of stentless xenograft aortic valves has increased substantially. Stentless design demonstrates superior hemodynamics compared with stented valves, with normal or near normal hemodynamics at rest and during exercise. Surgeons in Australia began using TSPV in 1994. Most of the published mid, to long-term results for TSPV have been from 'The Clinical Investigators of the TSPV' [1]. The purpose of this study is to describe the Australian experience with TSPV in the aortic position and to examine the clinical, functional and structural outcomes in 543 patients up to eight-year follow up.

2. Material and methods

2.1. Patient population

A cohort of 543 consecutive patients who underwent aortic valve replacement with TSPV between June 1994 and December 2003 by three surgeons at three different units in Australia was reviewed. The patients were selected on the basis of general suitability for bioprosthetic replacement and none were excluded on the grounds of age, risk or co-morbidity. The patients were identified through a prospectively maintained surgical database and medical charts were reviewed retrospectively in order to complete missing data of interest. The preoperative clinical characteristics of the patient cohort are described in Table 1.

2.2. Surgical technique

The native aortic valve was exposed through a transverse aortotomy above the sinotubular junction. The native aortic valve was excised and the annulus completely debrided in standard fashion. A discrepancy of more than 10% between sino tubular and aortic annular diameters required additional procedures in 62 (11.4%) patients (Table 2). All valves were inserted using the standard technique, the proximal suture line with 4-0 interrupted ethibond and the distal suture line with running 4-0 prolene after locating the top of the commissural posts.

2.3. Follow-up

Patients were followed up individually by their physicians. All out-of-hospital deaths were cross referenced between the State Mortality Databases and the hospitals’ patient database. The study was censored on 31st March 2004. All patients underwent early transthoracic echocardiography (TTE) during their postoperative hospital stay and regular late TTE as part of long-term follow-up. Patients
were either anticoagulated (Warfarin) for three months and then changed to low dose aspirin, or just given low dose aspirin according to surgeon preference.

2.4. Statistical methods

Postoperative complications were analyzed according to the guidelines reported by Edmunds et al. [2]. Statistical analyses were done with the Number Cruncher Statistical System (NCSS). Actuarial survival was calculated using the lifetable method. Results were expressed as percentages of the mean and percentages of the standard deviation of the means.

3. Results

3.1. Clinical outcomes

Mean age was 73.5 years (range: 36–92 years) (Table 1). At the time of surgery 74.4% of the patients were older than 70 years. At the time of censoring the study (March 2004) the total follow-up was 2131 patient years, with a mean of 3.92 valve years per patient (maximum of 9.5 years). Preoperatively, 94.3% of patients were in NYHA class II–IV. At 8 years 76.3% and 21.9% were in NYHA class I and II, respectively.

### Table 1

Preoperative clinical characteristics (n=543)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (mean ± S.D.)</td>
<td>73.6 ± 8.4</td>
<td></td>
</tr>
<tr>
<td>Male:female ratio</td>
<td>292:251</td>
<td>54:46</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>41</td>
<td>7.5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>232</td>
<td>42.7</td>
</tr>
<tr>
<td>Diabetes</td>
<td>87</td>
<td>16.0</td>
</tr>
<tr>
<td>Heart failure</td>
<td>92</td>
<td>16.9</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>63</td>
<td>11.6</td>
</tr>
<tr>
<td>Impaired renal function (creatinine 150 μmol/l)</td>
<td>28</td>
<td>5.1</td>
</tr>
<tr>
<td>Coronary artery disease *</td>
<td>272</td>
<td>50.0</td>
</tr>
<tr>
<td>Carotid stenosis</td>
<td>24</td>
<td>4.4</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>9</td>
<td>1.6</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>93</td>
<td>1.7</td>
</tr>
<tr>
<td>Angina</td>
<td>287</td>
<td>52.8</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td>21</td>
<td>3.86</td>
</tr>
</tbody>
</table>

NYHA class

- I: 31, 5.7
- II: 196, 36.0
- III: 251, 46.2
- IV: 65, 1.9

Previous cardiac intervention

- CABG: 19, 3.5
- AVR #: 11, 2.0
- Pacemaker: 6, 1.1
- PTCA: 9, 1.6
- Others: 13, 2.4

Aortic valve lesion

- Aortic stenosis: 432, 79.5
- Aortic regurgitation: 40, 7.4
- Mixed lesion: 71, 13.1

Mixed lesion

- Single vessel disease: 42.8
- Double vessel disease: 26.7
- Trippe vessel disease: 27.9
- Others: 2.6

Pulmonary homograft: 2

Pericardial valve: 6

Mechanical valve: 3

3.2. Operative data

The operative data are summarized in Table 2. Two surgeons preferred to correct discrepancies of more than 10% between the sinotubular and aortic annular diameter, which required additional relatively minor procedures. Valve sizes used in 74.3% of patients were 25, 27 and 29 mm. Average cross-clamp time for isolated aortic valve replacement decreased from 126.37 min in the beginning of the series (1995) to 88.42 min towards the end (2003) of the series.

### Table 2

Operative data

<table>
<thead>
<tr>
<th>Valve pathology</th>
<th>n (%)</th>
<th>Mean ± S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degenerative</td>
<td>96 (17.7)</td>
<td></td>
</tr>
<tr>
<td>Congenital bicuspid</td>
<td>102 (18.8)</td>
<td></td>
</tr>
<tr>
<td>Calcification</td>
<td>265 (48.8)</td>
<td></td>
</tr>
<tr>
<td>Rheumatic</td>
<td>38 (7.0)</td>
<td></td>
</tr>
<tr>
<td>Endocarditis</td>
<td>7 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Prosthetic failure</td>
<td>11 (2.0)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>24 (4.4)</td>
<td></td>
</tr>
</tbody>
</table>

Associated procedures

- CABG: 246 (45.3)
- MV repair: 10 (1.8)
- Asc. aorta replacement: 1 (0.2)
- MV replacement: 1 (0.2)
- Miscellaneous*: 4 (0.7)

Bypass and cross-clamp times (min)

- With concomitant surgery: 262 (48.3)
- Bypass time: 162.6 ± 35.3
- Cross-clamp time: 120.5 ± 24.2

Without concomitant surgery

- With bypass time: 281 (51.7)
- Cross-clamp time: 91.1 ± 19.8

Total patients: 543 (100)

Bypass time: 134.1 ± 38.9

Cross-clamp time: 102.3 ± 26.8

Valve size implanted (label size mm)

- 21: 40 (7.4)
- 23: 97 (17.9)
- 25: 182 (33.5)
- 27: 118 (21.7)
- 29: 106 (19.5)

Procedure for ST and AA diameter discrepancy

- Total: 62 (11.4)
- Dacron patch reduction of ST diameter: 18 (3.3)
- Reduction aortoplasty: 3 (0.6)
- Pericardial patch enlargement of ST diameter: 8 (1.5)
- Plication of ST junction: 11 (2.0)
- LV myomectomy: 17 (3.1)
- Rotation of distal suture line: 5 (0.9)

3.3. Hemodynamics

The postoperative echocardiographic data are shown in Table 3. The average mean systolic gradient for all valves at 6 years was 7.42 mmHg and the peak gradient was 13.82 mmHg. The effective orifice area varied from 1.73 cm² (23 mm valve) to 1.96 cm² (29 mm valve). Fig. 3 shows postoperative aortic insufficiency (AI) as assessed by color Doppler echocardiography. Mild AI increased from 7% of the patients in the first postoperative year to 40% of the patients in the eighth postoperative year. Moderate AI was noted in 5% of the patients on long-term follow-up and in all these patients AI was transvalvular. During follow-up no...
patient underwent replacement for progressive insufficiency.

3.4. Early mortality

Nineteen perioperative deaths (3.5%) occurred either during initial hospitalization or < 30 days after operation. Four patients had difficulty weaning from CPB; of these one died on table and three died on the day of operation. Five patients died of low cardiac output and three had fatal perioperative myocardial infarctions. One patient developed right ventricular failure and required RVAD, but died on the second postoperative day. One patient developed ARDS. The causes for the early ‘valve related’ five deaths include CVA, worsening MR following AVR, worsening LV outflow obstruction and sudden unexplained death in two patients.

3.5. Late mortality

In this series there were 47 late deaths. Of these 14 were ‘valve related’ deaths; two occurred because of endocar-
ditis, one patient died because of anticoagulation related hemorrhagic stroke, two patients developed late aortic insufficiency and CHF and could not be re-operated because of other associated co-morbidities. Nine patients died of unexplained causes.

The non-valve related deaths (33) included eight patients who died of malignancy. In all of these patients the most recent echocardiogram showed normal valve function with no evidence of endocarditis or thrombosis.

The overall freedom from death was 94.7% at 1 year, and 79.3% at 8 years (Fig. 1a). The overall freedom from valve related death was 98.4% at 1 year and 93.2% at 8 years (Fig. 1b).

3.6. Late events (Table 4)

Late thromboembolism was documented in 21 patients: 15 had cerebral transient ischemic attack, six had a stroke. Fig. 2c shows the freedom from thromboembolic complications – 89.2% at 8 years. Infective endocarditis developed in eight patients. Three had endocarditis in the first postoperative year. Out of eight patients with endocarditis, five required explant of the infected valves and most of them showed leaflet perforations. Antibiotics alone cured the infection in two patients and one patient was not fit for further surgery and died in spite of aggressive medical therapy. Freedom from infective endocarditis at 8 years was 97.9% (Fig. 2a). None of the patients developed hematicylic anemia or valve thrombosis. Major bleeding events in the form of gastrointestinal bleed and epistaxis was documented in five patients (all of whom were therapeutically anticoagulated). Freedom from any bleeding event at 8 years was 98.5% (Fig. 2b).

3.7. Explants and reoperation

Seven patients had reoperation for TSPV explant (Table 5) (Fig. 1c). One had TSPV implanted and then rapidly re-explored for bleeding; explantation of the TSPV was necessary because of aorto-mitral discontinuity. Five had explants for endocarditis; one had explant at 7.8 years for calcific structural failure, originally inserted in a 36-year-old patient.
The quest for the ideal prosthetic valve is far from over. Mechanical valve replacement became popular in the 1960s, but in the later decades when the complications associated with manufacture and anticoagulation were better defined and understood, the pendulum swung in favor of bioprostheses [3]. The pulmonary autograft is not widely popular among surgeons and access to aortic homograft is restricted even in hospitals with an active tissue bank. In four of these patients TSPV was replaced by homografts. None of the patients underwent reoperation for late development of significant aortic regurgitation. There have been no instances of primary valve dysfunction because of cusp perforation, rupture, significant pannus or tissue creep. The rate of structural deterioration (calcification in one patient) was 0.04% per patient year and the rate of reoperation (seven patients) was 0.33% per patient year. Actuarial freedom from structural deterioration at 8 years (Fig. 1d) was 97.5%.

4. Discussion

The quest for the ideal prosthetic valve is far from over. Mechanical valve replacement became popular in the 1960s, but in the later decades when the complications associated with manufacture and anticoagulation were better defined and understood, the pendulum swung in favor of bioprostheses [3]. The pulmonary autograft is not widely popular among surgeons and access to aortic homograft is restricted even in hospitals with an active tissue bank. Currently the most frequently used valves in the aortic position are mechanical devices followed by the bioprostheses.

A bioprosthetic device capable of combining the properties of biological valves with the durability of mechanical valves would represent a substantial step forward. The wide variety of available prostheses in itself demonstrates that the ideal prosthesis does not yet exist and this many times leads to unjustified commercial competition among the manufacturers. In an attempt to circumvent some of the drawbacks of both mechanical and stented bioprosthetic valves, stentless valves were developed more than 15 years ago [4]. Stentless valve technology uses the native aortic root to ‘physiologically’ support the prosthesis and dissipate valve stress by maintaining the relationship between the sinuses of Valsalva and the valve cusp, which should allow for greater leaflet durability. Westaby et al. [5] have shown that when compared to a stented device, leaflet movement of the stentless valve appeared normal during the cardiac cycle, owing to a wider flow jet and more rectangular flow profile accompanied by an increased flow volume and elongation of the deceleration period of ejection. For stented prostheses the systolic pressure gradients remain the same throughout ejection and increase significantly with exercise and with impaired leaflet motion during the onset of diastole [6]. They postulated that removal of adverse stress relationships between tissue and stents may translate into improved valve durability.

The hemodynamics for the Toronto SPV are similar to those of the cryopreserved allograft, but with a significantly lower degree of aortic insufficiency. Long term structural durability and functional integrity for the TSPV are as yet unknown.

We have presented mid- to long-term results of 543 patients who underwent AVR with TSPV at three different centers in Australia. Our early and late outcomes are comparable to those in other published series. However, our patients, with a mean age of 73.6 years, are older than in other similar stentless valve series and our 45.3% rate of concomitant CABG is higher compared with 15–32% in other series [7].

The most commonly used implantation technique for the TSPV remains the double suture line in the subcoronary position. Subtle technical modifications include the type of aortic root incision, plasty of the aortic root or ascending aorta and reduction or enlargement of the sinotubular junction. The geometric arrangement of the TSPV is such that the diameter of the valve at the level of the commissure is similar to that of the annulus, that is, it is a prosthesis with parallel sides and generally symmetrical commissures. For this reason it is vital to measure the diameter of the aortic annulus (AA) and the sinotubular junction (ST) in order to ensure that the recipient root also

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**Table 4**

<table>
<thead>
<tr>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%/pt year</td>
</tr>
<tr>
<td>Early</td>
<td></td>
</tr>
<tr>
<td>Embolism</td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>6</td>
</tr>
<tr>
<td>TIA</td>
<td>4</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>3</td>
</tr>
<tr>
<td>Bleeding event</td>
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</tr>
<tr>
<td>Structural valve dysfunction</td>
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</tr>
<tr>
<td>Nonstructural valve dysfunction</td>
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</tr>
<tr>
<td>Paravalvular leak</td>
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<tr>
<td>Hemolytic anemia</td>
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<tr>
<td>Thrombosis</td>
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</tr>
<tr>
<td>Explant (all causes)</td>
<td>1</td>
</tr>
<tr>
<td>Death (all causes)</td>
<td>19</td>
</tr>
<tr>
<td>Death (valve related)</td>
<td>5</td>
</tr>
</tbody>
</table>

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**Table 5**

<table>
<thead>
<tr>
<th>Sex, age at initial implant (year)</th>
<th>Original valve pathology</th>
<th>Time to redo (year)</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>M (85)</td>
<td>Tricuspid, calcific</td>
<td>0</td>
<td>Dehiscence at aorto-mitral junction</td>
</tr>
<tr>
<td>F (79)</td>
<td>Tricuspid, calcific</td>
<td>0.3</td>
<td>Endocarditis with leaflet perforation</td>
</tr>
<tr>
<td>M (63)</td>
<td>Bicuspid, calcific</td>
<td>1.5</td>
<td>Multifocal endocarditis</td>
</tr>
<tr>
<td>M (76)</td>
<td>Tricuspid, calcific</td>
<td>3</td>
<td>Endocarditis</td>
</tr>
<tr>
<td>F (66)</td>
<td>Tricuspid, calcific</td>
<td>3</td>
<td>Strepto. Pyogenes endocarditis</td>
</tr>
<tr>
<td>M (76)</td>
<td>Tricuspid, calcific</td>
<td>4.2</td>
<td>Strepto. Faecalis endocarditis, leaflet perforation</td>
</tr>
<tr>
<td>M (36)</td>
<td>Tricuspid</td>
<td>7.8</td>
<td>Calcification and stenosis of SPV</td>
</tr>
</tbody>
</table>
has parallel sides. In our series 21.7% (in a subgroup of 286 patients) underwent some additional procedure for ST, AA discrepancy. In general, the implantation time of stentless xenografts is longer than that of a stented valve by 20–30 min.

The relative contraindications to use of the stentless valves are calcified or aneurysmal aortic root, bicuspid aortic valve with opposed coronary ostia, and other coronary ostial anomalies. Many of these conditions can be dealt with by technical modifications.

The hospital mortality after stentless aortic valve replacement has been reported to vary widely between 0.8 to 8%, but it has always proven absolutely comparable with and often lower than mortality reported for stented bioprosthesis [8–10]. In a recent metaanalysis of the outcome with stentless valves, risk factors for hospital mortality were female gender, old age, NYHA class, diagnosis of aortic stenosis, small aortic annulus, co-existent coronary disease requiring surgery and duration of aortic cross clamp [8]. As recent reports have shown [11], the favorable hemodynamic behavior of stentless valves may be particularly helpful in patients with ventricular dysfunction. Accordingly, institutions with longstanding expertise in stentless valve surgery are increasingly extending this treatment modality to patients with aortic valve disease and advanced left ventricular dysfunction with promising results [11,12]. This explains in part the apparent discrepancy in hospital mortality among recent clinical surveys.

In most of the midterm results published so far stentless bioprostheses have exhibited hemodynamic properties clearly superior to stented bioprostheses as regards transvalvular pressure gradients, effective orifice area and regression of left ventricular hypertrophy [12,13]. This has led to a current hypothesis that more prompt and thorough regression of left ventricular hypertrophy may account for the survival advantage observed with stentless valve replacement.

Several investigations have shown that mean systolic gradient across the TSVP decreases over the first year of implantation and its effective orifice area increases [14]. The reason for this is believed to be remodelling of the left ventricle outflow tract and healing of the valve in the patient’s aortic root.

In the different retrospective studies reported so far, 8-year survival with TSPV has been between 92–98% [8]. In the current study, we noted freedom from reoperation at 8 years to be 95.9% and freedom from structural deterioration 97.5%.

In this series we observed an increase in mild to moderate echocardiographic AI over time. Ninety-three percent of patients had no AI with the early post-op TTE and at 8-year follow-up 40% patients had mild and 5% had moderate AI. Two patients developed severe AI but were not considered suitable for re-do AVR. No patient in this series underwent explant for isolated significant AI. In our series there is no SVD leading to significant AI as only 7.4% of patients had AI preoperatively. It is reasonable to assume therefore that development of AI is due primarily to poor leaflet apposition from commissural stretching at the sinotubular junction or sinus of Valsalva, with or without dilatation of the ascending aorta. Not until 2002 were there reports of SVD because of calcification of the TSPV. In a recent series 25% of the 12 explants were because of calcification of valve leaflets leading to AS [15]. The only SVD in our series was a 36-year-old male patient who developed severe calcification of TSPV 8 years after implantation.

In our series overall survival at 8 years as reflected by freedom from death from all causes was 79.3%. Freedom from valve related death was high at 93.2% at 8 years. Mortality was primarily because of malignancies in the noncardiac group.

Although still in the early stages, because the number of prostheses which have been in situ for more than 8 years is small, it would appear that the trend for prosthetic failure is no better for stentless valves than stented devices or homografts. If this proves to be the case, then clearly the answer for increased durability lies not in a stent but in the quality of the xenograft tissue.

To conclude, TSPV is associated with excellent hemodynamics early after surgery and up to 8 years after surgery. The prevalence of hemodynamically significant AI remains low. The patients enrolled in this study will continue to be followed up and will serve as the basis for future reference.

Acknowledgments

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References


