INTRODUCTION

A stented bioprostheses in the aortic position has the disadvantage of presenting high transvalvular gradients as well as incomplete regression of left ventricular hypertrophy.1 The stent can cause non-physiological mechanical stress, with valvular calcification and consequent dysfunction.2 In contrast, the presence of a rigid stent produces a residual obstruction in transaortic flow, reducing effective area, and impeding complete resolution of left ventricular hypertrophy.3 This has been shown to have a negative effect on ventricular function following aortic valve replacement4 and, therefore, on long-term survival.5

Homografts have been demonstrated to have excellent hemodynamic performance6 but their clinical use is restricted due to the limited number of donors.7 When compared with stented prostheses,7 stentless prostheses have been credited with better hemodynamic performance, earlier and more complete regression of left ventricular hypertrophy,8,9 and improved ventricular function in patients with aortic insufficiency and left

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Reemplazo valvular aórtico con bioprótesis no soportada de Cryolife O'Brien

Introducción y objetivos. El xenoinjerto de Cryolife O'Brien es una bioprótesis no soportada, construida por valvas no coronarias de 3 válvulas aórticas porcinas. El objetivo de este estudio es investigar los resultados preoces después del reemplazo valvular aórtico con este xenoinjerto compuesto.

Métodos. Desde octubre de 1993, la bioprótesis Cryolife O'Brien ha sido implantada en 210 pacientes. La edad media fue de 70,9 ± 7,5 años (intervalo, 23 y 83 años). La indicación fue estenosis aórtica en 132 casos, insuficiencia aórtica en 25 casos y doble lesión en 53 casos. Se ha estudiado la función valvular, mediante ecocardiografía preoperatoria, en el momento del alta y a los 6 y 12 meses del postoperatorio.

Resultados. La mortalidad a 30 días fue del 5,2% (11/210). Los gradientes medios se reducen y el índice de área efectiva aórtica aumenta con el tiempo. El índice de masa ventricular izquierda, el grosor de la pared y el espesor del septo también se reducen de forma precoz en el postoperatorio.

Conclusiones. El uso de la bioprótesis no soportada de Cryolife O'Brien ha mostrado unos resultados satisfactorios en el seguimiento a un año. Será necesario realizar seguimientos futuros para analizar el comportamiento de esta bioprótesis a largo plazo.

Palabras clave: Cirugía. Ecocardiografía. Bioprótesis no soportada.
ventricular dysfunction, leading to better quality of life and improved survival rates among recipients.

The objective of the present study is to examine initial results of using the Cryolife O’Brien stentless prosthesis in aortic valve replacement, thru a prospective cohort study.

METHODS

From October 1993 to October 2004, 210 patients received a Cryolife O’Brien prosthesis in the aortic position in our service. Mean age was 70.9 (7.5) years (range 23-83); 185 patients (88.1%) were >65 years; 110 (52.4%) were men; 100 (47.6%) were women; 128 (60.9%) were in New York Heart Association (NYHA) functional class III-IV.

Perioperative data on patients appear in Table 1.

Sinotubular dilation, extensive calcification of the aortic root, and the unfavorable position of coronary ostia, were exclusion criteria for implantation of the prosthesis.

Implanted valve sizes were: 21 mm in 20 patients (9.5%); 23 mm in 61 (29%); 25 mm in 58 (27.6%); 27 mm in 56 (26.7%); and 29 mm in 15 (7.1%). In 129 patients (61.4%), valve size was $\geq 25$ mm.

Mean extracorporeal circulation time was 83.68 (22) min for all series; 58.2 (11.4) min for isolated valve replacement; and 89.1 (19.7) min for valve replacement combined with other procedures.

Valves Under Study

The Cryolife O’Brien stentless porcine xenograft (Cryolife International, Marieta, GA, USA) is a composite prosthesis, constructed from 3 noncoronary valves obtained from 3 porcine valves, fixed in glutaraldehyde under low or near-zero pressure. Valves are adjusted for size and symmetry to ensure synchronic opening and maximum coaptation. Once adjusted, the 3 valves are sewn together along the free edge of the aortic wall to the commissures. The base of the valve is sewn with a continuous suture to ensure its integrity. A significant difference by comparison with other stentless valves is the absence of any other type of artificial material.

In all cases, the prosthesis was implanted in supra-annular position, using continuous suture, as described elsewhere. The size chosen was one size larger that that found when measuring the annulus with a Hegar dilator.

Echocardiography

Transthoracic echocardiography (TTE) was performed preoperatively, at discharge, at 6 months and at 12 months. Preoperatively and at discharge, studies were performed in the same hospital, but at 6- and 12 months they were not. These follow-up studies took place in patients’ referring hospitals and the validity, and reliability of the measurements were determined by calculating the inter-class correlation coefficient for each parameter.

Left ventricular systolic and diastolic diameters, posterior wall in diastole, and interventricular wall in diastole were measured.

Left ventricular ejection fraction (LVEF) was calculated using the Teichholz formula. Peak and mean gradients were calculated with the modified Bernoulli equation. Effective area was calculated with the continuity equation.

Left ventricular mass (LVM), in grams, was calculated from measurements of interventricular wall (IVW) in diastole, posterior wall thickness (PW) in diastole, and left ventricular diastolic diameter (LVdD), all in centimeters, using The American Society of Echocardiography modified cube method, as follow:

$$\text{LVM (g)} = 0.8 \times [1.04 \times (\text{IVT} + \text{PW} + \text{LVdD}) - (\text{LVdD})] + 0.6$$

Effective area and left ventricular mass values were indexed by body surface area in $m^2$.

Follow-Up

Follow-up required patients to attend outpatient clinics and, at the time of writing, 168 patients have attended...
all check-ups; 16 (7.6%) have yet to complete 1 year of follow-up; and 4 (1.9%) have been lost to the study. Mean follow-up is 301.4 (8.4) days.

Following Edmunds et al., we collected data on morbidity and mortality after cardiac valve operations for subsequent publication.

Statistical Analysis

Statistical analysis was with SPSS 11.0 (Statistical Package for the Social Sciences, Chicago IL, USA). Continuous variables are presented as mean (SD) and categorical variables as percentages.

Continuous variables were analyzed with Student t test and χ² test, and discrete variables with Fisher exact test.

To detect significant changes in echocardiographic data over time we used Student t test for paired data in related samples.

Stepwise backward logistic regression was used to analyze predictors of in-hospital mortality. We analyzed the following variables: gender, age, chronic obstructive pulmonary disease (COPD), kidney failure, coronary heart disease, diabetes, high blood pressure, previous stroke, pulmonary artery hypertension (PAHT), preoperative atrial fibrillation, weight, height, body surface area, body mass index, extracorporeal circulation time, and aortic clamping time.

The percentage of complication-free patients at 1 year was calculated according to Kaplan-Meier.

In all cases, a P value less than .05 was considered significant.

RESULTS

In-hospital mortality at 30 days was 5.2% (11 of 210) for all series and 4.2% (7 of 167) for isolated aortic valve replacement. Six patients died of multiorgan failure, 1 of sepsis, 1 of hemorrhage, 1 of pulmonary embolism, 1 of respiratory insufficiency, and 1 of mesenteric ischemia.

Logistical regression analysis found in-hospital mortality was predicted by: extracorporeal circulation time >90 min; aortic clamping time >75 min; and preoperative atrial fibrillation. Presence of coronary heart disease was associated with increased mortality but was not statistically significant (Table 2).

Of 199 patients who survived surgery, 2 presented peripheral embolisms during the first year (1%): 1 in the humeral artery and 1 in the popliteal artery, at 2 days, and 5 months, respectively. These were non-anticoagulated patients who had presented atrial fibrillation. The episodes were resolved by embolectomy. At >1 year, 98.47% (0.88%) of patients were free of thromboembolic complications.

Three patients presented early prosthetic endocarditis (2%) at 2, 3, and 5 months, respectively, without prosthetic dysfunction. These patients were reoperated, 2 for aortic annular abscess and 1 for sepsis not responding to antibiotic treatment. All 3 died following reoperation. At 1 year, 98.38% (0.93%) of patients were free of endocarditis.

Five patients have been reoperated (2.5%). Three of these (described above) were operated for prosthetic endocarditis; 1 had prosthetic stenosis due to defective implantation technique; 1 had mild periprosthetic insufficiency, and hemolytic anemia with substantial clinical repercussions. After 1 year, 97.22% (1.23%) of patients were free from reoperation. During the first year, 9 patients (4.5%) died: 3 patients with prosthetic endocarditis died following reoperation; 1 sudden death; 1 had acute myocardial infarction; 1 had congestive heart failure; 1 had kidney failure; 1 had respiratory insufficiency; and 1 had a tumor. Survival at 1 year was 94.65% (1.65%).

Comparison of preoperative functional class with functional class at 12 months shows improvement in all 168 patients who have completed 1-year follow-up: 161 (95.8%) are in functional class I and 7 (4.1%) in functional class II.

At 1 year, aortic insufficiency was not present in 113 patients (67.3%), and was only trivial in 40 (23.8%) and mild in 15 (8.9%). Echocardiographic data are in Table 3.

Comparison of left ventricular diastolic diameter measurements showed significant reduction at discharge (P<.001) versus preoperatively. However, measurements at 6 and 12 months did not vary significantly by comparison with data collected at discharge.

Left ventricular systolic diameter measurements reduced significantly at discharge (P=.008) versus preoperatively. Data at 12-months showed further significant reduction versus data collected at discharge (P=.049).

We found a significant improvement (P=.003) in ejection fraction at 1-year versus preoperatively and at discharge (P=.001).

Interventricular wall in diastole showed significant reduction (P<.001) at 6 months versus preoperatively and at discharge (P=.007). Subsequent measurements did not vary significantly.

Posterior wall in diastole measurements reduced significantly (P=.015) at 6 months versus preoperatively.

### TABLE 2. Factors Predicting in-Hospital Mortality*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
<th>β</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECC &gt;90 min</td>
<td>2.07</td>
<td>1.26-3.39</td>
<td>.002</td>
<td>.57</td>
</tr>
<tr>
<td>Aortic clamping &gt;75 min</td>
<td>2.71</td>
<td>1.48-4.97</td>
<td>.007</td>
<td>.186</td>
</tr>
<tr>
<td>Preoperative AF</td>
<td>2.58</td>
<td>1.10-6.07</td>
<td>.045</td>
<td>.138</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>2.15</td>
<td>1.06-4.34</td>
<td>.059</td>
<td>.130</td>
</tr>
</tbody>
</table>

*ECC indicates extracorporeal circulation; AF, atrial fibrillation; CI, confidence interval; OR, odds ratio.
TABLE 3. Echocardiographic Data*

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (n=219)</th>
<th>At Discharge (n=199)</th>
<th>6 Months (n=188)</th>
<th>2 Months (n=68)</th>
<th>P*</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVDd, mm</td>
<td>51 (9.4)</td>
<td>47.1 (10)†</td>
<td>47.5 (7.7)†</td>
<td>47.2 (7.3)†</td>
<td>&lt;.0001</td>
<td>0.83</td>
</tr>
<tr>
<td>LVsD, mm</td>
<td>33 (9.6)</td>
<td>32.3 (10.3)†</td>
<td>31.1 (7.8)†</td>
<td>30 (7)‡‡</td>
<td>&lt;.0001</td>
<td>0.85</td>
</tr>
<tr>
<td>EF, %</td>
<td>61.1 (14.2)</td>
<td>59.7 (14.9)</td>
<td>63 (12.6)</td>
<td>63.9 (11.7)‡‡</td>
<td>.003</td>
<td>0.76</td>
</tr>
<tr>
<td>IVWd, mm</td>
<td>15.1 (3.5)</td>
<td>15.1 (3.3)</td>
<td>13.7 (3.3)‡‡</td>
<td>13.2 (2.8)‡‡</td>
<td>&lt;.0001</td>
<td>0.80</td>
</tr>
<tr>
<td>PWd, mm</td>
<td>13 (2.6)</td>
<td>13.2 (2.5)</td>
<td>12.2 (2.5)†</td>
<td>11.8 (2.4)‡‡</td>
<td>&lt;.0001</td>
<td>0.75</td>
</tr>
<tr>
<td>LVM, g</td>
<td>307 (102)</td>
<td>282 (105)†</td>
<td>253 (97)‡‡</td>
<td>237 (78)‡‡</td>
<td>&lt;.0001</td>
<td>0.79</td>
</tr>
<tr>
<td>LVMI, g/m²</td>
<td>176 (58)</td>
<td>160 (60)†</td>
<td>143 (52)‡‡</td>
<td>136 (43)‡‡</td>
<td>&lt;.0001</td>
<td>0.77</td>
</tr>
</tbody>
</table>

*ICC indicates inter-class correlation coefficient; LVDd, left ventricular diastolic diameter; LVsD, left ventricular systolic diameter; EF, ejection fraction; LVMI, left ventricular mass index by body surface area; LVM, left ventricular mass; PWd, posterior wall in diastole; IVWd, interventricular wall in diastole.
†Statistically significant versus preoperative data.
‡Statistically significant versus data at discharge.
§1-year follow-up versus preoperative data.

We found further significant reduction at 1 year versus preoperatively (P<0.001) and at discharge (P=.026).

Left ventricular mass reduced significantly at discharge (P<0.001) versus preoperatively; and at 1 year versus discharge (P=.007).

Similarly, left ventricular mass index per m² of body surface area reduced significantly (P<.001), and reduction at 6 months was significant versus discharge (P=.02), although subsequent variation was not significant.

Mean transvalvular aortic gradient (Table 4) reduced significantly at discharge following valve replacement (P<.001); at 6 months this reduction continued (P<.001) versus discharge; and at 12 months, versus 6 months (P=.007).

Effective aortic area (P<.001) and effective aortic area index versus body surface area (P<.001) also improved significantly versus preoperatively; variation during the first year was not significant. Values of area and area index were optimal and were >0.8 cm²/m² in all patients.

DISCUSSION

Stentless aortic valve implantation was first reported in 1965, by Binet et al.,1,4 and in 1966, by O’Brien and Clareborough.15 With the development of tissue fixing using glutaraldehyde and the relatively simple implantation of mounted prostheses, interest in stentless valves fell away; however, stented bioprostheses in the aortic position have the disadvantage that mechanical stress appears in the valve, which is associated with the stent and restrictive hemodynamic performance with relatively high residual gradients in small sized valves.16

To avoid these inconveniences of stented bioprostheses, a growing number of surgeons began to use aortic homografts. Independently, Ross et al17 in 1962 and Barratt-Boyes18 in 1964 started to implant homografts using the technique described previously by Duran and Gunning.19

However, the availability of homografts is limited by the scarcity of donors. In 1988, David et al20 reintroduced the use of stentless porcine bioprostheses fixed in glutaraldehyde. The composite porcine valve reported by O’Brien and Clareborough in 1966, was reintroduced in 1991 with glutaraldehyde used for preservation.21

Aortic valve replacement with stentless bioprostheses is associated with excellent hemodynamic performance and clinical course,22,23 despite the greater technical complexity. The presence of residual gradient elevation continues to be the most important factor in the persistence of left ventricular hypertrophy after aortic valve replacement. Absence of the stent and greater effective areas ensure low residual obstruction, as shown by low postoperative gradients and rapid regression of left ventricular hypertrophy, even in patients with small aortic annulus.

Limitations of the Study

Our study does have certain limitations. First, we have not compared this prosthesis with any other type of valvular replacement. The short follow-up period has prevented us from obtaining information about the durability of this type of prosthesis. Echocardiographic data corresponding to 6- and 12-month follow-up were obtained in 4 hospitals and, therefore, by different observers; consequently, we analyzed the reliability of these measurements by calculating the inter-class correlation coefficient for each parameter.

CONCLUSIONS

Both ventricular diameter and left ventricular mass show substantial early reduction, and these changes are significant in the echocardiographic study performed at discharge, some 5 to 7 days postoperation; this reduction continues consistently during the first year.
Using the Cryolife O’Brien xenograft presents some specific advantages by comparison with other stentless prostheses. For example, implantation is simpler and faster due to the use of a single suture, resulting in only slightly longer extracorporeal circulation and aortic clamping time than in the conventional stented prosthesis. This benefits older patients, particularly if they receive other associated procedures.

Secondly, supraannular implantation permits the use of a larger size than could be deployed in a conventional bioprosthesis, with greater valvular orifices and lower residual gradients; this is also favored by absence of ventricular muscle in the base of the prosthesis. In our series, data on mean gradients and effective aortic area are similar to those reported elsewhere and better than published data on other types of third generation stented porcine prosthesis.

Even though the durability of these valves remains to be determined, they show excellent hemodynamic performance and are a good choice for aortic valve replacement in patients previously selected for bioprosthesis implantation, in particular for patients with a small aortic annulus, as found in degenerative aortic valve stenosis in the older patient.

REFERENCES


**TABLE 4. Changes in Mean Aortic Transvalvular Gradient, Effective Aortic Area, and Body Surface Area Index**

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (n=210)</th>
<th>At Discharge (n=199)</th>
<th>6 Months (n=188)</th>
<th>1 Year (n=168)</th>
<th>( P_{\alpha} )</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>mG, mm Hg</td>
<td>50.7 (21.9)</td>
<td>12.8 (9.2)†</td>
<td>9 (6)‡</td>
<td>7.8 (4.1)†‡‡‡‡</td>
<td>&lt;.0001</td>
<td>0.86</td>
</tr>
<tr>
<td>EAA, cm²</td>
<td>0.67 (0.4)</td>
<td>1.93 (0.9)†</td>
<td>2.21 (0.8)†‡</td>
<td>2.14 (0.7)†‡</td>
<td>&lt;.0001</td>
<td>0.75</td>
</tr>
<tr>
<td>EAAI, cm²/m²</td>
<td>0.38 (0.2)</td>
<td>1.11 (0.5)†</td>
<td>1.27 (0.4)†‡</td>
<td>1.32 (0.9)†‡</td>
<td>&lt;.0001</td>
<td>0.75</td>
</tr>
</tbody>
</table>

*EAA indicates effective aortic area; EAAI, effective aortic area index by body surface area; ICC, inter-class correlation coefficient; mG, mean gradient.
†Statistically significant versus preoperative data.
‡Statistically significant versus data at discharge.
§Statistically significant versus data at 6 months.
II1-year follow-up versus preoperative data.
Data are presented as mean (SD).