Hemodynamic and clinical outcomes with the Biocor valve in the aortic position: An 8-year experience

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Objectives: The aim of this study was to analyze the 8-year experience, survival, prosthetic complications, and hemodynamics of patients who received the Biocor valve, a new-generation tissue valve, in the aortic position.

Methods: From May 1992 through May 2001, 257 consecutive patients (129 women and 128 men; mean age, 75 ± 6 years; age range, 45-91 years) received 258 aortic Biocor porcine prostheses. One female patient who received 2 Biocor valves in the aortic position during 2 consecutive operations was entered twice in the statistical analysis. Twelve (4.6%) patients had previous aortic valve operations. Preoperatively, 82 (32%) patients were in New York Heart Association functional class III or IV. Associated surgical procedures included coronary artery bypass grafting in 56 (21.7%) patients, aortic annular enlargement or aortoplasty in 20 (8%) patients, and others in 8 (3%) patients. Echocardiography was performed in the majority of long-term survivors (91.6%). Follow-up included 1215 patient-years and was 100% complete, with a median time of 5 patient-years (range, 0.4-10.5 years).

Results: There were 16 (6.2%) early deaths. According to a univariate analysis, New York Heart Association functional class III or IV, concomitant procedures, ejection fractions of less than 40%, and urgent operations were identified as significant perioperative risk factors. At follow-up, 75 patients died; 8-year actuarial Kaplan-Meier survival was 48% ± 5%. At 8 years, the actuarial freedom from valve-related death was 92% ± 2.6%, the freedom from thromboembolism was 93% ± 2%, the freedom from anticoagulant-related hemorrhage was 95% ± 2%, the freedom from endocarditis was 99% ± 0.6%, the freedom from paravalvular leak was 96% ± 1.5%, the freedom from all valve-related complications was 78% ± 4.5%, and the freedom from structural valve deterioration was 95% ± 3.7%. At 8 years, the actuarial freedom from structural valve deterioration was 89% ± 10% and 95.8% ± 4% in patients younger and older than 65 years, respectively. At 10 years, in patients older than 65 years, the actual freedom from structural valve deterioration was 97.9% ± 2.1%, and the freedom from reoperation was 97% ± 1.3%. New York Heart Association status was I or II in 90% of patients at the end of follow-up. The mean echocardiographic follow-up time was 4.6 ± 2 years. By using Doppler echocardiography, the peak and mean transprosthetic gradients were determined to be 30.8 ± 9.3 mm Hg and 16.6 ± 5.3 mm Hg, respectively. Mean mass/volume ratio and left ventricular end-diastolic volume were 1.37 ± 0.17 g/mL and 63.4 ± 22.6 mL/m², respectively. The majority of patients showed a persistent left ventricular hypertrophy.
Conciliation: The Biocor is an effective bioprosthesis with a low incidence of valve-related complications comparable with that of other second-generation bioprostheses. This stented porcine prosthesis provides satisfactory results in terms of hemodynamics, valve durability, and freedom from reoperation.

Second-generation tissue valves have been processed and engineered to enhance their durability and their hemodynamic performance compared with those of first-generation bioprostheses. The Biocor prosthesis (Biocor Industria e Pesquisas Ltda, Belo Horizonte, Brazil) is a triple-composite porcine tissue valve fixed in glutaraldehyde at zero pressure (the so-called resting state) and mounted on a flexible acetal copolymer (Celcon) stent. This second-generation porcine valve has been used in our institution since 1992 (Figure 1).

The aim of this study was to analyze the 8-year clinical performance, complication rate, and hemodynamic performance of the Biocor porcine bioprosthesis implanted in a consecutive series of patients who underwent isolated aortic valve replacement.

Patients and Methods

Between May 1992 and May 2001, 257 consecutive patients (129 women and 128 men; mean age, 75 ± 6 years; median age, 75 years; age range, 45-91 years) underwent 258 isolated aortic heart valve replacements at our institute. One female patient who received 2 Biocor valves in the aortic position during 2 consecutive operations was entered twice in the statistical analysis. The analysis was prosthesis oriented, and observations were censored when the bioprosthesis was replaced. The patients’ data were prospectively collected and updated in our prosthesis database. Patients’ demographic data are detailed in Table 1.

Thirty-two percent (82/258) of patients were in New York Heart Association (NYHA) functional class III or IV. Twelve (4.5%) patients had previously received a different prosthesis in the aortic position. Concomitant procedures included coronary revascularization (56/258), aortic annular enlargement or aortoplasty (20/258), and others (8/258). Mean aortic prosthetic size was 23.6 ± 1.8 mm (median, 23 mm; range, 21-27 mm). The indexed effective orifice area was greater than 1 cm²/m² in all patients (mean, 2.24 ± 0.4 cm²/m²; median, 2.10 cm²/m²; range, 1.6-4.0 cm²/m²), but there were 5 patients in whom the effective orifice area was between 1 and 0.85 cm²/m² (only 2 patients had an indexed effective orifice area equal to 0.85 cm²/m²). Explanted bioprostheses underwent pathologic examination, as previously reported by our department for other valve types.2

Echocardiographic Analysis

Patients underwent 2-dimensional echocardiography to evaluate hemodynamic results. The majority of surviving patients (153/167) underwent 2 consecutive echocardiograms between June 2000 and December 2002. We included in the analysis the hemodynamic results of 10 patients who died some time after the first echocardiogram. The mean echocardiographic follow-up time was 4.6 ± 2 years. The simplified Bernoulli equation was used to calculate mean and peak pressure gradients across the valve. Left ventricular volumes were calculated by using an ellipsoid biplane area-length method.3 Left ventricular myocardial mass was calculated by multiplying the myocardial volume by the specific weight of myocardial muscle (1.05 g/mL).4 The left ventricle was defined as normal when the left ventricular end-diastolic volume was less than 70 mL/m² and the mass/volume ratio (M/V) was between 0.8 and 1.2 g/mL. The ejection fraction was calculated as follows: (end-diastolic volume − end-systolic-volume)/end-diastolic volume.

Surgical Technique

Median sternotomy, cardiopulmonary bypass, moderate hypothermia, and aortic crossclamping were used in all patients. Cardioplegic arrest was achieved by using antegrade and retrograde cold blood cardioplegia repeated at 20-minute intervals.

Aortic prostheses were implanted through a transaortic approach. Mean aortic crossclamp and cardiopulmonary bypass times were 82 ± 43 minutes and 113 ± 38 minutes, respectively. Prostheses were inserted by using multiple interrupted 2-0 Ticon sutures reinforced by Teflon pledgets with the noneverted suturing technique. Patients received continuous oral anticoagulation with warfarin sodium (target international normalized ratio, 2.0-3.0). The treatment is usually started on the second postoperative day and continues until the third postoperative month. Patients with chronic atrial fibrillation and patients with left atrial dilatation, left ventricular dilatation, or both were anticoagulated indefinitely.

Patient Follow-up

Follow-up data were collected on an annual basis through direct visits, questionnaires, or telephone interviews. Follow-up was closed in December 2002, and the cumulative time was 1215 patient-years; it was 100% complete. Median and mean follow-up time was 5 patient-years (range, 0.3-10.5 years).

Statistical Analysis

Edmunds and colleagues5 guidelines for morbidity and mortality reporting were used for definition of postoperative complications and prostheses-related events.

The linearized rate of postoperative complications and prostheses-related events was expressed as percentage per patient-year. The χ² test was used for statistical comparisons.

The estimate of overall survival was calculated by use of the Kaplan-Meier method and expressed as percentage ± SE or percentage ± 95% confidence interval. The 65-year-old patients were
included in the group of patients older than 65 years. We consider our data informative up to 8 years, with 21 patients at risk.

Actual freedom from complication was calculated by using the method of Grunkemeier and associates. 6

Results
Sixteen (6.2%) patients, 10 women and 6 men (mean age, 76.6 ± 1 years; age range, 71-83 years), died perioperatively (≤30 days). Sixty percent were in NYHA class III or IV, 25% had an urgent operation, and 50% had a concomitant procedure (1 with ventricular septal defect, 1 with aortoplasty, and 6 with coronary artery disease), and in 30% the ejection fraction was less than 40%. NYHA class III or IV, concomitant procedures, low ejection fractions, and urgent operations were identified as significant univariate risk factors (P < .05). Causes of death are detailed in Table 2.

Survival
Overall 8-year survival was 48% ± 5% (Figure 2). There were 75 (31%) late deaths: 21 (28%) were cardiac related, and 14 (18%) were valve related. Actuarial freedom from valve-related death was 92% ± 2.6% at 8 years (linearized rate of 1.1%/patient-year, Table 3). Causes of late death are detailed in Table 2. At the end of follow-up, 90% of patients were in functional class I or II, 80% of patients were anticoagulated, and 67% were in sinus rhythm. Therefore 92% of surviving patients improved or remained functionally stable, and 8% of patients had a worsening of functional status.

Thromboembolism
Twelve major thromboembolic events occurred in 11 patients, 1 early and 11 late (linearized rate of 0.9%/patient-year). Among these patients, 64% had an embolic stroke before surgical intervention, 62% were in atrial fibrillation, and 75% were anticoagulated. Embolism was fatal in 6 patients, causing 1 early and 5 late deaths. Prosthetic thrombosis was the cause of a late death in an 84-year-old woman affected by chronic atrial fibrillation and bearing patient-prosthesis mismatch. Actuarial freedom from thromboembolism and thrombosis was 93% ± 2% at 8 years (Table 3).

Hemorrhagic Events
Six patients had anticoagulation-related major hemorrhage, which was fatal in 4 cases; the linearized rate was 0.5%/
patient-year. Eight-year actuarial freedom from anticoagulant-related hemorrhage was 95% ± 2% (Table 3).

**Paravalvular Leak**
Seven patients who underwent aortic valve replacement because of a bicuspid aortic valve (1 patient), calcific degenerative valve stenosis (5 patients), and subacute native valve endocarditis (1 patient) had a paravalvular leak. The linearized rate was 0.66%/patient-year. Six of these patients underwent reoperation. The mean interval between implantation and paravalvular leak was 1.26 ± 2 years (median interval, 0.5 years). Eight-year actuarial freedom from leak was 96% ± 1.5% (Table 3).

**Endocarditis**
Two patients had endocarditis, and they were medically treated (linearized rate of 0.16%/patient-year). Actuarial freedom from endocarditis was 99% ± 0.6% at 8 years (Table 3).

**Structural Valve Deterioration (SVD)** occurred in 3 patients (linearized rate of 0.24%/patient-year). The first case of SVD occurred in a 53-year-old man who underwent a prosthetic replacement after 5.5 years, and the second and the third cases of SVD occurred in 58- and 78-year-old men who had received the Biocor valve 8 and 9 years earlier, respectively. In both cases the diagnosis was based on echocardiography, but their general clinical status contraindicated a new valve operation. Overall 8-year actuarial freedom from SVD was 95% ± 3.7%. According to age, 8-year actuarial freedom from SVD was 89% ± 10% in patients younger than 65 years of age and 96% ± 4% in patients older than 65 years ($P = .004$, log-rank test; Figure 3). Overall 10-year actuarial freedom from SVD was 90.3% ± 6.8% (Figure 4), and it was 97.9% ± 2.1% in patients older than 65 years.

**Reoperations**
Eight patients underwent reoperation; the linearized rate was 0.66%/patient-year. Most reoperations (75%) were performed on the first postimplantation year. Eight-year actuarial (Table 3) and actual freedoms from reoperation were 95% ± 1.8% and 96.1% ± 1.4%, respectively. In patients younger than 65 years, the reoperation causes were SVD (1 patient) and paravalvular leak (1 patient). In older patients left ventricular outlet obstruction (1 patient) and paravalvular leak (5 patients) were the causes. Actual 8-year freedom from reoperation was 85.4% ± 9.6% in patients younger than 65 years and 97% ± 1.3% in patients older than 65 years.

**TABLE 2. Cause of death**

<table>
<thead>
<tr>
<th>Cause</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early deaths:</td>
<td></td>
</tr>
<tr>
<td>Cardiac related</td>
<td>7</td>
</tr>
<tr>
<td>Neurologic</td>
<td>2</td>
</tr>
<tr>
<td>Cerebral embolism</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>2</td>
</tr>
<tr>
<td>Sudden</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
</tr>
<tr>
<td>Late deaths:</td>
<td></td>
</tr>
<tr>
<td>Cardiac related (1.7%/patient-year)</td>
<td>21</td>
</tr>
<tr>
<td>Thrombosis (0.08%/patient-year)</td>
<td>1</td>
</tr>
<tr>
<td>Thromboembolism (0.4%/patient-year)</td>
<td>5</td>
</tr>
<tr>
<td>Cerebral hemorrhage (0.3%/patient-year)</td>
<td>4</td>
</tr>
<tr>
<td>Sudden (0.3%/patient-year)</td>
<td>4</td>
</tr>
<tr>
<td>Other noncardiac (3.3%/patient-year)</td>
<td>40</td>
</tr>
</tbody>
</table>

**Valve-Related Complications**
There were 35 valve-related complications in 34 patients, including hemorrhage, thromboembolism, thrombosis, endocarditis, paravalvular leak, SVD, and sudden death. The linearized rate was 2.8%/patient-year. Actuarial freedom from valve-related complication was 78% ± 4.5% at 8 years (Table 3).

**Echocardiography**
Doppler echocardiographic data are summarized in Table 4 according to valve size. Mean and peak transprosthetic gradients for all valves were 16.6 ± 5.3 mm Hg and 30.8 ± 9.3 mm Hg, respectively. By grouping prosthetic size (21-27 mm, 23-27 mm, and 25-27 mm), the mean and peak gradients were significantly related to smaller size. The mean ejection fraction value was 60.1 ± 9.5. Average body surface area was 1.73 ± 0.16 m². Valve size was significantly related to body surface area. The mean values of the M/V ratio and left ventricular end-diastolic volume were 1.37 ± 0.17 g/mL and 63.4 ± 22.6 mL/m², respectively. The majority of patients (83.6%) had an M/V ratio of greater than 1.2 g/mL. In the 5 patients with an indexed effective orifice area of less than 1 cm²/m², the echocardiogram showed an M/V ratio of 1.39 g/mL, and the difference between these few patients and the entire population was not significant ($P = .82$).

**Discussion**
In the time interval of this study, 455 tissue valves (Biocor and Carpentier-Edwards Perimount) were implanted in the isolated aortic position by all the surgeons of our unit. Our indications for the use of bioprostheses were usually identical to those reported by the American Heart Association. Nonetheless, the final choice was up to the surgeon, depending on operative table findings. This study summarizes our experience with the use of the Biocor porcine prosthesis implanted in the aortic position.
Calcification was the major cause of failure of the first-generation porcine bioprosthesis (70%-80%), whereas primary cusp tearing was the major cause of failure of the first-generation pericardial bovine bioprosthesis (80%-90%). Therefore improvements were introduced in both tissue valve models to enhance their long-term performance. The Biocor prosthesis is a new-generation porcine valve, introduced on the market in 1982, composed of 3 different cusps mounted in a Celcon stent, covered by Dacron fabric, and fixed with glutaraldehyde at zero pressure.1 At our institute, the clinical use of the Biocor valve began in 1992, and intermediate14 and long-term15 results comparable with those observed with the Hancock II16 and Carpentier-Edwards17 pericardial prostheses have been observed.

Clinical Results
Compared with the 65% 8-year survival of the sex- and age-matched Italian population (1999 census data), the survival of the aortic patients of this series was significantly lower \( (P = .001) \). Compared with our results with the Hancock II prosthesis (a second-generation porcine valve),18 we observed a lower survival with the Biocor valve, most probably related to the 8-year older average age of the Biocor patients \( (P = <.05) \). Similarly, several other series performed with different tissue valves, either first- and second-generation porcine prostheses or second-generation pericardial prostheses,15-17,19-22 apparently reported better survivals than ours. However, we stress that in these comparisons our results are penalized by the older population age and by the small number of patients at risk at the end of follow-up, which in our series was 21 patients at 8 years and decreased to 4 patients at 10 years.

The confounding effect of older operative age on survival is well illustrated by comparing our results with those obtained with Carpentier-Edwards Perimount prostheses and published by Dellgren and colleagues.21 These authors report excellent survival at 10 years (50% ± 8%; 10 patients at risk at 10 years) by analyzing a population similar to our series in number (254 patients vs 258 patients) and with female prevalence (54% vs 50.3%) but with significantly younger patients (mean age, 71.3 years vs 75 years; \( P < .05 \)).

In our series the majority of patients had mild left ventricular hypertrophy, including the 5 patients with an indexed effective orifice area of between 1 and 0.85 cm²/m². Among these, only 2 patients definitely had a mismatch according to the Pibarot criteria.23 We observed a single late
death among these 5 patients, and the cause of death was a valve thrombosis, which cannot be related to the hypertrophy-arrhythmia complex of mismatch. Aortic root enlargement procedures are suggested in this clinical setting; however, Carrier and associates \(^{24}\) and Sommers and coworkers \(^{25}\) observed that after such procedures, the operative mortality is twice that observed with standard aortic valve replacement. Recently, Freed and colleagues \(^{26}\) re-

Figure 3. Eight-year actuarial freedom from SVD according to age.

Figure 4. Ten-year actual freedom from SVD. Circles depict confidence interval.
ported normalization of left ventricular mass in elderly women who received a small aortic valve (19 mm), suggesting care should be taken with the more complex procedures. In our Biocor series the aortic annulus enlargement procedure, which was done in 8 patients, was without complications; nonetheless, similarly neither the presence of prosthesis-patient mismatch nor the presence of a small prosthesis were risk factors for death. This finding mitigates the utility of aortic root enlargement, especially in small old ladies with a high risk of bleeding, in case of minimal technical errors.

Comparing our hemodynamics with those obtained with the Carpentier-Edwards Pericardial valve, under the same left ventricular function, peak and mean gradients were significantly lower with the pericardial bioprostheses ($P < .05$). These data might explain why two thirds of our patients had a persistent mild left ventricular hypertrophy compared with one third of patients receiving pericardial valves. It is obvious that all stented tissue valves, including Hancock II, Biocor, and Carpentier-Edwards (either pericardial or supra-annular porcine valves) have inferior hemodynamics when compared with those of the stentless bioprostheses. This hemodynamic advantage does not necessarily translate into a survival advantage. Luciani and associates reported superior results in terms of survival and event-free survival in favor of the stentless valve. Nevertheless, we stress that in this study the age of the patients receiving stentless valves was significantly younger. Therefore we continue to favor the use of stented bioprosthesis because we believe that the significantly longer aortic crossclamp and cardiopulmonary bypass times of their stentless group might adversely affect early and late survival of a population as old as their stented one.

Overall freedom from valve-related complications is comparable with that obtained with last-generation porcine and pericardial tissue valves by Mykén and coworkers, the very narrow Biocor valve sewing ring could also be blamed. In conclusion, this clinical experience shows that the Biocor porcine prosthesis guarantees results similar to those previously stated by others, with the same valve. In the literature there is a wide range of rates of this complication, which is related to several patient and surgeon factors.

**Freedom From Reoperation**

Actual freedom from reoperation because of SVD was excellent in patients older than 65 years, a finding comparable with that observed with Hancock II and Carpentier-Edwards pericardial valves, but 7 reoperations were required because of paravalvular leak. The rate of this complication was disturbing. We blame the severely calcified and frail aortic annulus tissue of elderly patients; nonetheless, as previously pointed out by Mykén and coworkers, the very narrow Biocor valve sewing ring could also be blamed.

In conclusion, this clinical experience shows that the Biocor porcine prosthesis guarantees results similar to those obtained with other second-generation prostheses in term of hemodynamics, valve durability, and freedom from reoperation.

We thank Di Marco Francesca, MD, for his assistance in preparing the echocardiogram data collection.

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**TABLE 4. Echocardiographic data**

<table>
<thead>
<tr>
<th>Valve size (mm)</th>
<th>No. of patients</th>
<th>Peak gradient (mm Hg)</th>
<th>Mean gradient (mm Hg)</th>
<th>EF (%)</th>
<th>M/V (g/mL)</th>
<th>LVEDV (mL/m²)</th>
<th>BSA (m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>27</td>
<td>35 ± 9</td>
<td>19.6 ± 6.3</td>
<td>63 ± 8</td>
<td>1.38 ± 0.17</td>
<td>63 ± 17</td>
<td>1.6 ± 0.13</td>
</tr>
<tr>
<td>23</td>
<td>67</td>
<td>30.6 ± 6.8</td>
<td>16.6 ± 4.7</td>
<td>61 ± 9</td>
<td>1.36 ± 0.14</td>
<td>60 ± 18</td>
<td>1.7 ± 0.14</td>
</tr>
<tr>
<td>25</td>
<td>45</td>
<td>31.7 ± 9</td>
<td>16.5 ± 4.3</td>
<td>59 ± 9</td>
<td>1.38 ± 0.18</td>
<td>66 ± 30</td>
<td>1.8 ± 0.15</td>
</tr>
<tr>
<td>27</td>
<td>14</td>
<td>21 ± 9</td>
<td>11 ± 4.5</td>
<td>54 ± 11</td>
<td>1.35 ± 0.26</td>
<td>72 ± 27</td>
<td>1.9 ± 0.13</td>
</tr>
</tbody>
</table>

EF, Ejection fraction; M/V, mass/volume ratio; LVEDV, left ventricular end-diastolic volume; BSA, body surface area.
References


