Mid-Term Comparative Follow-Up After Aortic Valve Replacement with Carpentier-Edwards and Pericarbon Pericardial Prostheses

Thierry Le Tourneau, MD; Christine Savoye, MD; Eugene P. McFadden, FRCPI; Daniel Grandmougin, MD; Hubert-François Carton, MD; Jean-Luc Hennequin, MD; Arnaud Dubar, MD; Georges Fayad, MD; Henri Warembourg, MD

Background—The first generation of pericardial valves had a high rate of premature deterioration. The aim of this study was to compare the outcome after aortic valve replacement with second generation pericardial prostheses (Pericarbon and Carpentier-Edwards).

Methods and Results—Between 1987 and 1994, 162 patients underwent aortic valve replacement with either a Pericarbon (n=81, 69±11 years) or a Carpentier-Edwards (n=81, 70±11 years) pericardial prosthesis. Mean follow-up was 4.4±2.7 years for Pericarbon and 4.8±2.4 years for Carpentier-Edwards valves (P=0.27), giving a total follow-up of 745 patient-years. Thirty-day mortality and 5-year actuarial survival were, respectively, 6.2% and 63.2±5.7% in the Pericarbon group and 6.2% and 63.5±5.6% in the Carpentier-Edwards group. At 8 years, freedom from (and linearized rates per patient-year) thromboembolism, structural failure, and all valve-related events were, respectively, 91.8±3.6% (1.4%), 76.9±8.7% (2.5%), and 58.4±9.3% (5.6%) in the Pericarbon group and 94.4±2.7% (1%), 100% (0%, P<0.01), and 88.8±3.7% (2%, P<0.05) in the Carpentier-Edwards group. There were 9 (11.1%) Pericarbon structural failures related predominantly to severe calcification and stenosis. The actual reoperation rate was 7.4% (1.6% per patient-year) in the Pericarbon group for fibrocalcific degeneration (n=3), periprosthetic leak (n=1), endocarditis (n=1), and aortic dissection (n=1). There was neither structural valve failure nor valve reoperation in the Carpentier-Edwards group. Echocardiographic review of 70 patients from 85 survivors (82.3%) found 4 additional Pericarbon valves with signs of early structural failure but no Carpentier-Edwards valve with such changes.

Conclusions—Eight years after aortic valve replacement, Pericarbon pericardial prostheses compared unfavorably with Carpentier-Edwards pericardial prostheses, with a high incidence of structural valve failure and reoperation. (Circulation. 1999;100[suppl II]:II-11–II-16.)

Key Words: valves ▪ surgery ▪ prosthesis ▪ complications

First generation pericardial valves have been abandoned because of poor clinical results and a high rate of deterioration characterized by leaflet tears and valve incompetence.1–6 Second generation pericardial valves (Carpentier-Edwards, Pericarbon) have now been available for over 10 years but little is known about their mid-term comparative results. The main advantages of pericardial valves are their low thrombogenicity, permitting the avoidance of oral anticoagulation, and their alleged improved hemodynamic performance compared with porcine bioprostheses.7–11 The aim of this retrospective study was to compare mid-term outcome in patients with 2 different types of pericardial valves (Carpentier-Edwards, Pericarbon) implanted in the aortic position between 1987 and 1994 in our institution.

Methods

Patients
We retrospectively reviewed the medical records of all patients who underwent isolated aortic valve replacement with second generation pericardial valves in our institution between July 1987 (first implantation) and December 1994. Patients received either a Carpentier-Edwards (Baxter Healthcare Corp) or a Pericarbon (Sorin Bio-medica) pericardial prostheses. Patients undergoing isolated mitral valve replacement or double valve replacements were excluded from this study, but there were no exclusion for concomitant procedures (such as coronary artery bypass grafting).

Surgery
All operations were performed through a median sternotomy under cardiopulmonary bypass using mild hypothermia; the heart was protected and arrested with antegrade cardioplegia. The main reason for the choice of pericardial prosthesis was its improved hemody-
Pericardial prosthetic valve implanted. Echocardiographic examination was obtained in 32 nonoperated patients of the 38 survivors (84.2%) in the Pericarbon group and 38 patients from 47 survivors (80.8%) in the Carpentier-Edwards group. Doppler data, including the permeability index (subvalvular/transvalvular velocity-time integral ratio) and the mean and maximal transvalvular gradients were recorded. Established structural dysfunction was defined as dysfunction requiring reoperation (symptoms such as heart failure, syncope, angina and/or Doppler-echocardiographic evidence of aortic valve deterioration with mean transvalvular gradient $\geq 40$ mm Hg or severe aortic regurgitation). Early structural dysfunction was defined as Doppler-echocardiographic evidence of aortic valve deterioration with a mean transvalvular gradient $\geq 30$ mm Hg and/or a maximal gradient $\geq 55$ mm Hg or the presence of moderate aortic regurgitation. All patients gave informed consent for Doppler-echocardiographic examination in our institution during the review period.

Statistical Analysis
The recommendations of the Society of Thoracic Surgeons and the American Association for Thoracic Surgery were followed. Results are expressed as mean $\pm$ SD. Comparisons between groups were performed with $\chi^2$ tests or with paired or unpaired Student’s t tests, as appropriate. Calculation of the linearized rates included early and event-free actuarial survival rates were calculated by the Kaplan-Meier method. The log-rank test was used to compare actuarial events. P $\leq$ 0.05 were considered significant.

Results

Patient Population
The patient population consisted of 162 consecutive patients who underwent aortic valve replacement with a pericardial prosthesis. Mean age was 70 $\pm$ 11 years (range 36 to 87 years). There were 90 men (55%) and 72 women (45%). Eighty-one patients received a Carpentier-Edwards prosthesis (Model SA, size 19 to 29). There were no differences in age, sex ratio, and number of patients in atrial fibrillation between the 2 groups (Table 1). There were also no differences in mean NYHA functional class before operation (Pericarbon: 2.42 $\pm$ 0.54 versus Carpentier-Edwards: 2.44 $\pm$ 0.65), after operation (Pericarbon: 1.60 $\pm$ 0.52 versus Carpentier-Edwards: 1.70 $\pm$ 0.56), or at the end of follow-up (Pericarbon: 1.64 $\pm$ 0.56 versus Carpentier-Edwards: 1.70 $\pm$ 0.58). The main reasons for valve replacement were calcified stenosis (139 patients), rheumatic fever (8), aortic regurgitation of another etiology (7), prosthetic valve dysfunction (6), and other reasons (2).

Associated procedures included 1 mitral valvuloplasty, 21 aortocoronary bypass procedures (8 in the Pericarbon group and 13 in the Carpentier-Edwards group), 4 ascending aortic operations (2 in each group), and 2 carotid endarterectomies. Respective aortic cross-clamp time and total cardiopulmonary bypass time were 92 $\pm$ 16 minutes and 110 $\pm$ 19 minutes in the Pericarbon group compared with 94 $\pm$ 21 minute ($P=0.60$) and 113 $\pm$ 28 minutes ($P=0.80$) in the Carpentier-Edwards group. The mean size of implanted valves did not differ between the 2 groups (Pericarbon: 22.8 $\pm$ 2.2 versus Carpentier-Edwards: 22.6 $\pm$ 1.9, $P=0.49$), and the distribution of the size of the implanted valves did not differ between the 2 groups.

Mortality
Five patients in each group died within 30 days of the operation, giving a mortality rate of 6.2%. The cause of early death was cardiac failure in 6 patients, infectious complications in 2 patients, and sudden death in 1 patient after discharge. The cause of death remained unknown in 1 patient.

There were 30 late deaths in the Pericarbon group and 28 in the Carpentier-Edwards group. In the Pericarbon and the Carpentier-Edwards groups, respectively, the cause of late death was cardiac-related in 5 (16.7%, 1.4% per patient-year) and 7 (25%, 1.8% per patient-year) patients, valve-related in 8 (26.7%, 2.2% per patient-year) and 4 (14.3%, 1% per patient-year) patients, and noncardiac in 17 (56.6%, 4.7% per patient-year) and 17 (60.7%, 4.3% per patient-year) patients. The overall death rate was 43.2% (35 patients) in the Pericarbon group and 40.7% (33 patients) in the Carpentier-Edwards group at the time of follow-up. The actuarial survival rate including early mortality was 63.2 $\pm$ 5.7% (Pericarbon) and 63.5 $\pm$ 5.6% (Carpentier-Edwards) after 5 years and 42.5 $\pm$ 6.8% (Pericarbon) and 51.1 $\pm$ 7.7% (Carpentier-Edwards, $P=0.46$) after 8 years (Figure 1).

Valve-Related Complications
Valve-related complications are summarized in Table 2. Eight (26.7%, 2.2% per patient-year) of the 30 late deaths in

### TABLE 1. Clinical Characteristics of Both Groups

<table>
<thead>
<tr>
<th></th>
<th>Pericarbon (n=81)</th>
<th>Carpentier-Edwards (n=81)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>71 $\pm$ 9 (36-86)</td>
<td>70 $\pm$ 10 (41-87)</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>45 (55%)/36 (45%)</td>
<td>45 (55%)/36 (45%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>5 (6%)</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>Mean NYHA class</td>
<td>2.4 $\pm$ 0.5</td>
<td>2.4 $\pm$ 0.6</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcified stenosis</td>
<td>70</td>
<td>69</td>
</tr>
<tr>
<td>Rheumatic fever</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Prosthetic valve dysfunction</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Data presented are mean $\pm$ SD (range) or number of patients.
the Pericarbon group were valve-related: 1 patient had fatal endocarditis, 2 had thromboembolic complication, 1 died suddenly, 1 died after aortic valve and aortic replacement for aortic dissection, and 3 died as a result of structural valve failure. Four (14.3%, 1% per patient-year) of the 28 late deaths in the Carpentier-Edwards group were valve-related: 2 had thromboembolic complications and 2 died suddenly. The actuarial rate of freedom from valve-related death was 90.5%±3.8% in the Pericarbon group and 93.4%±3.3% in the Carpentier-Edwards group after 5 years and 80.8%±7.4% in the Pericarbon group and 93.4%±3.3% (P=0.16) in the Carpentier-Edwards group after 8 years.

There were no significant differences between groups in the rates of valve-related death, thromboembolism, endocarditis, bleeding, and nonstructural dysfunction (significant perivalvular leak in 1 Pericarbon). However, clinical and echocardiographic follow-up demonstrated 9 Pericarbon valves with structural dysfunction after 8 years, for a linearized rate of 2.5% per patient-year, but no valve with structural dysfunction in the Carpentier-Edwards group. The actuarial rate of freedom from structural dysfunction was 76.9%±8.7% in the Pericarbon group and 100% (P<0.01) in the Carpentier-Edwards group after 8 years.

Six patients required valve reoperation in the Pericarbon group, giving an actuarial rate of freedom from reoperation of 77.1%±9.7% (linearized rate of reoperation: 1.7% per patient-year), and of 100% (0% per patient-year, P<0.05) in the Carpentier-Edwards group. Indications for valve reoperation in the Pericarbon group were fibrocalcific degeneration with severe stenosis (n=3), periprosthetic leak (n=1), endocarditis with severe regurgitation (n=1), and aortic dissection (n=1). Among the 9 patients with known structural valve dysfunction, 3 died without reoperation (1 was considered inoperable, and 2 died suddenly just before reoperation), 3 were reoperated on during the follow-up, and 3 were reoperated on after the end of follow-up (Table 3). Mean delay between valve implantation and the diagnosis of structural dysfunction was 5.6±2.6 years (range 2.6 to 9.9 years). The valves removed in patients with echocardiographic evidence of fibrocalcific degeneration with severe stenosis demonstrated calcification of the commissural and basal regions of the leaflets. Cusp tears were observed in 1 valve removed but were associated with severe calcification and stenosis. Of the 3 valves removed after the end of follow-up, 2 had severe calcification and stenosis but one had an important leaflet tear along the basal region that resulted in prolapse of 2 cusps without significant calcification.

Finally, the actuarial rate of freedom from reoperation or structural valve failure was 68.9%±8.7% in the Pericarbon group and 100% (P<0.01) in the Carpentier-Edwards group after 8 years.

**Echocardiographic Follow-Up**

Echocardiographic examination demonstrated 4 additional valves with signs of early structural dysfunction in the Pericarbon group but none in the Carpentier-Edwards group.

**TABLE 2. Valve-Related Complications During the Follow-Up Period**

<table>
<thead>
<tr>
<th></th>
<th>Pericarbon (n=81)</th>
<th>Carpentier-Edwards (n=81)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%Pt-year</td>
</tr>
<tr>
<td>Valve-related death</td>
<td>8</td>
<td>2.2</td>
</tr>
<tr>
<td>Embolism</td>
<td>5</td>
<td>1.4</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>3</td>
<td>0.8</td>
</tr>
<tr>
<td>Bleeding</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>Nonstructural dysfunction</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>Structural dysfunction</td>
<td>9</td>
<td>2.5</td>
</tr>
<tr>
<td>Valve reoperation</td>
<td>6</td>
<td>1.7</td>
</tr>
<tr>
<td>All valve-related events</td>
<td>20</td>
<td>5.6</td>
</tr>
</tbody>
</table>

%Pt-year indicates percentage per patient-year. *P<0.05 vs Pericarbon, †P<0.01 vs Pericarbon.
After exclusion of patients with established structural valve dysfunction and valves with signs of early structural dysfunction, echocardiographic analysis during the review period revealed a better hemodynamic profile of Carpentier-Edwards pericardial prostheses, with respect to the mean and maximal transvalvular gradient and the permeability index (Table 4).

**Discussion**

The aim of this retrospective study was to compare the outcome after aortic valve replacement with 2 types of second generation pericardial prostheses implanted from 1987 to 1994 in our institution. The results showed that Pericarbon pericardial prostheses compared unfavorably with Carpentier-Edwards pericardial prostheses after a mean follow-up period of 4.6 years. Despite a similar rate of survival in the 2 patient groups, Pericarbon valves demonstrated a high incidence of structural valve failure (11.1%), and valve reoperation (7.4%) compared with Carpentier-Edwards pericardial prostheses (0%).

Bioprosthetic valves consists of biological material resulting in a low incidence of thromboembolic complications, permitting the avoidance of anticoagulation. Compared with porcine bioprostheses, pericardial valves have an alleged improved hemodynamic profile, and it was hoped that short- and long-term results might be better. However, the first generation of pericardial valve has been abandoned because of early valve failure due to design failure,1,2 or tissue preparation failure.3 The Pericarbon valve consists of 2 glutaraldehyde-fixed (0.5%) bovine pericardial sheets mounted on a low profile flexible plastic stent (Delrin) covered by polyester fabric which is coated with a thin film of carbon (Carbofilm). One sheet forms the 3 leaflets and is sutured to the second sheet, which lines the inner surface of the stent. This particular design was developed in order to achieve better distribution of mechanical stress and to avoid mechanical injury by direct leaflet-to-fabric contact.13,14 However, to our knowledge, Pericarbon valves have no specific postfixation anticalcification treatment.

The Carpentier-Edwards pericardial valve consists of 3 glutaraldehyde-preserved bovine pericardial leaflets mounted inside the support frame with no stitches to the posts, in order to reduce the leaflet abrasion that limited the durability of previous pericardial valves. Another conceptual improvement was represented by complete strut flexibility achieved with an Elgiloy wire maintaining physiological aortic ring movements and decreasing shear stress. Pericardium for this valve is fixed with 0.625% buffered glutaraldehyde solution under very low pressure (free-floating method).15–19 After fixation, Carpentier-Edwards pericardial valves are treated with a sterilant solution (FET 80) consisting of formalin, ethanol, and tween 80 (polysorbate-80) to retard calcification.

*Figure 3.* Mean transvalvular gradient distribution in 70 of the 85 survivors (82.3%) at the end of follow-up, including 4 bioprostheses with signs of early structural dysfunction.

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**TABLE 3. Patient Characteristics and Doppler-Echocardiographic Findings for Pericarbon Valves With Structural Dysfunction**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age</th>
<th>Sex</th>
<th>Valve Size</th>
<th>Time From Implantation, mo/y</th>
<th>Doppler-Echocardiographic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>85</td>
<td>F</td>
<td>23</td>
<td>31/2.6</td>
<td>Stenosis + moderate regurgitation*</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>M</td>
<td>23</td>
<td>33/2.7</td>
<td>Stenosis†</td>
</tr>
<tr>
<td>3</td>
<td>78</td>
<td>F</td>
<td>19</td>
<td>44/3.6</td>
<td>Stenosis + endocarditis with secondary moderate regurgitation*</td>
</tr>
<tr>
<td>4</td>
<td>79</td>
<td>F</td>
<td>23</td>
<td>56/4.6</td>
<td>Stenosis + moderate regurgitation†</td>
</tr>
<tr>
<td>5</td>
<td>41</td>
<td>F</td>
<td>23</td>
<td>64/5.3</td>
<td>Stenosis†</td>
</tr>
<tr>
<td>6</td>
<td>71</td>
<td>F</td>
<td>23</td>
<td>68/5.5</td>
<td>Stenosis*</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>M</td>
<td>23</td>
<td>89/7.3</td>
<td>Stenosis + leaflet tear with severe regurgitation†</td>
</tr>
<tr>
<td>8</td>
<td>76</td>
<td>F</td>
<td>21</td>
<td>106/8.7</td>
<td>Stenosis‡</td>
</tr>
<tr>
<td>9</td>
<td>65</td>
<td>M</td>
<td>23</td>
<td>119/9.9</td>
<td>Leaflet tear with severe regurgitation‡</td>
</tr>
</tbody>
</table>

* Died without reoperation, † reoperated, ‡ reoperation after the end of follow-up.

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*Data represent results after exclusion of valves with structural dysfunction requiring reoperation and valves with signs of early structural dysfunction.*

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*P* < 0.05 vs Pericarbon, † *P* < 0.01 vs Pericarbon, ‡ *P* < 0.001 vs Pericarbon.
Analyses of the causes of primary tissue failure showed that early acute valvar lesions were the main cause of failure in the first generation pericardial valves,1–6,20 whereas the main cause of primary tissue failure was degenerative changes with fibrosis, shrinking, and calcification of the leaflets in porcine biological valves.10,21,22 In addition to acute leaflet tears, calcifications are known to occur in pericardial bioprostheses as well as in porcine valvular bioprostheses, leading to progressive degeneration.3,20–25 The main failure of Pericarbon valves was described as severe calcification of the commissural areas and basal regions of the leaflets, causing cusp stiffening and stenosis.14,24 Indeed, all but 1 valve with structural dysfunction in our study had severe calcification with significant stenosis. Valve failure due to leaflet tears has been occasionally observed,14 as was the case in 2 patients in this study. In one case, the leaflet tear was associated with calcification and stenosis; the second case was a late structural failure 9 years after implantation where the valve removed had a large tear without significant calcification.

The fact that no structural failures were seen in the Carpentier-Edwards group may be due in part to the relatively short length of follow-up (4.8±2.4 years, 0 to 8 years). However, in a recent study Aupart et al18 reported only 4 structural valve failures requiring reoperation in a series of 589 (0.7%) aortic valves replacements with Carpentier-Edwards prostheses, giving a linearized rate of structural valve deterioration of 0.2% per patient-year (mean follow-up: 4.1 years). In another study,19 the linearized rate of Carpentier-Edwards structural valve failure was only 0.9% per patient-year after a mean follow-up of 9.1 years. This very low incidence of structural valve failure is in marked contrast with the relatively high incidence of Pericarbon structural valve failure in our study (11.1%), where a linearized rate of 2.5% per patient-year was observed. This rate of Pericarbon structural valve failure is comparable with the findings of a previous study published in 199414 that described 7 (5.9%) aortic valve failures requiring reoperation on a mean period of 4.6 years in 119 patients. In another study,27 4 patients with aortic Pericarbon prostheses in a series of 92 patients (4.3%) experienced a structural valve failure after an actuarial follow-up of only 4 years. Thus the results of our study, in conjunction with previously published data, suggest that Pericarbon valves in the aortic position have a low rate of structural valve failure 5- to 10-fold that of Carpentier-Edwards pericardial prostheses for a follow-up of 4 to 5 years. The main difference between the 2 pericardial prostheses seems related to earlier and more marked development of calcification in Pericarbon prostheses; this may be due to the lack of anticalcification treatment compared with Carpentier-Edwards prostheses, leading to earlier degeneration. However, the rate of leaflet tears is reduced compared with the first generation of pericardial prostheses.

Systematic echocardiographic screening during the review period, performed on a large number (82.3%) of survivors by the same experienced investigator (C.S.), allowed us to compare the hemodynamic profiles of the 2 valves, after exclusion of valves with obvious changes of structural dysfunction. Carpentier-Edwards valves had a slightly but significantly better hemodynamic profile than Pericarbon valves with respect to mean and maximal transvalvular gradient as well as permeability index. Distribution of mean transvalvular gradient (including those valves with signs of early structural failure) confirmed the better hemodynamic profile of Carpentier-Edwards at the end of follow-up (Figure 3). Because systematic echocardiographic examination within 3 months of implantation was not performed in our institution, we cannot determine if this result was due to a difference in the initial postoperative hemodynamic profile or to a deterioration in the hemodynamic profile of the Pericarbon valves since the operation.

The lack of randomization between the 2 types of pericardial valves is the main limitation of this study. The study population was composed of 162 consecutive patients who underwent aortic valve replacement with a pericardial prosthesis by the same experienced cardiac surgeons. Only 2 types of aortic pericardial prostheses were used in our institution from 1987 to 1997: the Pericarbon valve and the Carpentier-Edwards valve. Moreover, by chance, the number of patients and the sex ratio were similar in the 2 groups, as were the baseline patients characteristics, valve size, associated procedures, cardiopulmonary bypass time, and mean follow-up period.

In conclusion, this study demonstrated that Pericarbon pericardial prostheses compared unfavorably with Carpentier-Edwards pericardial prostheses in the aortic position after a mean follow-up period of 4.6 years, despite a similar rate of survival in both groups. We believe that a randomized control trial may no longer be considered ethical, as there is cumulative evidence that Pericarbon prostheses exhibit a high rate of structural dysfunction compared with Carpentier-Edwards prostheses.

References


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