Carpentier-Edwards Pericardial Valve in the Aortic Position: 25-Years Experience

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Background. The Carpentier-Edwards pericardial valve was designed to minimize structural valve deterioration. Excellent durability and low incidence of valve-related complications have been reported. The objective of the present study was to analyze clinical results after 25 years of experience with this valve implanted in the aortic position. The effect of patient age at the time of surgery was also evaluated.

Methods. This is a retrospective cohort study of 2,405 patients from November 1981 to March 2011. Primary outcomes of interest were survival and freedom from major adverse effects such as thromboembolic, endocarditis, and reoperation.

Results. Sixty percent were male, with a mean age of 71 ± 9 years old. Actuarial survival rates including early deaths averaged 78% ± 2%, 55% ± 2%, and 16% ± 2% after 5, 10, and 20 years of follow-up, respectively. The freedom rate of valve reoperation for prosthesis dysfunction and all other causes averaged 98% ± 0.2%, 96% ± 1%, and 67% ± 4% at 5, 10, and 20 years. Patients younger than 60 years of age had a 15-year survival averaging 54% ± 5% compared with patients aged between 60 and 70 years of age averaging 46% ± 3% and with patients older than 70 years of age averaging 28% ± 3% (p = 0.001). Survival at 5, 10, and 20 years for patients who had concomitant CABG (coronary artery bypass grafting) were 78% ± 1%, 55% ± 2%, and 9% ± 3% compared with no concomitant CABG (84% ± 1%, 62% ± 2%, and 22% ± 3% (p < 0.001)).

Conclusions. Carpentier-Edwards pericardial valve implantation in the aortic position is secure and durable. The effects of age influence reoperation rate and survival as well as a concomitant coronary artery bypass procedure.

approved by the Ethical Committee at the Montreal Heart Institute.

Valves were implanted according to standard surgical techniques. Biologic valves usually implanted in patients older than 65 years of age, but patient preference was the primary determinant of valve selection.

Primary outcomes of interest were recorded as defined in Guidelines recently published (Guidelines for reporting morbidity and mortality after cardiac valvular operations) [9]. Causes of death were obtained from hospital records or autopsy when available. Early mortality and complications were defined as those occurring during the hospital stay or within 30 days of valve implantation.

Statistical Analysis
Continuous data are presented as the mean ± SD. Categoric data are presented as percentages. Survival, freedom from reoperation, thromboembolic events, and combined endpoint curves were obtained with the Kaplan-Meier method (NCSS 2007, Kaysville, UT). Differences between groups of patients were analyzed using the log-rank tests.

Preoperative Parameters
Aortic valve replacements were performed in 2,405 patients during the study period. Sixty percent (1,450 of 2,405) were male and 40% (955 of 2,405) were female, with a mean age of 71 ± 9 years (ranging from 18 to 90 years). Preoperative left ventricular ejection fraction averaged 0.56 ± 0.13. Most patients (853 of 2,405 and 1,316 of 2,405) were in the New York Heart Association (NYHA) functional class 2 and 3 at the time of surgery. The majority of patients (2,278 of 2,405, 95%) did not have a previous cardiac surgery.

Eighty-five percent of patients (2,044 of 2,405) underwent aortic valve replacement for aortic stenosis with a preoperative aortic peak transvalvular gradient averaging 49 ± 23 mm Hg. Twelve percent of patients (294 of 2,405) were operated for aortic regurgitation, 2% (37 of 2,405) for prosthetic valve dysfunction, and 1% (30 of 2,405) for acute bacterial endocarditis.

During the AVR procedure, 42% (1,005 of 2,405) of patients had concomitant coronary artery bypass grafts (CABG) and 6% (134 of 2,405) had enlargement of the aortic annulus. Aortic cross-clamp time and cardiopulmonary bypass time averaged 80 ± 28 and 109 ± 39 minutes, respectively (Table 1). Fifteen percent of patients had a valve size 19 implanted, 38% a size 21, 31% a size 23, 13% a size 25, 2% a size 27, and 1% a size 29.

Results
Survival and Functional Status
One hundred seventeen (117 of 2,405, 4.9%) patients died during the first 30 days after surgery. Cardiac failure and noncardiac problems were the main causes of early death. Postoperative complications included bleeding and tamponade and atrioventricular block as the 2 most frequent events (Table 2). Percentage of late death was 28% and total death including early deaths at 30 years was 33%. Causes of death were principally unknown (40%) followed by cardiac insufficiency (21%) and myocardial infarction (10%). Major complications included combined endpoints (hemorrhage, cardiac insufficiency, myocardial infarction, endocarditis, and thromboembolic events) 9%, prosthesis dysfunction 4%, explant 4%, thromboembolic events 3%, and endocarditis 2% (Table 3).

Actuarial survival rates including early deaths averaged 78% ± 2%, 55% ± 2%, 34% ± 2%, and 16% ± 2% after 5, 10, 15, and 20 years of follow-up, respectively (Fig 1). Seventy-five percent (1,808 of 2,405) of patients were in NYHA functional class 1 or 2 at the last follow-up averaging 6 ± 9 years after surgery (Table 3).

Valve-Related Complications and Reoperation
Thromboembolic events represented 3% (80 of 2,405) of late complications and included 33 cases of fatal thromboembolic events (1%). Seventy-five percent of patients were not anticoagulated at the time of the event. The 5, 10, and 20-year freedom rate from thromboembolism averaged 97% ± 0.4%, 94% ± 1%, and 79% ± 6%, respectively. The freedom rate from prosthetic valve endocarditis

### Table 1. Preoperative Parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Carpentier-Edwards (n = 2,405)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>71 ± 9</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>1,450 (60%)</td>
</tr>
<tr>
<td>Pre-op LVEF (%)</td>
<td>56 ± 13</td>
</tr>
<tr>
<td>Pre-op peak gradient (mm Hg)</td>
<td>49 ± 23</td>
</tr>
<tr>
<td>Surgical indication</td>
<td></td>
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<tr>
<td>Stenosis</td>
<td>2,044 (85%)</td>
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<tr>
<td>Regurgitation</td>
<td>294 (12%)</td>
</tr>
<tr>
<td>Prosthesis dysfunction</td>
<td>37 (2%)</td>
</tr>
<tr>
<td>Active endocarditis</td>
<td>30 (1%)</td>
</tr>
<tr>
<td>CPB (minutes)</td>
<td>109 ± 39</td>
</tr>
<tr>
<td>Cross-clamp (minutes)</td>
<td>80 ± 28</td>
</tr>
<tr>
<td>NYHA functional classes</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>101 (4%)</td>
</tr>
<tr>
<td>II</td>
<td>853 (35%)</td>
</tr>
<tr>
<td>III</td>
<td>1,316 (55%)</td>
</tr>
<tr>
<td>IV</td>
<td>113 (5%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>22 (1%)</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>127 (5%)</td>
</tr>
<tr>
<td>CABG</td>
<td>77 (61%)</td>
</tr>
<tr>
<td>AVR</td>
<td>37 (29%)</td>
</tr>
<tr>
<td>MVR</td>
<td>9 (7%)</td>
</tr>
<tr>
<td>TVR</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Multiple valve repairs</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (4%)</td>
</tr>
<tr>
<td>None</td>
<td>2,278 (95%)</td>
</tr>
<tr>
<td>Concomitant procedures</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>1,005 (42%)</td>
</tr>
<tr>
<td>Aortoplasty enlargement</td>
<td>134 (6%)</td>
</tr>
</tbody>
</table>

AVR = aortic valve replacement; CABG = coronary artery bypass surgery; CPB = cardiopulmonary bypass; LVEF = left ventricular ejection fraction; MVR = mitral valve replacement; NYHA = New York Heart Association; TVR = tricuspid valve replacement.
Aged 98% ± 0.3%, 98% ± 0.5%, and 95% ± 2% at 5, 10, and 20 years after surgery (Fig 2).

Ninety-one (91 of 2,405, 4%) patients showed evidence of prosthetic valve dysfunction necessitating explantation and replacement of the valve in 89 patients. Two patients refused redo surgery. Calcified stenotic prostheses and infection were the 2 most common causes of prosthetic dysfunction (Table 4). Reoperations for explantation and replacement of the prosthesis were performed 6 ± 4 years after the initial surgery in all patients, including those with a preoperative diagnosis of endocarditis. Patients with a diagnosis of structural valve deterioration without evidence of endocarditis (63 of 89) underwent reoperation 11 ± 5 years after the initial valve replacement. The overall freedom rate of valve reoperation for prosthetic valve dysfunction averaged 98% ± 0.2%, 96% ± 1%, and 67% ± 4% at 5, 10, and 20 years after initial surgery (Fig 3).

**Effect of Age on Survival and Reoperation**

Patients younger than 60 years of age at implantation had a 15-year survival averaging 54% ± 5% compared with patients between 60 and 70 years of age averaging 46% ± 3% and with patients older than 70 years of age averaging 28% ± 3% (p = 0.001) (Fig 4).

The freedom rate from reoperation for prosthetic valve dysfunction averaged 98% ± 1%, 90% ± 3%, 60% ± 6%, and 30% ± 8% at 5, 10, 15, and 20 years after surgery in patients younger than 60 years of age compared with 99% ± 0.3%, 95% ± 1%, 90% ± 3% at 5, 10, and 15 years after surgery in patients aged between 60 and 70 years old, and 100%, 99% ± 0.5% at 5 and 10 years after surgery in patients older than 70 years of age (p = 0.001) (Fig 5).

Reoperation from all causes including endocarditis was performed on average at 12 ± 4 years after the initial valve implantation for patients less than 60 years of age, at 10 ± 5 years for the 60 to 70 year old group, and at 6.8 ± 0.7 years for patients older than 70 years.

There were 54 prostheses explanted (54 of 89, 61%) in patients younger than 60 years of age, 28 (28 of 89, 32%) prostheses explanted in patients aged between 60 to 70 years old, and 7 (7 of 89, 8%) explants in patients older than 70 years of age (Table 4). After surgery for prosthesis explant and replacement, 39 out of the 89 (44%) patients died. Average time to postoperative mortality in that population was 2.8 ± 3.6 years.

**Effect of Concomitant CABG Procedure**

A total of 1,005 patients had concomitant CABG with the AVR procedure. Survival at 5, 10, 15, and 20 years for patients who had concomitant CABG were 78% ± 1%, 55% ± 2%, 27% ± 3%, and 9% ± 3%, respectively, compared with 84% ± 1%, 62% ± 2%, 44% ± 2%, and 22% ± 3% in patients undergoing isolated AVR (p < 0.001) (Fig 6).
Echocardiographic Follow-Up

Seven hundred eighty-five patients had an echocardiographic follow-up at 6 ± 9 years after surgery. Transaortic mean gradient averaged 17 ± 8 mm Hg and maximal gradient averaged 24 ± 16 mm Hg for the total population.

Comment

The present study showed that the freedom rate from reoperation for structural valve deterioration (SVD) averaged 99% in patients older than 70 years of age at implantation throughout the 30-year period of the study. Rates of reoperation increased significantly in the
younger groups of patients. Moreover, prosthetic valve endocarditis remains the first cause of valve reoperation in elderly patients and the second cause after SVD in younger patients. Studies examining the experience with the CE pericardial valves in the aortic position had shown beneficial effects on durability and hemodynamic results compared with other bioprostheses [4–8]. This improvement in durability is due to decreased stress-induced structural deterioration through infrastent tissue mounting, better tissue orientation combined with improved tissue preservation techniques, and to flexible and distensible struts [10]. Early and late mortality and complications after bioprosthetic aortic valve replacement were similar to other studies when compared with the present analysis [4, 6, 8]. Long-term survival after surgery remains highly dependent on age groups at the time of implantation. Patients younger than 60 years have better 15-year survival than the other age groups, but the patients 70 and older have a higher rate of freedom from reoperation for SVD. However, even if patients 60 years and less experienced more reoperations, the low mortality risk of reoperation versus the increase risk of hemorrhage secondary to the anticoagulation, makes the option to use the bioprosthetic valve a good one for the younger patients [11, 12]. Moreover, patients may benefit later from percutaneous valve inserted in the old bioprosthetic valve, an approach that is not possible through a mechanical valve [13, 14]. Reoperation in the elderly patients was performed at a mean of 7 years after the initial implantation, at 10 years for the 60 to 70 years of age and at 12 years for patients less than 60 years. Age and valve position are the 2 most determinants of longevity of the bioprosthesis, with increasing durability in the elderly in the aortic position [4]. In our study the rate of reoperation among patients greater than 70 years was low, possibly secondary to reduced life expectancy, a blunted immune response, and reduced hemodynamic stress on the bioprosthesis [15]. Patients younger than 60 years were at highest risk for prosthesis explantation due to structural valve

Table 4. Causes for Surgical Explantation of the Prosthesis by Age Group

<table>
<thead>
<tr>
<th>Causes</th>
<th>Under 60 years (n = 54)</th>
<th>60–70 years (n = 28)</th>
<th>Over 70 years (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic dehiscence</td>
<td>1 (2%)</td>
<td>1 (4%)</td>
<td>0</td>
</tr>
<tr>
<td>Infection</td>
<td>13 (24%)</td>
<td>9 (32%)</td>
<td>4 (57%)</td>
</tr>
<tr>
<td>Stenosis and calcification</td>
<td>28 (52%)</td>
<td>12 (43%)</td>
<td>2 (29%)</td>
</tr>
<tr>
<td>Leafllet tear</td>
<td>10 (19%)</td>
<td>6 (21%)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>1 (2%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>1 (2%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Fig 3. Freedom rate from reoperation for explantation of the prosthesis at 25 years for all related causes, including prosthesis valve dysfunction and endocarditis; mean ± standard error. (— = aortic valve replacement, Carpentier-Edwards [AVR CE]).
deterioration characterized by valve restenosis and calcification of the prosthesis followed by infection and tearing of a leaflet. Indeed, tissue degeneration after 15 years of biologic valve longevity certainly changes the strength of the leaflets. Influence of gender could also be a cause of SVD because women have a higher prevalence of dihydrotinate treatment use which could promote early valve Ca$^{++}$. Comparison of structural valve deterioration with other
tissue valves is difficult because there are not enough comparative studies and many factors could differ in different studies about the long-term experience of these valves. The low incidence of leaflet tear with the CE is the result of design improvement. David and colleagues [16] demonstrated that the Hancock II valve has an overall 8 years freedom from SVD of 93%. The Biocor porcine bioprosthesis (St. Jude Medical, St. Paul, MN) had a 10-year freedom from SVD of 78% [17]. Jamieson and colleagues [7] reported in 1995 their 17-year experience with the CE standard porcine valve and freedom from SVD was inferior to the pericardial valve at 15 years with 58% freedom with the porcine versus 80% with the pericardial.

Aside from SVD and reoperation for any other causes, thromboembolism remains a concern with an overall rate of 3% in this study with 1% being fatal thromboembolism, which is comparable to what is published in the literature (0.8%) [7]. The effect of concomitant CABG procedures affected the overall survival, probably related to the long-term progression of the coronary artery disease. Patients with concomitant CABG had a lower long-term survival, as expected.

Study Limitations
This is a retrospective study with a long period of observation extending to 30 years. Underestimation of complications could be possible as recall bias during the telephone interviews. Surgical techniques and patient selection may have changed during the study period. Nevertheless, we use biologic valves in a greater number of patients and in younger patients at the present time. Thus, results of the present study give an accurate perspective to the result that patients could expect in our current clinical practice. Because of a long follow-up period and different standards of practice according to the anticoagulation regimen, that data for the entire cohort could not be included in this paper due to too many missing data. We included only data for patients who had thromboembolism.

Conclusions
Carpentier-Edwards pericardial valve implantation in the aortic position is secure and durable. Patient age at the time of surgery influences the rate of reoperation and survival after implantation of the prosthesis. Patients younger than 60 years old have a better survival at long-term follow-up but concerns still remain regarding the constant rate of reoperation for structural valve deterioration in that population. Patients under age 60 would benefit by having a closer follow-up approaching 10 years post implantation of the prosthesis.

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