Long-term evaluation of Carpentier-Edwards porcine bioprosthesis for rheumatic heart disease

Hsi-Yu Yu, MDa
Yi-Lwun Ho, MDb
Shu-Hsun Chu, MDc
Yih-Sharng Chen, MDa
Shoei-Shen Wang, MDa
Fang-Yue Lin, MDa

Objectives: The clinical results of Carpentier-Edwards standard bioprosthesis have been extensively studied for valvular heart surgery in America and Europe. However, the data of long-term performance of Carpentier-Edwards standard porcine valve in areas with a high prevalence of rheumatic heart disease are still lacking. In this study, we assessed the clinical performance of Carpentier-Edwards standard porcine bioprostheses in a patient group with high prevalence of rheumatic heart disease.

Methods: A total of 872 patients underwent valvular heart surgery with Carpentier-Edwards standard porcine bioprostheses replacement between 1975 and 1999 and the results were analyzed. Rheumatic etiology counts for 95% of the patients. Mean age of operation was 40 ± 14 years (mitral valve), 43 ± 19 years (aortic valve), and 45 ± 13 years (double valve). Follow-up was 95.6% complete and continued up to 24 years (total 7017 patient-years) with mean of 8.9 ± 5.1 years.

Results: The operative mortality rate was 5.85%. Actuarial patient survival rates after discharge at 5, 10, 15, and 20 years were 92.5%, 83.8%, 72.3%, and 35.8%, respectively. A total of 442 cases received reoperation due to failure of bioprostheses. The mean duration to valve failure is 12.2 ± 0.4 years. Actuarial estimate of freedom from structural valvular failure at 5, 10, 15, and 20 years were 96.3%, 63.7%, 24.4%, and 7.7%, respectively.

Conclusion: The long-term result of Carpentier-Edwards standard bioprostheses in the present patient group is satisfactory. However, freedom from valve failure is lower than that of Western series. Younger age at operation and higher prevalence of rheumatic etiology in this area are possible causes.

The clinical experience reported in recent Western series has provided valuable information with regard to the structural durability and valve-related complications of biological valve substitutes.1-4 Younger age at operation is a significant risk factor for structural valve deterioration and reoperation.4 The freedom from structural valvular dysfunction of Carpentier-Edwards (CES) porcine bioprosthesis has been reported to range from 70.8% to 87.0% at 10 years.1-3 However, the data of long-term performance of CES porcine valve in an area where rheumatic heart disease prevails is still lacking. Rheumatic heart disease has been endemic disease in Asian developing countries for the past 30 years.5,6 Therefore rheumatic valvular dysfunction was the major disease category for operation with CES valve in this area. We hypothesized that the clinical performance of CES bioprosthesis in Southeast Asia might be different from that of Western countries due to different etiology of operation. We conducted the present study to assess and follow up those
patients undergoing valvular replacement with CES porcine valves. This study was designed to (1) evaluate the effect of age on patient survival, (2) assess the freedom from valve failure, and (3) evaluate the effect of valve site on patient survival and structural valvular failure.

Materials and Methods

Patients
CES porcine bioprostheses were implanted in 872 patients (1060 bioprostheses) from 1975 to 1999 in a single hospital (Figure 1). Supra-annular–type bioprostheses were not available until 2000 in our country; all the bioprostheses in this study were standard type (model 2625(A) and 6625(M)). Over 90% of those operations were performed between 1977 and 1984. Operations were performed mainly by 6 doctors. Ninety-five percent were rheumatic heart disease in nature. Rheumatic heart disease was diagnosed from clinical history and serological and echocardiographic studies, as well as pathological findings. The operation was performed through median sternotomy with standard cardiopulmonary bypass and cardioplegic cardiac arrest. The cardioplegic solution was self-formulated solution before early 1980, commercialized solution (St Thomas Hospital solution) from early 1980 to 1990, and cold blood cardioplegia after 1990. CES porcine bioprosthesis was irrigated thoroughly before implantation to remove preservative solution. Suturing was performed with interrupted 2-0 Ticron in eversion technique with Teflon pledgets or multiple single stitches without pledgets, according to operators’ preference. During follow-up in outpatient clinics, anticoagulant therapy with warfarin (prothrombin time was controlled at 1.5 to 2 times of control value) was prescribed for a 3-month course except for patients with atrial fibrillation with large atrium or patients with history of emboli, who needed longer anticoagulant therapy.7

Follow-up
Follow-up was conducted retrospectively by chart review (in 78%), patient investigation (14.8%), and telephone/mail follow-up (6.6%). Operative mortality included any cardiac death that occurred within 30 days after the operation or before hospital discharge. Late mortality included any cardiac death that occurred during the follow-up period. Valve-related events were categorized in accordance with the guideline for reporting morbidity and mortality devised by the American Association of Thoracic Surgery and the Society of Thoracic Surgeons ad hoc committee.8 Structural valve failure was diagnosed and documented by clinical

<table>
<thead>
<tr>
<th>TABLE 1. Cause of early and late mortality</th>
<th>Mortality numbers (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early</strong></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>25 (2.87)</td>
</tr>
<tr>
<td>Intractable arrhythmia</td>
<td>6 (0.69)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>4 (0.46)</td>
</tr>
<tr>
<td>Stroke</td>
<td>3 (0.34)</td>
</tr>
<tr>
<td>Infection</td>
<td>2 (0.23)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>4 (0.46)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>7 (0.80)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>51 (5.85)</td>
</tr>
<tr>
<td><strong>Late</strong></td>
<td></td>
</tr>
<tr>
<td>Acute myocardial infarct</td>
<td>6 (0.69)</td>
</tr>
<tr>
<td>Stroke</td>
<td>16 (1.83)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>73 (8.37)</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>3 (0.34)</td>
</tr>
<tr>
<td>Sudden death</td>
<td>3 (0.34)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>7 (0.80)</td>
</tr>
<tr>
<td>Noncardiac cause</td>
<td>33 (3.78)</td>
</tr>
<tr>
<td>Unknown</td>
<td>13 (1.49)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>154 (17.66)</td>
</tr>
</tbody>
</table>

Actuarial survival rate was presented as survival ± S.E.

Figure 2A. Actuarial survival after CES bioprosthesis implantation.
presentation and reoperative findings before mid 1980 or by the above criteria as well as echocardiographic study after mid 1980, when we generalized 2-dimensional Doppler echocardiogram into clinical use at our hospital.

Statistics
Data were expressed as mean ± standard deviation. Simple morbid events were reported as a simple percentage. Time-related events were reported as linearized rate (number of events divided by the total patient-years) or plotted as Kaplan-Meier survival curve, actuarial life table, or actual rate. Statistical comparison between groups was computed by Student t test, chi-square test, or log-rank test according to specific data type. P < .05 was considered significant.

Results
Patients
There were 406 men (46.6%) and 466 women (53.4%). There were 161 (18.5%) aortic valve replacements (AVR), 523 (60.0%) mitral valve replacements (MVR), and 188 (21.6%) both aortic and mitral valve replacements (DVR). The ages ranged from 9 to 81 years; mean age at operation was 40 ± 14 (MVR), 43 ± 19 years (AVR), and 45 ± 13 years (DVR).

Actuarial survival rate was presented as survival ± S.E.

P = .23 between MVR and AVR group by log rank test

P = .03 between MVR and DVR group by log rank test

P < .01 between AVR and DVR group by log rank test

Figure 2B. Effects of valve site on survival after CES bioprosthesis implantation.
(DVR). The total follow-up was 95.6% complete during the 6-month closing interval before our study period. The total cumulative follow-up was 7017 patient-years, with mean of 8.94 ± 5.08 years.

Patient Survival
The overall operative mortality was 5.85% (51 of 872 patients). As divided by decades, the operative mortality rate were 6.36%, 6.28%, and 0.00% in the periods before 1980, between 1980 and 1990, and after 1990, respectively. The overall late mortality was 154 of 785 cases (2.19% per patient-year). The causes of early and late mortality are listed in Table 1. The actuarial survival rate of all discharged cases at 5, 10, 15, and 20 years were 92.5%, 83.8%, 72.3%, and 35.8%, respectively (Figure 2, A). The survival rate of patients receiving DVR was initially similar to that of single valve replacement but became worse than that of patients receiving either MVR or AVR at about 8 years after operation (P = .03 and P < .01; respectively, Figure 2, B). Patients younger than 40 years had better survival curve than those older than 40 years (Figure 2, C). Both sexes had similar survival curves (P = .21).

Structural Valve Failure
During the follow-up period, 442 cases (56.3%) received reoperation due to bioprostheses failure. The linearized rate was 6.30 per patient-year. The predominant pathology at reoperation of explanted valve was calcification on the leaflets, making the leaflets thickened and fused. Another major finding was linear tear of the leaflet, which was

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>Survival</th>
<th>Survival</th>
<th>Survival</th>
<th>Survival</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40 y/o</td>
<td>(362)</td>
<td>98.6±0.6%</td>
<td>94.7±1.1%</td>
<td>90.2±1.7%</td>
<td>82.7±2.9%</td>
</tr>
<tr>
<td>≥ 40 y/o</td>
<td>(423)</td>
<td>96.2±0.9%</td>
<td>90.1±1.4%</td>
<td>78.7±2.4%</td>
<td>63.5±3.9%</td>
</tr>
</tbody>
</table>

Actuarial survival rate was presented as survival ± S.E.

P<0.001 by log rank test

Figure 2C. Survival after CES bioprosthesis implantation according to age younger or older than 40 years.
usually associated with valve incompetence. Occasionally, perforation holes in the leaflets were found, in patients for whom history of prosthetic valve endocarditis (PVE) sometimes could be traced. The mean duration to valve failure is 12.2 ± 0.4 years. Actuarial freedom rates from valve failure at 5, 10, 15, and 20 years were 96.3%, 63.7%, 24.4%, and 7.7%; respectively (Figure 3, A). Actual rate of freedom from reoperation was also plotted (Figure 4). These 2 methods began to show differences only after 10 years because of the relatively small number of mortality of valve failure cases. Male and female patients had similar freedom from valve failure rates ($P = .80$). The patients were subgrouped as (1) ≥60 years, (2) between 40 and 60 years, (3) between 20 and 40 years, and (4) ≤20 years. The median valve survival duration was 13.08, 12.30, 11.96, and 10.86 years in groups 1, 2, 3, and 4, respectively (Figure 3, B). Only groups 1 and 4 were statistically significant ($P = .03$). Valvular sites (mitral, aortic, and both) also affected the mean survival duration of CES porcine bioprostheses (Figure 3, C). Mean survival duration of DVR (11.07 years) was worse than either AVR (12.26 years; $P = .003$) or MVR (11.96 years; $P = .03$). Whether warfarin was used did not influence freedom from valve failure rate ($P = .29$). Freedom from reoperation rate among valves replaced before 1980 was not different from those replaced after 1980 ($P = .11$; Figure 3, D).

**Discussion**

**Patient Survival**

The present study documented better survival and worse freedom from valve failure rate in our patient group than several published big series.$^{1-4}$ Age difference is the most possible cause. Long-term actuarial survival estimates at 5, 10, and 15 years have been reported by Fann and colleagues$^{4}$ to be 77 ± 1%, 54 ± 2%, and 32 ± 3%, respectively, for the AVR with porcine bioprosthesis (Hancock valve) and respective rates for MVR were 70 ± 1%, 50 ± 2%, and 32 ± 3%. Similar data have also been reported by Fiane and colleagues,$^{11}$ whose actuarial survival rates at 5 and 10 years were 73.2 ± 5.2% and 52.1 ± 6.6% for AVR with CES bioprosthesis and 76.7 ± 4.2% and 61.6 ± 4.8% for MVR. In the present study, long-term actuarial survival estimates at 5, 10, and 15 years were 94.4%, 88.5%, and 82.7%, respectively, for AVR and the respective rates for MVR are 91.6%, 88.5%, and 82.7%. The mean age of patients in the present study is younger than those of other studies [40 ± 14 years (MVR) and 43 ± 19 years (AVR), Table 2]. In the data reported by Fann and coworkers,$^{4}$ the

![](image-url)
mean age at operation was 58 ± 13 years (MVR) and 60 ± 15 years (AVR). The age discrepancy between this report and that of other major series can be attributed to the etiology of valvular heart disease. In our hospital, most of the patients (95%) underwent valvular replacement at that time due to rheumatic origin,12 while rheumatic disease only accounts for 47% in Western series.1 This cohort of younger rheumatic patients is also documented by other series, such as John and colleagues and Duran and coworkers,13,14 both of which were also based on patients of rheumatic etiology. The main reasons for the high prevalence rate of rheumatic fever and rheumatic heart disease in these Asian areas are subtropic climate, crowded population, and poor economic status at that time, as well as prevalence of streptococcal infections.15

By analyzing respective perioperative mortality rates in 3 separate decades (before 1980: 6.36%, 1980 to 1990: 6.28%, and after 1990: 0.00%), no differences of operative outcome could be found between self-formulated or commercialized cardioplegic solution (separated by early 1980),

<table>
<thead>
<tr>
<th>Group</th>
<th>1 year</th>
<th>5 years</th>
<th>10 years</th>
<th>15 years</th>
<th>20 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. at risk</td>
<td>Survival</td>
<td>No. at risk</td>
<td>Survival</td>
<td>No. at risk</td>
</tr>
<tr>
<td>(1)≥60 y/o</td>
<td>(91)</td>
<td>96.7%</td>
<td>(46)</td>
<td>94.7%</td>
<td>(17)</td>
</tr>
<tr>
<td>(2)40-60 y/o</td>
<td>(333)</td>
<td>99.7%</td>
<td>(289)</td>
<td>98.3%</td>
<td>(167)</td>
</tr>
<tr>
<td>(3)20-40 y/o</td>
<td>(311)</td>
<td>99.4%</td>
<td>(265)</td>
<td>96.8%</td>
<td>(174)</td>
</tr>
<tr>
<td>(4)&lt;20 y/o</td>
<td>(50)</td>
<td>100.0%</td>
<td>(39)</td>
<td>96.6%</td>
<td>(20)</td>
</tr>
</tbody>
</table>

group (1) and (2), p= 0.46; group (1) and (3), p= 0.12; group (1) and (4), p= 0.03;
group (2) and (3), p= 0.18; group (2) and (4), p= 0.08; group (3) and (4), p= 0.21;
group (1)+(2)+(3) and group (4), p= 0.21

Figure 3B. Actuarial survival curve of freedom from valve failure, grouped by age.
while marked improvement could be found after 1990, due to advance in operative technique, cardiopulmonary bypass, and myocardial protection, as well as intensive care unit and ward nursing techniques.

Structural Valve Dysfunction

On the other hand, age was discovered to be a significant risk factor for primary tissue failure of bioprostheses by many authors. In the present report, our data were compatible with those series, either by actuarial or actual rate. The mean age of operation was younger in this study, which could explain why the freedom from structural valvular dysfunction is lower than those of the Western series (Table 2).

To compare structural valve failure rate in specific age groups, we picked out a subgroup of 40 to 50 years old with either MVR (n = 121) or AVR (n = 22) to study. In MVR cases, the freedom from structural valve failure at 5, 10, 15, and 20 years are 99.1 ± 0.9%, 63.1 ± 5.1%, 16.6 ± 4.3%, and 13.3 ± 4.0%, respectively, which are quite similar to that reported by Fann and colleagues (97%, 65%, 21% at 5, 10, 15 years, respectively) and by Jamieson and colleagues (12% and 0% at 15 and 20 years, respectively) for the same age MVR subgroup. In AVR cases, the freedom from structural valve failure at 5, 10, 15, and 20 years are 100 ± 0.0%, 80 ± 10%, 44 ± 13%, and 7.5 ± 7%, respectively, which are also similar to that reported by Fann and colleagues (100%, 70%, 47% at 5, 10, 15 years, respectively) and by Jamieson and coworkers (42% and 26%, at 15 and 20 years, respectively) for the same age subgroup with AVR. This finding suggests age to be an important determining factor of structural valve failure in both the West and the East.

The high prevalence of rheumatic heart disease may partially explain the progression of structural valve dysfunction, which was supported indirectly by the pathology of explanted valves (calcification, linear tear, and perforation). Valvular sites (mitral, aortic, or both) also affected the mean

---

Figure 3C. Actuarial survival curve of freedom from valve failure, grouped by valve implantation sites in mitral or aortic sites.
The survival duration of CES porcine bioprostheses in this study. Mean rates durability of AVR (12.26 years), MVR (11.96 years), and DVR (11.07 years) were better than those reported by Bernal and colleagues (92.9 months for AVR, 101.6 months for MVR, 84.3 months for DVR).

Later year of operation had higher rate of structural valve dysfunction in our data (Figure 3, D), which is compatible with that reported by Fann and colleagues. One possible explanation is the early detection of structural valve dysfunction with improved technology. The 2-dimensional Doppler echocardiography was generalized in our hospital since mid 1980, so many of the patients in the first time period (1975 to 1980) could not be followed by this method. Besides this, it also implies that structural valve failure rate is not inversely related to economic status. (Gross national income in Taiwan at 1976 to 1979 and 1980 to 1985 were 850 and 1846 New Taiwan Dollar, respectively.)

### Limitations

Much of our data was collected before 1996, when Edmunds and colleagues published the guideline for reporting the long-term results of valvular surgery; some of our parameters might not be wholly the same with suggested formats.

Another limitation is that because 95% of our cases were rheumatic in nature, no sufficient nonrheumatic cases can be compared to elucidate whether disease nature is one factor influencing structural valve dysfunction rate.

Another limitation is homogeneity of valves used in our hospital (CES), so no comparison can be made with other major types of first- or second-generation bioprostheses with respect to the durability of different valves in rheumatic patients.

The other limitation is the young age group in our early operation population (Figure 1). This means most patients older than 60 years were censored at less than 5 years, so we...
cannot obtain reliable CES reoperation rate in that age group. This is one possible explanation why structural valvular failure rate of AVR in the present study is higher than that by other reports.

Conclusions
The long-term results of CES bioprostheses in this patient group are satisfactory. However, freedom from valve failure is lower than that of Western series. These differences are due to younger age at operation and higher prevalence of rheumatic etiology in this area.

References


