EARLY AND LATE SURVIVAL FOLLOWING REPLACEMENT OF PROSTHETIC HEART VALVES

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From May 1975 to December 1988, 62 patients underwent 66 replacements of prosthetic heart valves, due to structural valve failure in 37, prosthetic valve endocarditis (PVE) in 17, periprosthetic leak in 5, thrombosed valve in 3, hemolysis in 2, and prophylactic removal in 2. Before reoperation, 3 patients were in NYHA Class I, 24 in Class II, 21 in Class III, and 18 in Class IV. Replacements of valve prostheses were at the mitral position in 33 patients, at the aortic position in 16, at the aortic and mitral position in 9, at the mitral and tricuspid position in 5, at the tricuspid position in 2, and at the pulmonary position in 1. There were 6 early deaths (9.1%), and 13 late deaths (7.2 ± 0.4%/patient-year). Clinical improvement of the current survivors was good. The follow-up duration was 4 months to 11.4 years (mean 3.5 years), and the cumulative follow-up was 180 patient-years (100% complete). Patients undergoing replacement of 2 prostheses showed a higher early mortality rate (35.7%) than those who received replacement of 1 prosthesis (1.9%) (p<0.01). The actuarial survival including early deaths was compared using the generalized Wilcoxon test. Survival was better in patients with replacement of one prosthesis than in those with replacement of 2 prostheses (p<0.001), and was better in NYHA Class I to III patients than in Class IV patients (p<0.05). Replacement of 1 prosthesis for patients with primary tissue failure of bioprostheses showed no operative mortality and a good 5 year survival rate (96 ± 4 %). High risk factors for replacement of prosthetic valves included double valve replacement, NYHA Class IV and PVE.

PROSTHETIC heart valve replacement is a method that compensates for a severely impaired and non-reconstructable native heart valve. Although useful for symptomatic and hemodynamic improvement of the patient, valve replacement cannot be considered a definitive treatment since the "ideal" prosthetic valve does not exist! The risk of replacement of heart valve prostheses must always be accounted for when assessing the long-term prognosis of patients who receive artificial heart valve devices. Theoretically, all patients with bioprostheses of limited durability should be reserved for replacement of prostheses. As the number of patients who have prosthetic valve replacements increases and the follow-up period is prolonged, the number of patients who need replacement of prostheses also increases. The operative and late results of replacement of valve prostheses are the important factors for the long-term prognosis of patients with heart valve prostheses. The aim of this study was to assess the influence of preoperative hemodynamics (NYHA Class),

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Single valve replacement
Double valve replacement

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Japanese Circulation Journal Vol.55, February 1991 89
procedures of redo-operation (replacement of 1 or 2 valve prostheses) and causes of further surgery (structural valve failure; prosthetic valve endocarditis and others) on early and late survival.

PATIENTS AND METHODS

Between May 1975 and December 1988, 62 patients underwent 66 replacements for implanted prosthetic valves. There were 32 men and 30 women, aged 6 to 71 years (mean 47.5 years). Mechanical prostheses were removed in 13 patients (19.7%), bioprostheses in 52 (78.9%), and both valves in 1 (1.4%). At redo-operation, mechanical prostheses were implanted in 33 patients (50.0%), bioprostheses in 31 (47.0%), and both valves in 2 (3.0%). Patients with valved conduit and left ventricular rupture who needed replacement of the mitral prosthesis were excluded from this study. Sixty-two patients had initial replacement of the prosthetic valve in the same anatomical position; one of them underwent first and second redo-operation in the mitral and aortic position separately during a four-year period. Three patients underwent second replacement of the prosthetic valve. One patient had a third replacement of the prosthetic valve. There was no operative mortality at the second or third replacement of the prostheses. Replacement of valve prostheses were at the mitral position in 33 patients, the aortic position in 16, the aortic and mitral position in 9, the mitral and tricuspid position in 5, the tricuspid position in 2, and the pulmonary position in 1. In the 14 patients who received double valve replacement at redo-operation, 8 cases are included in which initial prosthetic valve implantations for diseased native valves were performed as associated operation in addition to replacement of prosthetic valves.

The causes for replacement of valve prostheses were structural valve failure in 37 patients, prosthetic valve endocarditis (PVE) in 17, periprosthetic leakage in 5, thrombosed valve in 3, hemolysis in 2, and prophylactic removal of bioprostheses in 2, one of whom had left atrial thrombus and the other had heart failure due to increased regurgitation of the native tricuspid valve. Three patients were in the New York Heart Association (NYHA) Functional Class I, 24 in Class II, 21 in Class III, and 18 in Class IV before redo-operation (Table I).

Early mortality was defined as death occurring within 30 days of operation. All deaths occurring after 30 days were included in late mortality. Follow-up information was obtained from re-examination at our hospital or from follow-up letters sent to the patients or the referring physicians and was completed over a six-month closing interval ending in June 1989. Follow-up data were obtained in all patients after hospital discharge. The follow-up duration was from 4 months to 11.4 years (mean 3.5 years). A cumulative total of 180 patient-years (pt-yrs) was available for analysis. To clarify the prognosis of the replacement of prosthetic valve, actuarial survival was calculated including early deaths. Actuarial survival was calculated by the Kaplan-Meier method using STAX* program (a software system custom-designed for life table). A patient dying from hepatoma because of a non-cardiac death was calculated as a discontinuation of follow-up. The actuarial rates were expressed as the per cent of event-free patients (mean ±1 standard error). The generalized Wilcoxon test and chi-square test were used for the statistical analysis of the data. A p value less than 0.05 was considered significant.

RESULTS

Early mortality: There were 6 early deaths (9.1%); 5 in patients with a removed bioprosthetic valve (9.6%) and 1 in whom mechanical valves were removed (7.1%), a difference of which was not significant (Table II). Replacement of 1 prosthesis showed a mortality of 1.9% (1/52) in contrast to 35.7% (5/14) in patients with replacement of 2 prostheses (p<0.01). A patient with replacement of 1 prosthesis in the aortic position underwent a second redo-operation. She had liver cirrhosis and died from multiple organ failure. Five patients who had undergone replacement of 2 prostheses died from low cardiac output syndrome or multiple organ failure.

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TABLE I  RELATIONSHIP BETWEEN NYHA FUNCTIONAL CLASS BEFORE REDO-OPERATION AND SURGICAL PROCEDURE OF REPLACEMENT (RPL) OF PROSTHETIC HEART VALVES

<table>
<thead>
<tr>
<th>NYHA Class before redo-operation</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>One prosthesis RPL</td>
<td>3 (1*)</td>
<td>21 (3)</td>
<td>16 (2)</td>
<td>12 (5)</td>
<td>52 (10)</td>
</tr>
<tr>
<td>Two prostheses RPL</td>
<td>0</td>
<td>3 (2)</td>
<td>5 (2)</td>
<td>6 (4)</td>
<td>14 (8)</td>
</tr>
<tr>
<td>Total</td>
<td>3 (1*)</td>
<td>24 (5)</td>
<td>21 (4)</td>
<td>18 (9)</td>
<td>66 (18)</td>
</tr>
</tbody>
</table>

( ) : death, \*: hepatoma.

TABLE II  CAUSES OF EARLY AND LATE DEATHS

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Age</th>
<th>Sex</th>
<th>Causes of reoperation</th>
<th>NYHA</th>
<th>Procedures of reoperation</th>
<th>Causes of early/late death</th>
</tr>
</thead>
<tbody>
<tr>
<td>TM</td>
<td>56</td>
<td>F</td>
<td>PTF</td>
<td>II</td>
<td>reMVR (SJM), TVR (SJM)</td>
<td>LOS, DOT*</td>
</tr>
<tr>
<td>TH</td>
<td>63</td>
<td>M</td>
<td>PTF</td>
<td>IV</td>
<td>reMVR (CEP), TVR (CEP)</td>
<td>LOS*</td>
</tr>
<tr>
<td>WS</td>
<td>58</td>
<td>F</td>
<td>PTF</td>
<td>III</td>
<td>reAVR (SJM), reMVR (SJM)</td>
<td>LOS, MOF*</td>
</tr>
<tr>
<td>SH</td>
<td>55</td>
<td>M</td>
<td>PTF (A, M)</td>
<td>IV</td>
<td>reAVR (SJM), reMVR (SJM), TAP</td>
<td>LOS, MOF*</td>
</tr>
<tr>
<td>MT</td>
<td>32</td>
<td>M</td>
<td>PTF</td>
<td>IV</td>
<td>reAVR (H), OMC</td>
<td>PVE</td>
</tr>
<tr>
<td>IT</td>
<td>50</td>
<td>F</td>
<td>PTF</td>
<td>IV</td>
<td>reMVR (SJM), TVR (SJM)</td>
<td>CHF</td>
</tr>
<tr>
<td>ZA</td>
<td>21</td>
<td>F</td>
<td>PTF</td>
<td>II</td>
<td>reMVR (SJM), AVR (SJM)</td>
<td>Sudden death</td>
</tr>
<tr>
<td>AH</td>
<td>41</td>
<td>M</td>
<td>PVE, active</td>
<td>IV</td>
<td>rereMVR (CEP)</td>
<td>Sudden death</td>
</tr>
<tr>
<td>KT</td>
<td>71</td>
<td>F</td>
<td>PVE, active</td>
<td>IV</td>
<td>reAVR (CEP)</td>
<td>PVE</td>
</tr>
<tr>
<td>OF</td>
<td>39</td>
<td>F</td>
<td>PVE, active</td>
<td>IV</td>
<td>reMVR (SJM), TAP</td>
<td>PVE</td>
</tr>
<tr>
<td>SK</td>
<td>30</td>
<td>M</td>
<td>PVE, active</td>
<td>III</td>
<td>reAVR (BS), MVR (H)</td>
<td>PVE</td>
</tr>
<tr>
<td>KJ</td>
<td>59</td>
<td>M</td>
<td>PVE, active</td>
<td>I</td>
<td>reAVR (CEP), Manougui*</td>
<td>Hepatoma</td>
</tr>
<tr>
<td>YT</td>
<td>66</td>
<td>M</td>
<td>PVE, healed</td>
<td>III</td>
<td>reAVR (SJM)</td>
<td>LOS, MOF*</td>
</tr>
<tr>
<td>YT</td>
<td>62</td>
<td>F</td>
<td>PVE, healed</td>
<td>IV</td>
<td>reMVR (SJM), TAP</td>
<td>Redo-operation</td>
</tr>
<tr>
<td>KM</td>
<td>42</td>
<td>M</td>
<td>PVE, healed</td>
<td>II</td>
<td>reMVR (BS)</td>
<td>CHF</td>
</tr>
<tr>
<td>SK</td>
<td>48</td>
<td>M</td>
<td>TV (M, T)</td>
<td>IV</td>
<td>reMVR (CEP), reTVR (CEP)</td>
<td>LOS*</td>
</tr>
<tr>
<td>MM</td>
<td>22</td>
<td>F</td>
<td>PL</td>
<td>II</td>
<td>reMVR (CEP), TAP</td>
<td>Redo-operation</td>
</tr>
<tr>
<td>KT</td>
<td>21</td>
<td>M</td>
<td>PL</td>
<td>II</td>
<td>reAVR (H)</td>
<td>PTF, PL</td>
</tr>
<tr>
<td>WK</td>
<td>56</td>
<td>M</td>
<td>Hemolysis</td>
<td>III</td>
<td>reAVR (CEP)</td>
<td>MOF</td>
</tr>
</tbody>
</table>


Late survival: There were 13 late deaths (late mortality 7.2±0.4%/pt-yr); 4 PVE, 2 congestive heart failure, 2 redo-operation except replacement of prostheses, 2 sudden deaths, 1 heart failure due to primary tissue failure\* of Hancock valve (certified by autopsy), one multiple organ failure, and one hepatoma (Table II). There were 5 deaths (5.9±0.7%/pt-yr) in patients with mechanical valves and 7 deaths (7.4±0.8%/pt-yr) in patients with bioprosthesis valves (p=NS). All current survivors but one (43/44) were in NYHA Class I or II. One patient has been put under chronic hemodialysis due to renal failure, after reoperation. There were 10 deaths (19.2%) in 52 patients who underwent replacement of 1 prosthesis and 8 deaths (57.1%) in 14 patients who underwent replacement of 2 prostheses. The overall survival rate was better in patients

who underwent replacement of one prosthesis than in those to whom replacement of 2 prostheses was performed \( (p<0.001) \) (Fig. 1). Survival at 5 years was \( 77\pm9\% \) in the group with replacement of 1 prosthesis and \( 18\pm16\% \) in the group with replacement of 2 prostheses. On the other hand, there were 9 deaths \( (18.8\%) \) in 48 patients who were in NYHA Class I to III before redo-operation and also 9 deaths \( (50.0\%) \) in 18 patients who were in Class IV. The overall survival rate was better in patients who were
in Class I to III than in those in Class IV (p<0.05) (Fig. 2). Survival rate at 5 years was 84±6% in Classes I to III and 19±16% in Class IV.

In the subgroup of patients undergoing replacement of 1 prosthesis, there were 5 deaths (12.5%) in 40 patients who were in NYHA Class I to III before redo-operation and 5 deaths (41.7%) in 12 patients who were in Class IV. The survival rate was bet-

Comparative actuarial survival of the patients who received replacement of one prosthesis or two prostheses because of primary tissue failure of bioprostheses.

Comparative actuarial survival of the patients who were in NYHA Class I to III Class IV before redo-operation in the subgroup of primary tissue failure of bioprostheses.

Survival in patients who were in Classes I to III than in those in Class IV (p<0.05) (Fig. 3). Survival at 5 years in this subgroup was 92±4% in Classes I to III and 32±24% in Class IV. On the other hand, in the subgroup of patients undergoing replacement of 2 prostheses the difference in survival was not significant between those 2 groups. There were 4 deaths (50.0%) in 8 patients in Classes I to III and also 4 deaths (66.7%) in 6 patients in Class IV. The survival rate at 5 years in patients who underwent replace-
Replacement of Prosthetic Valve

Actuarial survival was investigated from the causes of replacement of prostheses.

Structural valve failure: There were no deaths in the 2 patients with structural failure of the mechanical valve. They were in NYHA Class II and underwent replacement of 1 prosthesis each. On the other hand, there were 7 deaths (20.0%) in 35 patients with primary tissue failure of bioprostheses. Survival of the group with structural valve failure was 63 ± 17% at 5 years (Fig. 4).

In the primary tissue failure patients, there was 1 death (4.0%) in 25 patients who underwent replacement of 1 prosthesis and 6 deaths (60.0%) in 10 patients who underwent replacement of 2 prostheses. The overall survival in this subgroup was better in patients who underwent replacement of 1 prosthesis than in those who underwent replacement of 2 prostheses (p < 0.01) (Fig. 5). The survival rate at 5 years was 96 ± 4% in the group with 1 prosthetic replacement and 0% in the group undergoing replacement of 2 prostheses. On the other hand, there were 3 deaths (12.0%) in 25 patients who were in NYHA Classes I to III before redo-operation and 4 deaths (40.0%) in 10 patients who were in Class IV. The survival rate at 5 years was 84 ± 9% in Classes I to III and 38 ± 27% in Class IV. The overall survival rate in this subgroup was not significantly different between the 2 groups (Fig. 6).

Endocarditis: In 17 patients of PVE there were 7 deaths (41.2%), 3 of which were a recurrence of PVE. There were 4 deaths (50.0%) in 8 patients who had active PVE and 3 deaths (33.3%) in 9 patients who had healed PVE. The survival rate of the PVE group was 37 ± 21% at 5 years (Fig. 4). There were 6 deaths (40.0%) in 15 patients who underwent replacement of 1 prosthesis and 1 death (50.0%) in 2 patients who underwent replacement of 2 prostheses. There were 3 deaths (25.0%) in 12 patients in NYHA Classes I to III before redo-operation and 4 deaths (80.0%) in 5 patients in Class IV.

Other causes: In 12 patients with periprosthetic leak, thrombosed valve, hemolysis and prophylactic removal as the cause of valve prostheses replacement, there were 4 deaths (33.3%). The survival rate of this group was 74 ± 13% at 5 years. There were 3 deaths (30.0%) in 10 patients who underwent replacement of 1 prosthesis. There were 3 deaths (27.2%) in 11 patients in NYHA Classes I to III before redo-operation. A patient with thrombosis of the mitral and tricuspid prosthetic valves died in hospital. He was in shock before reoperation.

**DISCUSSION**

Replacement of prosthetic valves was associated with a higher operative mortality than at initial implantation as has been indicated in several reports. But, recent technical improvements and increased experiences have contributed to a decrease in risk almost to that of initial implantation. Various incremental risk factors of redo-operation have been indicated, including advanced Functional Class before redo-operation, prolonged aortic cross-clamp time, PVE, urgency of reoperation and advanced age. These risk factors are similar to those of initial prosthetic valve implantation. However, few studies have examined the late result of replacement of prosthetic valves.

The prognosis of patients undergoing replacement of 2 prostheses was worse than for those undergoing replacement of 1 prosthesis as seen in a study of an entire group of patients and a subgroup with primary tissue failure of bioprostheses. This may be caused by a larger operative invasion, namely prolonged aortic cross-clamp time, and a more decreased preoperative cardiac function which necessitates replacement of 2 prostheses. Before redo-operation, 43% of those undergoing replacement of 2 prostheses and 25% of those undergoing replacement of 1 prosthesis were in NYHA Class IV. Overall survival was also lower in Class IV patients than in Classes I through III in the entire patient group as well as the subgroup with a single prosthetic replacement. The prosthetic valve dysfunction rapidly lowers NYHA functional grades to Class IV and may show decreased cardiac reserve. We have had many patients progressing to Class IV or remaining in Class III or under before redo-operation, even though a similar grade of prosthetic valve disruption is present. There was no significant difference in survival be-
between NYHA Class I to III and Class IV in the subgroup of patients with primary tissue failure. However, it is predictable that this difference will become more obvious with the increase in the number of cases and the prolonged follow-up period. A report from the Mayo Clinic shows that before reoperation, patients in NYHA Class I or II show a better survival rate after reoperation than do those who are in Class III or IV\(^7\). We did not notice a difference between these 2 groups. Late mortality of initial native valve replacement showed that the survival rate after double prothetic valve implantation was worse than that after single prothetic valve implantation, and the presence of severe preoperative symptoms (Class IV) increased the risk of premature late deaths\(^12\). The risk factors for premature late deaths of patients undergoing replacement of the prothetic valve are not related to the type of prosthesis used, but was more affected by the surgical procedures performed as well as the patient’s cardiac function before redo-operation. The patients who needed a double prothetic valve implantation at redo-operation were at greater risk. These high-risk patients should be operated on at an early stage of prothetic valve dysfunction and cardiac failure before urgent surgery is necessitated. If 1 prothetic valve becomes dysfunctional while another valve is still intact in a Class IV patient implanted with 2 bioprostheses, replacement of the dysfunctional valve should be performed while the normally functioning prostheses should be allowed to remain intact.

In spite of the improvement in life expectancy afforded by prothetic heart valve replacement, the operation is, in general, palliative rather than curative. There has been an increase in the number of prothetic valve redo-operations in recent years because of the larger population at risk and the prolonged survival of patients undergoing valve replacement. Particularly, primary tissue failure is the most frequent cause of further surgery in patients with bioprostheses, because it accelerates beyond the fifth year of implantation\(^3,13—16\). It was noted in 53% of patients who underwent reoperation in this study. Reoperation for primary tissue failure of bioprostheses is a major concern. Generally, failure of bioprostheses occurs progressively and allows early recognition and elective reoperation in contrast with a dysfunctioning mechanical prostheses. Recently, scheduled reoperation has been performed without homologous blood transfusion under the conditions of an autologous preoperative blood donor program\(^17\). This is one of the advantages of reoperation for bioprostheses. However, reoperation of the bioprostheses is sometimes performed on an emergency basis\(^18\). In this study, 26.8% (10/35) of primary tissue failure patients were Class IV, and some needed urgent redo-operations. Replacement of 1 prosthesis for patients with primary tissue failure caused no early deaths and produced a good 5-year survival rate of 96±4%. This is important when selecting bioprostheses with limited durability. Based on previous results, bioprostheses may be selected for operation in younger adults, since this then allows them to be on a regimen of minimal or no medication after prothetic valve implantation.

Prothetic valve endocarditis as the cause of replacement of valve prostheses showed a more incremental decrease in survival compared with structural valve failure or other causes (Fig. 4). Particularly, 37.5% of active PVE cases (3/8) died with recurrence of PVE after redo-operation, and impaired preoperative hemodynamics in Class IV showed poor prognosis for replacement surgery of prothetic valves.

Late survival of this study were compared to that of initial prothetic valve implantation. Generally speaking, the 5-year and 10-year survival rates of patients who received isolated aortic or mitral valve replacement were about 80% and 60%, respectively. On the other hand, the 5-year and 10-year survival rates of primary aortic and mitral valve replacement patients were about 70% and 50%\(^19—23\). In our Hancock bioprosthesis series, the overall survival rate at 5 years, including early deaths, was 85% in patients undergoing isolated aortic or mitral valve replacement and 76% in those undergoing multiple valve replacement\(^24\). The overall survival rate of patients who underwent replacement of valve prostheses in this study and those who underwent initial implantation of the prothetic valve showed a similar survival curve in single valve replacement cases. However, this curve was less favor-

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able in the group of patients with replacement of 2 prostheses than in the those undergoing initial implantation for double valve replacement. Among current survivors, excellent clinical improvement was obtained after replacement of valve prostheses similar to initial valve implantation. Multiple valve replacement with bioprostheses should be restricted at initial implantation of the prosthetic valve since patients who receive double or triple bioprostheses will be at greater risk for replacement of 2 prostheses at redo-operation than those who have had a single valve replacement with bioprosthesis. Furthermore, the mechanical valve may be better suited to patients who need multiple valve replacement and who have no contraindication for anticoagulation therapy.

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