Long-Term Results of Aortic Valve Replacement With Mechanical Prosthesis or Carpentier-Edwards Perimount Bioprosthesis in Japanese Patients According to Age

Takahiro Nishida, MD; Hiromichi Sonoda, MD; Yasuhisa Oishi, MD; Hideki Tatewaki, MD; Yoshihisa Tanoue, MD; Yuichi Shiokawa, MD; Ryuji Tominaga, MD

Background: The long-term results of aortic valve replacement (AVR; n=737) with bileaflet mechanical prosthesis (MP) or Carpentier-Edwards Perimount bioprostheses (BP) were evaluated in different age groups.

Methods and Results: Since 1981, a total of 737 prostheses (424 bileaflet MP vs. 313 BP) were implanted for AVR in 278 patients aged ≥70 years (79 MP vs. 199 BP), in 191 patients aged 60–69 years (128 MP vs. 63 BP) and in 268 patients aged <60 years (217 MP vs. 51 BP). Follow-up was completed for 6,523 patient-years in 98.5% of cases. Among the patients ≥70 years, both the actuarial survival rate (P=0.0434) and freedom from valve-related morbidity (P=0.0205) were better in the BP group than in the MP group without any difference in occurrence of structural valve deterioration in both groups. Among the patients aged 60–69, anticoagulant-related complications occurred less often in the BP group (P=0.0134) without any difference in long-term survival. Among the patients aged <60, long-term survival was significantly better in the MP group, whereas freedom from anticoagulant-related events did not differ.

Conclusions: The use of BP is suitable in patients aged ≥70 years, while the use of bileaflet MP is preferable in patients aged <60 years. Among patients aged 60–69 years, the use of BP is acceptable because of the lower incidence of anticoagulant-related events and the equivalent long-term survival. (Circ J 2014; 78: 2688–2695)

Key Words: Heart valve; Outcome; Prosthesis
Long-Term Results of AVR

USA, n = 313). In the bileaflet MP group, CarboMedics valve (CarboMedics; Austin, TX, USA) was used in 184 patients, St. Jude Medical valve (SJM; St. Jude Medical, Minneapolis, MN, USA) was used in 230 patients and ATS valve (ATS Medical, Minneapolis, MN, USA) was used in 10 patients. We used 39 stentless BP (14 Toronto Stentless Porcine Valve and 25 Medtronic Freestyle) during the 1994–2004 period and 20 Mitroflow BP have been used since April 2013 for AVR. Because the design and the hemodynamic performance of these stentless BP and Mitroflow BP are different from CEP stented BP, we excluded the stentless BP and Mitroflow BP results from the present study. With regard to prosthesis selection, we explained and discussed the merits and demerits of both prostheses (BP and MP) with the patients before AVR, and the patients themselves decided on prosthesis type. This prosthesis selection procedure has been followed consistently throughout the last 30 years at Kyushu University. The predominant causes of valve disease were rheumatic or degenerative heart disease in all groups (Table 1). There were no significant differences in the logistic EuroSCORE or the number of concomitant cardiac procedures between the 2 groups (MP or BP) for each age group (Table 1).

The details of the surgical procedures and patient care have been previously described. In brief, all patients underwent surgery with standard cardiopulmonary bypass and moderate hypothermia (28–34°C). Either cold crystalloid or blood cardioplegia were delivered antegrade, retrograde or both. Evertting mattress sutures or horizontal mattress sutures with 2-0 braided polyester sutures reinforced with polytetrafluoroethylene (Teflon) felt pledgets were predominantly used to suture the valves.

After discharge from hospital, international normalized ratio of prothrombin time was measured at least every 4 weeks and maintained between 1.8 and 2.4 throughout the patient’s lifetime in those with MP, whereas warfarin was similarly used for the first 3 months after surgery and then terminated in patients with BP if they were in sinus rhythm.

Early postoperative followed by monthly or annual follow-
valve deterioration (SVD), we estimated the discriminative age only in the BP group because SVD was observed only in the BP patients. We evaluated the likelihood ratio and P-value repeatedly in each BP age group divided by a certain age (from 50 to 80 years old). The age with the highest likelihood ratio was then termed the discriminative age for SVD in the BP patients.

Comparison between the MP and BP groups was done for several adverse events in each age group using an actuarial life table (Kaplan-Meier method), and comparisons of estimates were made using the log-rank test. The level of statistical significance was set at P<0.05.

Results

Early Mortality

There were 17 early deaths within 30 days of surgery and in-hospital deaths within any time interval after surgery. The early mortality rate was 2.5% (8/278) among the patients ≥70 years of age, 2.1% (4/191) among the patients 60–69 years of age, and 1.9% (5/268) among the patients <60 years of age (Table 4). The cause of early death was predominantly low output syndrome (8 patients) resulting in multiple organ failure.

<table>
<thead>
<tr>
<th>Table 3. Optimal Age for Use of BP</th>
<th>Age (years)</th>
<th>LR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve-related death</td>
<td>72</td>
<td>9.2360</td>
<td>0.0024</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>72</td>
<td>9.1270</td>
<td>0.0025</td>
</tr>
<tr>
<td>All-cause death</td>
<td>69</td>
<td>13.7890</td>
<td>0.0002</td>
</tr>
<tr>
<td>Valve-related morbidity</td>
<td>62</td>
<td>27.4160</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Re-AVR</td>
<td>68</td>
<td>12.1480</td>
<td>0.0005</td>
</tr>
<tr>
<td>Bleeding events or thromboembolic events</td>
<td>62</td>
<td>6.1232</td>
<td>0.0133</td>
</tr>
</tbody>
</table>

To find the age differentiating good from bad outcome in the BP or MP groups, we repeatedly evaluated the interaction of prosthesis type (MP or BP) between the 2 age groups that were divided by a certain age (50–80 years old) using the proportional hazard model (Cox regression model). The age with the highest LR was termed the discriminative age. LR, likelihood ratios. Other abbreviations as in Table 1.

<table>
<thead>
<tr>
<th>Table 4. Mortality and Morbidity at 20 Years†</th>
<th>Age ≥70 years (n=278)</th>
<th>Age 60–69 years (n=191)</th>
<th>Age &lt;60 years (n=268)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>MP (n=79)</td>
<td>BP (n=199)</td>
<td>MP (n=128)</td>
</tr>
<tr>
<td>Mean follow-up period (years)</td>
<td>7.3±0.6</td>
<td>4.6±0.3</td>
<td>9.8±0.6</td>
</tr>
<tr>
<td>Maximum follow-up period (years)</td>
<td>23.2</td>
<td>21.0</td>
<td>25.5</td>
</tr>
<tr>
<td>Total patient-years</td>
<td>579.6</td>
<td>922.0</td>
<td>1,250</td>
</tr>
<tr>
<td>Freedom from death at 20 years (%)</td>
<td>38.4±18</td>
<td>68.5±20</td>
<td>78.0±6.2</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>31.0±15</td>
<td>58.5±19</td>
<td>57.4±9.4</td>
</tr>
<tr>
<td>All-cause death</td>
<td>7.1±4.5*</td>
<td>29.6±11</td>
<td>28.7±6.9</td>
</tr>
<tr>
<td>Freedom from adverse events at 20 years (%)</td>
<td>51.2±11*</td>
<td>57.5±24</td>
<td>41.8±9.2</td>
</tr>
<tr>
<td>Valve-related morbidity</td>
<td>100</td>
<td>75.1±21</td>
<td>100*</td>
</tr>
<tr>
<td>SVD</td>
<td>100</td>
<td>90.7±6.4</td>
<td>98.3±2.4</td>
</tr>
<tr>
<td>PVE</td>
<td>100</td>
<td>95.9±2.1</td>
<td>63.2±16</td>
</tr>
<tr>
<td>Re-AVR</td>
<td>65.3±12*</td>
<td>94.0±3.3</td>
<td>73.0±7.9</td>
</tr>
<tr>
<td>Bleeding events</td>
<td>89.9±4.5</td>
<td>95.6±2.0</td>
<td>71.3±6.2*</td>
</tr>
<tr>
<td>Thromboembolic events</td>
<td>57.6±11*</td>
<td>89.6±4.3</td>
<td>47.3±9.1*</td>
</tr>
</tbody>
</table>

Data given as mean±SEM. *Hospital mortality rate (%). †P<0.05 vs. BP in the same age group. ‡Kaplan-Meier method. Abbreviations as in Table 1.
Valve-Related Morbidity

Valve-related morbidity included all of the cases of SVD, PVL, bleeding events, thromboembolic events (TE) and prosthetic valve endocarditis. The frequency of valve-related morbidity was not significantly different between either the 3 age groups (P=0.6728 according to the Cox model; Table 2) or the 2 types of prosthesis (P=0.5049), but valve-related morbidity was significantly associated with the interaction between age and type of prosthesis (P<0.0001). On Kaplan-Meier analysis a significantly higher rate of freedom from valve-related morbidity was seen in the BP group than in the MP group for patients ≥70 years of age (P=0.0205; Figure 2A; Table 4). In contrast, a significantly higher rate of freedom from valve-related morbidity was observed in the MP group than in the BP group for patients <60 years of age (P<0.0001; Figure 2C; Table 4).

SVD

We defined SDV for both prosthesis types as deterioration of artificial valve resulting in reoperation, and also defined SVD in accordance with the American Society of Echocardiography guidelines. 12 Three patients were diagnosed as having SVD with severe AR of BP only on transthoracic echocardiography.
Bleeding Events
A total of 46 bleeding events (36 in the MP group vs. 10 in the BP group) were observed. A significant difference was observed in the occurrence of bleeding events between the 3 age groups (P=0.0225, Cox model; Table 2), but no significant differences were observed in either type of prosthesis (P=0.1300) or interaction between age and type of prosthesis (P=0.0690). The incidence of bleeding events was greater in the MP group (intracranial bleeding, n=26; gastrointestinal bleeding, n=6; pulmonary bleeding, n=4) than in the BP group (intracranial bleeding, n=7; gastrointestinal bleeding, n=3). The rate of freedom from bleeding events was significantly higher in the BP group than in the MP group for the ≥70-year age group (P=0.0139, Kaplan-Meier; Table 4). In contrast, no significant differences were observed in the rate of freedom from bleeding events in either the 60–69-year age group (P=0.1735) or <60-year age group (P=0.2140).

Anticoagulant-Related Events
Anticoagulant-related events included all of the bleeding events without performing re-AVR. A total of 16 cases of SVD were observed in the BP group (0.89%/patient-years), while no cases of SVD were observed in the MP group. The discriminative age for SVD evaluated on Cox regression was 71 years of age (highest likelihood ratio, 10.0590; P=0.0015).

A significant difference was observed in the occurrence of SVD between the MP and BP groups (P<0.0001, Cox model; Table 2). Among the patients ≥70 years of age, however, SVD was observed in only 1 patient in the MP group (0.11%/patient-years) thus, the difference in the freedom from SVD between the MP and BP groups was negligible (P=0.2636; Figure 3A). In contrast, a significantly higher incidence of SVD was observed in the BP group than in the MP group among both the patients 60–69 years of age (P<0.0001; Figure 3C) and those <60 years of age (P<0.0001; Figure 3E). The rate of freedom from SVD at 20 years in the BP group was 54.2±18% for the 60–69-year age group (Figure 3C; Table 4) and 29.5±15% for the <60-year age group (Figure 3E; Table 4).

Re-AVR
A total of 35 re-AVR were done. The predominant causes of reoperation were SVD (n=13) and PVL (n=9). The in-hospital mortality rate for re-AVR was 3.0% (1/35 patients). Significant differences were observed in the occurrence of re-AVR between the 3 age groups (P=0.0007, Cox model; Table 2) and in the interaction between age and type of prosthesis (P=0.0439). Re-AVR was not required in either the MP or BP group in the ≥70-year age group. No significant differences were observed between the MP and BP groups (P=0.0559, Kaplan-Meier) in the occurrence of re-AVR for the 60–69-year age group, suggesting that the use of BP is appropriate for AVR even among Japanese patients in this age group. In contrast, the rate of freedom from re-AVR was significantly higher in the MP group than in the BP group for the <60-year age group (P<0.0001).

TE
A total of 51 episodes of TE (42 in the MP group vs. 9 in the BP group) occurred. No significant differences were observed in the incidence of thromboembolism between the 3 age groups (P=0.4799) or with respect to the type of prosthesis (P=0.1274, Cox model; Table 2). A higher incidence of thromboembolism (brain infarction, n=34; transient ischemic attack, n=6; thromboembolism in the small intestine, n=1; thromboembolism in the peripheral artery, n=1) was observed in the BP group (brain infarction, n=9). The rate of freedom from TE was significantly higher in the BP group than in the MP group for the 60–69-year age group (P=0.0139, Kaplan-Meier; Table 4). In contrast, no significant differences were observed in the rate of freedom from TE in either the ≥70-year age group (P=0.2140) or <60-year age group (P=0.2140).

Anticoagulant-Related Events
Anticoagulant-related events included all of the bleeding events
Long-Term Results of AVR

Based on the present 30-year follow-up results for the patients treated with AVR with either bileaflet MP or CEP BP, we reconfirmed that bileaflet MP, such as the CarboMedics and SJM prostheses, have better durability and equivalent incidence of anticoagulant-related events and are preferable for use in relatively young patients <60 years of age, whereas BP, such as CEP, have better anti-thrombotic and bleeding characteristics and are preferable for use in elderly patients ≥ 70 years of age. In particular, CEP BP are excellent for use in elderly patients ≥ 70 years of age due to their lower rate of mortality and valve-related morbidity. This type of BP is thus the treatment of choice for both patients ≥ 70 years of age and those 60–69 years of age due to the excellent survival rate, equivalent rate of freedom from valve-related morbidity and lower incidence of anticoagulant-related events.

In the present series, a significantly lower freedom from SVD was observed in the BP group than in the MP group among the patients aged 60–69 years, although no significant differences were observed between the MP and BP groups in either valve-related death or cardiac death among these patients. Emery et al recommended the use of SJM MP due to its excellent (>90%) freedom from valve-related events at 20 years after age and MP in the patients <70 years of age.5 Based on the present 30-year follow-up results for the patients treated with AVR with either bileaflet MP or CEP BP, we reconfirmed that bileaflet MP, such as the CarboMedics and SJM prostheses, have better durability and equivalent incidence of anticoagulant-related events and are preferable for use in relatively young patients <60 years of age, whereas BP, such as CEP, have better anti-thrombotic and bleeding characteristics and are preferable for use in elderly patients ≥ 70 years of age. In particular, CEP BP are excellent for use in elderly patients ≥ 70 years of age due to their lower rate of mortality and valve-related morbidity. This type of BP is thus the treatment of choice for both patients ≥ 70 years of age and those 60–69 years of age due to the excellent survival rate, equivalent rate of freedom from valve-related morbidity and lower incidence of anticoagulant-related events.

In our previous report on the long-term results of MVR, we confirmed the benefits of BP in elderly patients ≥70 years of age and MP in the patients <70 years of age.5 Based on the present 30-year follow-up results for the patients treated with AVR with either bileaflet MP or CEP BP, we reconfirmed that bileaflet MP, such as the CarboMedics and SJM prostheses, have better durability and equivalent incidence of anticoagulant-related events and are preferable for use in relatively young patients <60 years of age, whereas BP, such as CEP, have better anti-thrombotic and bleeding characteristics and are preferable for use in elderly patients ≥ 70 years of age. In particular, CEP BP are excellent for use in elderly patients ≥ 70 years of age due to their lower rate of mortality and valve-related morbidity. This type of BP is thus the treatment of choice for both patients ≥ 70 years of age and those 60–69 years of age due to the excellent survival rate, equivalent rate of freedom from valve-related morbidity and lower incidence of anticoagulant-related events.
AVR in patients 60–70 years of age. Brown et al reported superior survival rates among patients 50–70 years of age treated with MP. Based on these data, cardiac surgeons may opt to select MP in the patients 60–69 years of age in order to avoid re-AVR due to SVD, given that both physicians and patients generally consider the risk of reoperation to be more serious than the risk of anticoagulant-related complications. In-hospital re-AVR mortality, however, has decreased, although repeat cardiac surgery itself is an operative risk factor. Leontiev et al reported in-hospital mortality for re-AVR without aortic root replacement to be 3.5% (3/86). In the present study, only 1 of the 35 patients who underwent re-AVR (including 5 cases of aortic root replacement) died after operation due to multiple organ failure (in-hospital mortality, 3.0%), whereas no in-hospital deaths were observed after 13 re-AVR due to SVD. In contrast, 8 fatal anticoagulant-related events occurred in the MP group, while no such fatal events were observed in the BP group (Fisher’s exact test) in the 60–69-year age group. Furthermore, a significantly greater freedom from anticoagulant-related events was observed in the BP group (Figure 3D) than in the MP group in the patients aged 60–69 years. Both Jamieson et al and Marchand et al reported excellent rates of freedom from SVD in patients undergoing AVR with BP among those between 61 and 70 years of age. Prasongsukarn et al and Hanania also demonstrated the benefits of BP use in this age group. These and the present findings indicate that the use of BP for AVR in patients 60–69 years of age is reasonable.

Recently, transcatheter AVR has become widely used to treat high-risk patients in Japan. Webb et al reported on the transplantation of a transcatheter valve-in-valve aortic valve in a patient with a degenerated bioprosthetic valve, resulting in good and safe clinical outcomes with stable valve function for 2 years. Such developments, including the use of transcatheter AVR, also support the use of BP in this age group.

Moreover, in the present study, both the long-term survival (Figures 1E, F) and freedom from valve-related events (Figure 2C) were significantly higher in the MP group among the relatively younger patients <60 years of age, while the incidence of anticoagulant-related events was slightly greater in the MP group among these younger patients (Figure 3F). Therefore, the use of MP is generally preferable in relatively younger patients requiring AVR. Emery et al reported a rate of anticoagulant-related events of only 0.6%/patient-years and recommended the use of MP in patients under 50 years of age. Weber et al also noted a reduced mid-term survival among patients treated with BP, with similar valve-related event rates in both age group and concluded that current evidence remains insufficient to recommend BP for AVR in patients under 60 years of age. Although these data also support the present conclusions, patients treated with MP have a potential risk of bleeding events due to anticoagulation as they age. Newly available anticoagulants, such as rivaroxaban and apixaban, may become strong alternatives to warfarin for reducing the rate of bleeding and thromboembolic complications associated with MP, although another new anticoagulant, dabigatran, has recently been prohibited for use in patients with MP. Further clinical studies comparing the efficacy of these new anticoagulants and warfarin in patients treated with MP are urgently needed.

Conclusions

Based on comparative evaluation of AVR with respect to our long-term experience with treating Japanese patients, the use of BP is suitable in elderly patients ≥70 years of age, while bileaflet MP appear to be preferable for patients <60 years of age. As for the intermediate age group 60–69 years of age, the use of BP, such as CEP, may be preferable for AVR, given that the incidence of anticoagulant-related events is lower than that of MP, while the long-term results are equivalent.

Disclosures

The authors declare no conflict of interest.

References

Long-Term Results of AVR

2695


