Comparison of the Effects of Aortic Valve Replacement Using 19-mm Carpentier-Edwards Perimount Bioprosthesis and 19-mm Medtronic Mosaic Bioprosthesis

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Objective: Short (≤3 months)- and middle (≥4 months)-term results of aortic valve replacement (AVR) using 19-mm Carpentier-Edwards Perimount (CEP) bioprosthetic valves and 19-mm Medtronic Mosaic (MM) bioprosthetic valves in patients with small aortic annulus were compared.

Patients and Methods: At our facility, AVR was performed using bioprostheses in 110 patients from April 1999 to March 2006. Of these patients, 40 were treated using 19-mm CEP (Group C), and 9 using 19-mm MM (Group M). Evaluation by inquiry, physical examination, and echocardiography was performed before, a short term after, and a middle term after surgery, and the effects of AVR were compared.

Results: The New York Heart Association (NYHA) functional class grade showed improvements in both groups. The aortic valve peak pressure gradient was 29.8 ± 10.1 mmHg in Group C and 53.8 ± 17.3 mmHg in Group M, being higher in Group M, a middle term after surgery. However, the left ventricular mass index (LVMI) showed improvements in both groups compared with the values before surgery, and the left ventricular ejection fraction (LVEF) was maintained. During the middle term after surgery, the frequency of cardiac events showed no significant difference between the two groups.

Conclusions: In the patients treated with 19-mm MM, the aortic valve peak pressure gradient was higher than in those treated with 19-mm CEP, but acceptable improvements in the LVMI, maintenance of the LVEF, and avoidance of cardiac events were observed in both groups. (Ann Thorac Cardiovasc Surg 2008; 14: 81–87)

Key words: aortic valve replacement, bioprosthetic valves, small aortic annulus

Introduction

With the recent aging of society, elderly patients receiving aortic valve replacement (AVR) are increasing, and the selection of bioprosthetic valves for this procedure takes into consideration their good durability and low incidence of valve-related complications. Patient-prosthesismismatch (PPM), first described by Rahimtoola ("Mismatch can be considered to be present when the effective prosthetic valve area, after insertion into the patient, is less than that of the normal valve"), is considered to be unavoidable as long as artificial stented valves are used because of their structure. Thereafter, Pibarot et al. further evaluated the effects on the hemodynamics, complications, and mortality rate, and many studies are...
also conducted today.

The Carpentier-Edwards Perimount (CEP) bioprosthesis (Baxter Healthcare Corp., Edwards Division, Santa Ana, Calif.) and Medtronic Mosaic (MM) bioprosthesis (Medtronic, Inc., Minneapolis, Minn.) are stented bioprostheses that are available in Japan among those widely used throughout the world. Because of the generally small physique of the Japanese, many Japanese patients have small aortic annulus, and small-sized bioprostheses must be selected with a possible increase in the risk of PPM.

Since in many of our patients we noted a relatively high aortic valve pressure gradient after AVR using a bioprosthesis, we reviewed short (≤3 months)-term and middle (≥4 months)-term results of AVR using 19-mm bioprostheses at our facility to evaluate the effects of the surgery.

**Patients and Methods**

From April 1999 to March 2006, 110 patients underwent AVR using bioprostheses among those who required AVR for aortic valve stenosis (AS), aortic valve regurgitation (AR), aortic valve stenosis and regurgitation (ASR), or thoracic aortic disorders that necessitated AVR (including those who underwent this procedure as part of complex surgery for disorders that included angina pectoris and combined valvular disease). Of these patients, 40 were treated using 19-mm CEP (Group C), and 9 with 19-mm MM (Group M). The preoperative data of each group are summarized in Table 1.

In Groups C and M, the following items were evaluated by inquiry, physical examination, and echocardiography at our facility before, a short term after, and a middle term after surgery. Concerning patients who could not be examined at our facility, we adopted data collected from interviews with the patients and their families or from the results of evaluations by their family doctors.

Evaluation items: New York Heart Association (NYHA) functional class, Echocardiographic Measurement (left ventricular morphology and function, aortic valve peak pressure gradient, left ventricular mass (LVM),⁹ left ventricular mass index (LVMI) = LVM/body surface area, cardiac event, and survival rate.

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- **Implanted bovine and porcine bioprostheses**
- The CEP is a bovine stented heart valve fixed with glutaraldehyde at low pressure, and the cusps are treated with a surfactant to restrict calcification. Clinical investigation began in 1981 in the United States and has been in clinical use in Japan since 1985 and in the U.S. and Europe since 1991.
- MM is a porcine stented heart valve fixed with glutaraldehyde at zero pressure and treated with α-aminooleic acid to reduce tissue calcification. It has been in clinical use in Europe since 1994, in Japan since 1999, and in the U.S. since 2000.

**Surgical technique**

AVR was performed under normal-temperature extracorporeal circulation and cold crystalloid cardioplegic solution. After the aortic valve was removed, calcifications observed at the aortic root or aortic annulus were removed as much as possible, and the size of the aortic annulus was measured with a sizer for each bioprosthesis. If valve replacement in the intra-annular position was possible, the prosthesis was sutured by everting mattress suture, but if not, it was sutured to the supra-annular position by interrupted suture. The operative profile of each group is summarized in Table 2.

**Statistical analysis**

The data were expressed as the mean ± standard deviation. The Student’s t-test was performed to examine differences between the two independent groups. Differences between the two groups concerning each intraindividual or interindividual factor were examined by repeated measures ANOVA. Further, the survival rate was calculated by the Kaplan-Meyer method, and differences in the survival rate between the two groups were examined by the log-rank test. Differences were considered significant at p < 0.05.

**Results**

**NYHA functional class**

Preoperative and latest postoperative subjective symptoms were evaluated according to the NYHA. The NYHA improved from a preoperative mean of 2.8 to a postoperative mean of 1.3 in Group C and from 3.3 to 1.9 in Group M. Although a higher percentage of patients in Group C were rated NYHA II, the differences between the two groups were insignificant (Fig. 1).
Aortic valve peak pressure gradient

In Group C, the aortic valve peak pressure gradients were 29.7 ± 10.9 mmHg a short term after surgery and 29.8 ± 10.1 mmHg a middle term after surgery. In group M, they were 45.4 ± 12.6 mmHg and 53.8 ± 17.3 mmHg, respectively. Compared with the preoperative pressure gradients calculated by excluding AR patients, in whom the aortic pressure gradient was not high (90.9 ± 27.2 mmHg in Group C, 77.0 ± 30.8 mmHg in Group M), the pressure gradient was significantly decreased in both groups in the short and middle terms after surgery (p<0.001). However, the postoperative pressure gradient was slightly higher in Group M than in Group C in both the short and middle terms after surgery (p=0.08) (Table 3, Fig. 2).
LVMI
In Group C, the LVMI was 171.4 ± 42.2 g/m² before surgery, 139.3 ± 41.4 g/m² a short term after surgery, and 118.9 ± 47.4 g/m² a middle term after surgery. In group M, it was 170.7 ± 15.2 g/m², 156.0 ± 34.6 g/m², and 136.4 ± 14.4 g/m², respectively. Although significant decreases (p<0.001) were observed in both groups during both the short and middle terms after surgery, the improvement tended to be greater in Group C (p=0.40) (Table 3, Fig. 3).

Left ventricular ejection fraction (LVEF)
In group C, the LVEF was 65.5 ± 11.9% before surgery, 65.2 ± 12.6% a short term after surgery, and 70.0 ± 12.2% a middle term after surgery. In group M, it was 64.7 ± 16.0%, 60.6 ± 16.5%, and 67.4 ± 17.5%, respectively. In both groups, the LVEF was similar to or better than the values before surgery, indicating satisfactory maintenance of the left ventricular function (p=0.01). However, no significant difference was observed between the two groups (p=0.56) (Table 3, Fig. 4).

Actuarial freedom from cardiac event
In Group C, heart failure was noted in 1 patient 1 months after surgery and in another 17 months after; hemolytic anemia was observed in 1 patient 34 months after surgery. In Group M, 1 patient developed cardiogenic cerebral infarction associated with paroxysmal atrial fibrillation 41 months after surgery. The actuarial freedom from cardiac event was 88.6% in Group C and 75.0% in Group M 53 months after surgery. No significant difference was noted between the two groups (p=0.79) (Fig. 5).

Actuarial survival rate
No death was observed in Group C. In Group M, 1 patient died as a result of cardiogenic cerebral infarction 42 months after surgery, and another died from pneumonia 43 months after surgery. The actuarial survival rate was...
100% in Group C and 100% in Group M 24 months after surgery, but 100% in Group C and 50% in Group M 53 months after surgery, with a significant difference between the two groups ($p=0.007$) (Fig. 6).

**Discussion**

The minimum label size of bioprosthetic cardiac valves available in Japan is 19 mm for both CEP and MM. They are used frequently for AVR with Japanese patients who exhibit a small aortic annulus. However, since the small orifice area of the 19-mm valve is very likely to cause the persistence of a high-pressure gradient, the use of a larger prosthesis with an enlargement of the aortic root (a stentless bioprosthesis) has been suggested to be useful. Annular enlargement surgery has been reported by Nicks et al., Konno et al., and Manouguian et al., but these procedures have also been reported to be more invasive. Each one requires slightly more complex surgical manipulations, a longer use of a cardiopulmonary bypass, and a longer aortic clamp time. In consideration of the progressive aging of candidates for these procedures, the safety of valve replacement should be improved further.

In AVR, CEP has shown excellent durability and a low incidence of complications over a period of 17 years since its introduction. MM is a new-generation bioprosthesis that has been used since 1994 in Europe, and excellent durability and a low incidence of complications have also been reported as midterm results. However, Kirsch et al. reported that relatively high pressure gradients persisted after AVR using 19-mm MM, i.e., a peak pressure gradient of 40.8 ± 12.1 mmHg and a mean pressure gradient of 23.4 ± 6.9 mmHg. Takakura et al. reported that the peak and mean pressure gradients after AVR using a 19-mm CEP were 27.7 ± 9.5 mmHg and 12.3 ± 4.8 mmHg, respectively, at rest and 50.4 ± 11.5 mmHg and 22.2 ± 4.8 mmHg, respectively, even under dobutamine stress (10 μg/kg/min), and were acceptable. Eichinger et al. compared mean aortic valve pressure gradient using 19-mm CEP and 19-mm MM and reported 11.4 ± 4.1 mmHg for CEP and 14.6 ± 5.0 mmHg for MM at rest and 20.7 ± 4.4 mmHg and 28.4 ± 9.0 mmHg, respectively, during 25 W exercise. Although the number of patients was small and no statistical evaluation was performed, the results with CEP appear to be better. Marquez et al. performed a hydrodynamic evaluation of various bioprostheses, including CEP and MM in vitro, and showed that the valve pressure gradient increases with the cardiac output and that the mean effective valve orifice area was associated with the valve pressure gradient. Moreover, they reported that the valve pressure gradient

![Fig. 4. Comparison of left ventricle ejection fraction.](image1)

![Fig. 5. Actuarial freedom from cardiac event.](image2)

![Fig. 6. Actuarial survival rate.](image3)
Various opinions about the importance of PPM are still being presented. Various opinions about the importance of PPM are still being presented. According to Walther et al., who evaluated 1,856 patients who received mechanical prostheses and 2,275 who received bioprostheses, moderate PPM was noted in 26.7% of all patients, but its frequency was higher in the bioprosthesis group, and it was an independent predictive factor for the short-term and long-term mortality rates. However, N.J. Howell et al. reported that even severe PPM with an indexed effective orifice area (EOA) < 0.6 cm²/m² did not affect the hospital mortality rate or middle-term survival rate. If so, the use of bioprostheses with a small orifice area should not necessarily be avoided.

A point that requires particular attention is that the label sizes of both CEP and MM used in this study were 19 mm, but the internal orifice diameter, which is a factor that affects the EOA, was 18.0 mm in CEP and 16.5 mm in MM. Also, the external sewing ring diameter, which is considered to be the maximum diameter of a bioprosthesis, was 26 mm in CEP and 25 mm in MM, so that the 19-mm MM is considered to be smaller than 19-mm CEP (values are those announced by the manufacturers). When the sizers provided by the manufacturers were compared, the diameter of the sizer part inserted into the annulus at suturing to the supra-annular position was 19.0 mm in the 19-mm CEP, but it was clearly smaller at 16.6 mm in the 19-mm MM (values measured using slide calipers) (Fig. 7). Therefore 19-mm MM may be usable for a small aortic annulus, which the sizer of a 19-mm CEP does not fit.

In 19-mm MM, a peak pressure gradient of 45.4 ± 12.6 mmHg remained early after surgery. The postoperative pressure gradient tended to be higher in Group M than in Group C, but it showed improvements compared with the preoperative values, and improvements in the LVMI and subjective symptoms and a sufficiently acceptable incidence of complications were obtained. The 19-mm MM may be underestimated in comparisons with other bioprostheses because of its label size. Beyond the persistence of postoperative high-pressure gradient, 19-mm MM has a smaller profile and is capable of fitting a smaller aortic annulus.

Limitations of study
In this study, the number of patients was small. And we did not evaluate PPM because the EOA was not measured in many patients by postoperative echocardiography. And a direct comparison of the pressure gradient between before and after surgery was difficult because the subjects included patients with AR, in whom the preoperative aortic valve pressure gradient was not high. Therefore the preoperative pressure gradient in patients with AS and ASR and the postoperative pressure gradient of all patients were compared as a reference.

Conclusions
Short-term and middle-term results of AVR using 19-mm CEP and 19-mm MM were compared. Although the postoperative aortic valve pressure gradient was higher and survival rate was lower in 19-mm MM than in 19-mm CEP, the improvement in the LVMI, maintenance of the LVEF, and incidence of cardiac event were acceptable in both groups.

References
2. Rahimtoola SH. The problem of valve prosthesis-pa-


