Aortic stenosis is an age-related disorder that is characterized by calcification of the aortic valve, local lipid accumulation, inflammation, and neo-angiogenesis. Because the aged population is increasing, increased numbers of patients are experiencing aortic stenosis, so the number of patients requiring aortic valve replacement (AVR) is increasing. AVR still remains the standard therapy for symptomatic severe aortic stenosis, although transcatheter aortic valve implantation is considered as an alternative therapy for elderly patients at high risk for perioperative complications. In Asian countries in particular, female and elderly patients with aortic valve stenosis often have a small aortic annulus. Prosthesis-patient mismatch (PPM) is the difference between the area of the implanted prosthetic valve and that of the patient’s native valve without a stenotic lesion. Previous studies have shown that PPM, defined as an effective orifice area index (EOAI ie, effective orifice area divided by body surface area (BSA)) <0.85 cm²/m², may negatively affect postoperative clinical status and survival.4,5 Thus, surgeons need a prospective strategy for selection of the best prosthesis and operative method to prevent PPM.

Background: When aortic valve replacement (AVR) is performed in patients with a small aortic annulus, prosthesis-patient mismatch (PPM) is of concern. We investigated the mid-term outcomes of AVR with a 17-mm mechanical prosthesis.

Methods and Results: Seventy-eight patients with aortic stenosis underwent AVR with a 17-mm St. Jude Medical Regent prosthesis. Echocardiography was performed preoperatively, at discharge, and at follow-up (mean follow-up, 33 months). Patients were divided into 2 groups: with and without PPM at discharge. Between-group differences in postoperative variables, particularly survival, were analyzed. Overall hospital mortality was 2.6%. Actuarial 1- and 5-year survival rates were 95% and 79%, respectively. Diabetes and renal insufficiency were associated with long-term mortality. Freedom from major adverse valve-related cardiac events at 1 year and 5 years was 97.3% and 93.9%, respectively. Diabetes was shown to be an independent risk factor for major adverse valve-related cardiac events. Echocardiography 13 months after AVR showed a significant increase in mean effective orifice area index, decrease in mean left ventricular-aortic pressure gradient, and decrease in mean left ventricular mass index. PPM at discharge did not influence long-term survival or left ventricular mass regression.

Conclusions: The 17-mm Regent prosthesis provided satisfactory clinical and hemodynamic results. It is a reliable choice for patients with a small aortic annulus. (Circ J 2012; 76: 365–371)

Key Words: Surgery; Valves; Valvular diseases

The 17-mm Regent prosthesis is an option in patients with a small aortic annulus, although there are few reports of mid-term outcomes after AVR with a 17-mm prosthesis in large series of patients. Thus, the primary objective of this study was to evaluate mid-term clinical outcomes after AVR with the 17-mm Regent prosthesis and the effect of PPM.

Methods

Patients
From February 2005 through December 2009, 78 patients (mean age, 72.9±7.7 years) with aortic stenosis underwent AVR with a 17-mm mechanical prosthetic valve (St. Jude Medical, St. Paul, MN, USA). The study group comprised patients who underwent AVR with 1 or more concomitant procedures other than mitral valve replacement; 73 (94%) patients were women and 35 patients (45%) were in New York Heart Association (NYHA) functional class III or IV preoperatively. Mean BSA was 1.44±0.12 m² (range, 1.21–1.77 m²). Clinical characteristics of the patients are shown in Table 1. Our study followed the guidelines of the Ethical Review Board of Jichi Medical
Follow-up

Follow-up transthoracic echocardiographic data were obtained for 35 (45%) of the 78 patients at 13.3±10.8 (mean±SD) months after surgery. The clinical status of each patient was evaluated by means of direct hospital visits and telephone interviews. Follow-up was 100% complete. Mean follow-up was 32.6±19.6 months (range, 5–70 months). A major adverse valve-related event was defined according to the guidelines for reporting after cardiac valve interventions.6

Statistical Analysis

Data are reported as mean±SD. Preoperative and postoperative echocardiographic data for all patients were compared and analyzed by paired Student’s t-test. Patients were divided into 2 groups: with and those without PPM at discharge. Differences between the groups were analyzed by chi-square test or unpaired Student’s t-test as appropriate. Logistic regression was used to identify factors associated with in-hospital death. Variables entered into multivariate analysis if univariate analysis yielded a P-value <0.15. Actuarial survival was calculated by the Kaplan-Meier method. A Cox proportional hazards model was used to identify predictors of survival and adverse events. Variables included in the multivariate analysis were those with P-value <0.15 in the univariate analysis. The log-rank test was used to compare differences in actuarial survival between groups. All analyses were performed with SPSS software (version 10.1; SPSS, Chicago, IL, USA). P<0.05 was considered significant.

Results

Operative Morbidity and Mortality

Overall hospital mortality was 2.6% (2 patients). The causes of hospital deaths were respiratory failure and intestinal necrosis. Univariate analysis identified renal insufficiency and preoperative dialysis as predictors of hospital mortality. However, multivariate regression analysis yielded no independent predictor of hospital death. One patient required perioperative intra-aortic balloon pumping and percutaneous cardiopulmonary support because of hemodynamic instability. Postoperatively, 1 patient suffered cerebral infarction. None required pacemaker implantation.

Clinical Follow-up and Valve-Related Events

Two patients were readmitted because of heart failure. One patient experienced late cerebral hemorrhage. Cerebral infarction, prosthetic endocarditis, structural failure of the prostheses, reoperation, and paravalvular leakage did not occur in any patient during the follow-up period. Freedom from major adverse valve-related cardiac events at 1 year, 3 years, and 5 years was 97.3%, 93.9%, and 93.9%, respectively (Figure 1). The linearized rate of valve-related cardiac events was 2.3 per 100 patient-years. Major adverse valve-related cardiac events are summarized in Table 2. Univariate analysis revealed that

| Table 1. Preoperative Patient Characteristics and Operative Data (n=78) |
|-----------------|-----------------|-----------------|
| Age (years)     | 72.9±7.7        |                 |
| Sex ratio (M/F) | 5/73            |                 |
| NYHA class      |                 |                 |
| I–II            | 43 (55.1%)      |                 |
| III–IV          | 35 (44.9%)      |                 |
| Body surface area (m²) | 1.44±0.12 (1.21–1.77) | |
| Valve pathology |                 |                 |
| Sclerotic degeneration | 57 (73.1%) | |
| Rheumatic       | 18 (23.1%)      |                 |
| Bicuspid        | 3 (3.8%)        |                 |
| Hypertension    | 50 (64.1%)      |                 |
| Diabetes        | 12 (15.4%)      |                 |
| Ischemic heart disease | 18 (23.1%) | |
| Atrial fibrillation | 5 (6.4%)   |           |
| Renal insufficiency* | 9 (11.5%)   |           |
| Preoperative dialysis | 6 (7.7%)  | |
| Stroke          | 1 (1.3%)        |                 |
| Ejection fraction <0.4 | 4 (5.1%)       |           |
| Cardiopulmonary bypass time (min) | 166±55 | |
| Cross-clamp time (min) | 136±41       |           |
| Reoperation     | 2 (2.6%)        |                 |
| Concomitant procedure | 29 (37.2%)   |           |
| Coronary artery bypass grafting | 13 (16.7%) | |
| Tricuspid annuloplasty | 12 (15.4%) | |
| Mitral valve repair | 4 (5.1%)    |           |
| Septal myectomy | 3 (3.8%)        |                 |
| In-hospital death | 2 (2.6%)      |           |

Number of patients (%) or mean±SD values are shown. *Serum creatinine >1.5 mg/dl.
NYHA, New York Heart Association.

University. All patients had previously granted permission for use of their medical records for research purposes.
Mid-Term Outcomes With 17-mm Regent for AVR

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Age, preoperative NYHA class III or IV, hypertension, diabetes, and a concomitant procedure were associated with a major adverse valve-related cardiac event. Multivariate analysis showed diabetes to be the only independent predictor of a major adverse valve-related cardiac event (Table 3). Freedom from reoperation was 100%. Long-term survival and freedom from cardiac death are shown in Figure 2. Of the 76 survivors, 9 (12%) died during the follow-up period: malignancy (n=2), heart failure (n=1), pneumonia (n=1), renal failure (n=1), and unknown (n=4). Actuarial 1-year, 3-year, and 5-year survival rate were 94.8%, 86.3%, and 78.7%, respectively. Univariate analysis identified age, diabetes, renal insufficiency, ejection fraction <0.4 and a concomitant procedure as predictors of long-term mortality. Multivariate analysis showed diabetes and renal insufficiency to be the independent predictors of long-term mortality (Table 3). Freedom from cardiac death at 1 year, 3 years, and 5 years was 98.6%, 95.2%, and 91.4%, respectively.

Functional NYHA Class Before Surgery and at Follow-up

All patients except the 2 who died in the hospital were assessed for physical capacity according to NYHA classification during follow-up: 75 patients (99%) improved to class II or better after AVR.
Echocardiographic Variables

Preoperative echocardiography yielded a mean aortic valve area index of 0.41±0.13 cm²/m², a mean left ventricular-aortic pressure gradient (LVAo-PG) of 59.0±21.5 mmHg, and a mean left ventricular mass index (LVMI) of 175±53 g/m². Follow-up echocardiography revealed a significant decrease in mean LVAo-PG (16.6±6.8 mmHg), a significant decrease in LVMI (116±32 g/m²), and a significant increase in mean EOA (0.97±0.21 cm²/m²). There was no significant difference between the preoperative and postoperative ejection fractions (0.60±0.14 vs. 0.63±0.07).

Effect of PPM on Long-Term Survival and Echocardiographic Variables

The EOA was obtained at discharge for 58 (74%) of 78 patients. Of these 58 patients, 18 (31%) had PPM with an
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EOAI <0.85 cm²/m² at discharge. Severe PPM with an EOAI <0.65 cm²/m² was found in 4 of the patients. No valve-related complication was seen in any of the 4 patients with severe PPM. There was no significant difference between the patients with and without PPM in terms of sex ratio or age. Mean BSA was greater in patients with PPM than in patients without PPM (1.52±0.08 m² with PPM vs. 1.40±0.10 m² without PPM, P<0.001). Follow-up echocardiographic variables of the patients in both groups are shown in Figure 3. Reduction in LVMI as well as LV Ao-PG at follow-up did not differ between the 2 groups. Neither was there a difference in long-term survival between the 2 groups (Figure 4).

Discussion

Elderly Japanese are shorter in stature than their Western counterparts, and the aortic annulus of the Japanese is smaller, proportionate to their body size. Therefore, we often need a strategy to deal with the problem of a small annulus. The EOAI, which correlates with the postoperative transvalvular gradient, has been used to characterize PPM. On the basis of the relation between the EOAI and corresponding gradient, Pibarot et al reported that the ideal EOAI should exceed 0.85 cm²/m² to avoid a residual pressure gradient.5–9 Thus, in the case of patients with a small aortic annulus, careful evaluation is needed to achieve an EOAI >0.85 cm²/m² after AVR surgery because PPM may predispose to an unfavorable outcome.4–6

The main consequence of PPM is generation of an abnormally high transprosthetic gradient across the aortic valve, resulting in increased left ventricular work. Incomplete regression of the residual gradient across the prosthesis has been associated with increased long-term mortality.10 The decrease in the LVMI is considered to be a result of favorable remodeling derived from AVR. PPM is also associated with a smaller decrease in the LVMI and more cardiac events during the follow-up period.11,12 Prevention of PPM has also been reported to improve postoperative functional class/exercise tolerance and the incidence of late sudden death.6,13 However, some investigators have reported that the influence of PPM on outcome after AVR surgery remains controversial.11,14–16 Various surgical strategies, such as aortic root enlargement and stentless valve implantation, have been used to avoid PPM. Enlargement of the aortic annulus is based on the premise that a large-sized prosthesis favorably influences late clinical outcome.17 Castro et al performed aortic root enlargement procedures in 114 patients to avoid PPM.18 However, aortic annulus enlargement has been shown to result in prolonged aortic cross-clamp times. In addition, recent advances in the design of prostheses have improved hemodynamic performance considerably. Therefore, we choose to forgo annular enlargement in favor of implantation of a high-performance mechanical valve for patients with a small aortic annulus. Supra-annular implantation of a larger valve is considered a feasible option in some institutions. However, because the subvalvular tissue is in close proximity to the prosthetic orifice when the valve is implanted in the supra-annular position, protrusion of subvalvular tissue into the prosthetic orifice, which can lead to valve dysfunction, is of concern, especially in AVR with a mechanical valve. Therefore, we generally use intra-annular positioning for implantation of a mechanical valve. The 17-mm St. Jude Medical Regent valve with an EOAI of 1.30 cm² can be used in patients with a BSA <1.5 m², resulting in an EOAI >0.85 cm²/m².

Only a few authors have reported their experience with a 17-mm mechanical prosthesis, and controversy remains as to whether this valve is beneficial and safe, especially in the long term. Previously, we reported good hemodynamics and a 38% decrease in LVMI after AVR with a 17-mm Regent valve, as well as favorable clinical status.19 Other groups have shown satisfactory clinical improvement and significant left ventricular mass regression after AVR with a 17-mm mechanical
prosthesis. These findings suggest that implantation of a 17-mm Regent valve provides not only excellent operative results but also good survival, associated with the better hemodynamic results. Minardi et al reported satisfactory hemodynamic performance in 19 patients with the 17-mm Regent valve under dobutamine stress as well as at rest.

Garatti et al also showed good early and long-term outcomes after AVR with a 17-mm mechanical valve, although their evaluation included only the 17-mm Sorin Bicarbon Slim prosthesis (Sorin Biomedica, Saluggia, Italy), and the 17-mm St. Jude Medical Hemodynamic Plus (St. Jude Medical). It must be noted that the follow-up periods were relatively short and the number of patients in each study was small. So, we need to look more carefully into the safety and effectiveness of the 17-mm valve in a large number of patients.

The drawback of a mechanical valve is lifelong anticoagulation, and close monitoring is required to prevent postoperative complications, including thromboembolism and anticoagulation-related bleeding. Some could argue that mechanical valves (vs. bioprostheses) will increase mortality and morbidity as a result of anticoagulation. However, in our series, we encountered cerebral hemorrhage in 2 patients, accounting for a linearized rate of 0.5% per patient-year, but no cerebral infarction. These complication rates are comparable to those of patients given a bioprosthesis. Aupart et al studied clinical outcomes of AVR in 1,133 patients who received a bioprosthesis and reported a bleeding complication rate of 0.3% per patient-year and thromboembolism rate of 0.6% per patient-year. Despite the need for lifelong anticoagulation in patients who receive a mechanical prosthesis, some reports have indicated no significant differences in postoperative quality of life, survival, or incidence of complications between mechanical and biological valves.

The effect of PPM on prognosis and cardiac function remains controversial. Mhoy et al indicated that PPM negatively influences long-term survival in specific patient groups such as those with low cardiac function or severe PPM. Moon et al reported that PPM had a negative impact on long-term survival only for patients 70 years of age or less. Vicchio et al showed that in patients over age 70, severe or moderate PPM did not influence long-term outcome, left ventricular mass regression or quality of life. In our series, there was no difference in survival or reduction in LVMI between patients with and without PPM, although the incidence of severe PPM was low. Also, our study included only a small number of patients with low cardiac function or severe PPM.

Another mechanical valve currently available for a small aortic annulus is the 16-mm ATS-Advanced Performance valve (ATS Medical, Inc, Minneapolis, MN, USA). Kobayashi et al reported on 15 patients in whom the 16-mm valve was implanted. There was no in-hospital mortality or significant postoperative reduction of LVMI despite a high incidence of PPM. However, some of their patients given the 16-mm valve showed no improvement in left ventricular diastolic function at mid-term follow-up.

Study Limitations
The limitations of our study should be taken into consideration. The main limitation is the relatively low echocardiographic follow-up rate. Most of our patients were followed up at another hospital or clinic, some of which were far from the hospital where the operation was performed. In addition, the study group comprised mostly elderly patients. Nearly half of the patients were unable to return for echocardiographic assessment. Whether or to what degree this low follow-up rate affected our survival and LVMI regression data is unknown. Furthermore, the low incidence of severe PPM in our series might have obscured the potential affect of PPM on outcomes.

Conclusions
In summary, the 17-mm Regent prosthesis produced satisfactory results in terms of survival, physical capacity, and hemodynamic performance. Thus, the 17-mm prosthesis could be a reasonable alternative, especially in patients with a small aortic annulus. Although we confirmed the safety and effectiveness of the prosthesis over 33 months of follow-up, we need to evaluate outcomes over a longer period and in a substantially large study group.

References


